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RESEARCH ARTICLE

Lung Nodule Detectability of Artificial Intelligence-assisted CT Image Reading in Lung Cancer Screening

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Abstract: ***Background***: Artificial Intelligence (AI)-based automatic lung nodule detection system improves the detection rate of nodules. It is important to evaluate the clinical value of the AI system by comparing AI-assisted nodule detection with actual radiology reports.

Objective: To compare the detection rate of lung nodules between the actual radiology reports and AI-assisted reading in lung cancer CT screening.

Methods: Participants in chest CT screening from November to December 2019 were retrospectively included. In the real-world radiologist observation, 14 residents and 15 radiologists participated in finalizing radiology reports. In AI-assisted reading, one resident and one radiologist reevaluated all subjects with the assistance of an AI system to locate and measure the detected lung nodules. A reading panel determined the type and number of detected lung nodules between these two methods.

Results: In 860 participants (57±7 years), the reading panel confirmed 250 patients with >1 solid nodule, while radiologists observed 131, lower than 247 by AI-assisted reading ($p<0.001$). The panel confirmed 111 patients with >1 non-solid nodule, whereas radiologist observation identified 28, lower than 110 by AI-assisted reading ($p<0.001$). The accuracy and sensitivity of radiologist observation for solid nodules were 86.2% and 52.4%, lower than 99.1% and 98.8% by AI-assisted reading, respectively. These metrics were 90.4% and 25.2% for non-solid nodules, lower than 98.8% and 99.1% by AI-assisted reading, respectively.

Conclusion: Comparing with the actual radiology reports, AI-assisted reading greatly improves the accuracy and sensitivity of nodule detection in chest CT, which benefits lung nodule detection, especially for non-solid nodules.

Keywords: Artificial intelligence, lung nodule, detectability, real-world study, radiologist observation, computed tomography.

1. INTRODUCTION

Lung cancer is the leading cause of cancer-related death worldwide [1], and its prognosis largely depends on the tumor stage at the time of diagnosis and treatment. Early-stage lung cancer often presents as a lung nodule that can be detected by Computed Tomography (CT). Several randomized controlled trials have shown that lung cancer CT screening can significantly reduce lung cancer-related mortality [2-5]. However, the clinical implementation of high-quality lung cancer screening is challenging. In a real-world clinical setting, multiple observers with different clinical experiences perform image reading. Some lung nodules may be overlooked due to their appearance or perception errors of the observer, which may be caused by fatigue, distraction, or inappropriate reading conditions in the case of too many nodules [6, 7].

Artificial intelligence (AI) algorithms learn highly discriminative image features from a large number of medical images and thereby gain the ability to analyze target lesions. Recently, multiple studies based on Convolutional Neural Networks (CNN) have been conducted to improve the detection, segmentation, and classification of lung diseases. Nas-

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rullah *et al.* proposed a deep 3D customized mixed link network (CMixNet) architecture to detect and classify lung nodules and reached a sensitivity of 94% and a specificity of 91%, which can reduce the misdiagnosis and false positive in lung cancer screening [8]. Rebouças Filho *et al.* proposed a 3D adaptive crisp active contour method (3D ACACM) to segment lung images, in which the average F-score of 40 chest CT scans achieved 99% [9]. They also used an optimum-path forest classifier to automatically identify three lung diseases in CT images, and the F-score reached 95% [10]. Bhandary *et al.* applied a modified AlexNet (MAN) framework to improve the classification accuracy during lung cancer assessment and attained an accuracy of 97% [11]. Ciompi *et al.* proposed a deep learning system based on multi-stream and multi-scale CNNs, which can classify lung nodules into 6 image feature categories, and its performance was comparable with human observers. In recent years, due to the availability of large datasets and the urgency of clinical demands, AI technology has developed rapidly in lung cancer screening. AI-based systems have reached a lung nodule detection accuracy of 82.2–97.6% [12-14]. Some studies have shown that AI can improve the differential diagnosis and management of lung nodules [15-18].

Most of the previous AI studies were designed to validate specific CNN algorithms, either for model optimization or for retrospective assessment of their performance using a specific dataset. At present, a challenging task is to rigorously validate an algorithm prior to clinical application because CNN models often have high performance for a given dataset but sometimes fail to process data in the actual clinical environment [19]. It is necessary to know whether the AI-assisted nodule detection improves the detection rate compared with real-world clinical practice. Therefore, we performed this study to compare the detection rate of lung nodules between the actual radiology reports and AI-assisted reading in lung cancer CT screening.

2. METHODS

2.1. Study Sample

This study is embedded in the Netherlands-China Big-3 disease screening: lung cancer, coronary atherosclerosis, and chronic obstructive pulmonary disease (NELCIN-B3) project [20]. This retrospective study conforms to the Helsinki Declaration of 1975, revised in 1983, and was approved by the local medical ethics committee (approval no. SGH-2018-56). The need for written informed consent was waived.

Patients who underwent chest CT from November to December 2019 at our institute were consecutively included. The inclusion criteria were as follows: (1) asymptomatic participants aged from 45 to 74 without chest discomfort; (2) underwent non-contrast thin-slice low-dose chest CT. The exclusion criteria were: (1) history of lung surgery and (2) none or incomplete diagnostic report. We evaluated the general population aged 45 to 74 years because they are considered to be the beneficiaries of lung cancer screening [21, 22].

2.2. CT Image Acquisition

Four CT systems (Revolution and HD750, GE Healthcare; Somatom Force, Siemens; Aquilion One, Canon) were used for non-contrast-enhanced chest CT scanning. The collimation of CT detector was 256×0.625 mm, 64×0.625 mm, 96×0.6 mm, and 320×0.5 mm, respectively. All subjects underwent an inspiratory CT scan during a single breath-hold in the supine position. The tube voltage was 120 kV or 100 kV. The tube current was 50-200 mAs, and the dose modulation was on. The slice thickness/interval was from 0.625/0.625 mm to 1.0/1.0 mm. The effective radiation dose was approximately 1.0 mSv to 2.0 mSv.

2.3. Radiologist Observation

According to the routine reporting procedure in our hospital, one resident drafted the diagnostic report, and a board--certified radiologist supervised the final version. A total of 14 residents with 2 to 5 years of experience in diagnostic thoracic imaging and 15 radiologists with 10 to 30 years of experience worked on reporting in this study.

One resident with 7 years of experience in diagnostic thoracic imaging extracted the data from the original radiological reports. The data items were patient characteristics (age and sex) and lesion description, including nodule component (solid, part-solid, or non-solid) and diameter.

2.4. Artificial Intelligence-assisted Reading

To compare the performance between radiologists and AI-assisted reading, two radiologists reevaluated the images with the assistance of an AI system, who were blinded to the original diagnostic reports, including one resident with 5 years of experience drafting the diagnostic report and a radiologist with 20 years of experience supervising and preparing the final version.

In this study, we used a commercially available AI-based lung nodule evaluation system (InferRead CT Lung, Infervision), which has been approved by the Food and Drug Administration (FDA) for clinical usage. This system can automatically detect and quantify lung nodules on chest CT images. Immediately after image acquisition, the CT console automatically transmitted the images to the AI server for segmentation and detection of lung nodules. Each patient's image transmission and processing took approximately 3 to 5 minutes. The radiologists can then read the results of the AI system on their image reading terminals that is shown in Fig. (**1**). Briefly, this system automatically depicts a suspected nodule with a bounding box and reveals its characteristics, including its components (solid, part-solid, or non-solid), diameter, and volume. Meanwhile, the system allows for interactive decision-making with radiologists, who can modify the above parameters according to their own interpretation.

2.5. Establishment of Artificial Intelligence System

The training and validation of this AI system have been reported [23, 24]. From January 2012 to June 2017, the CT

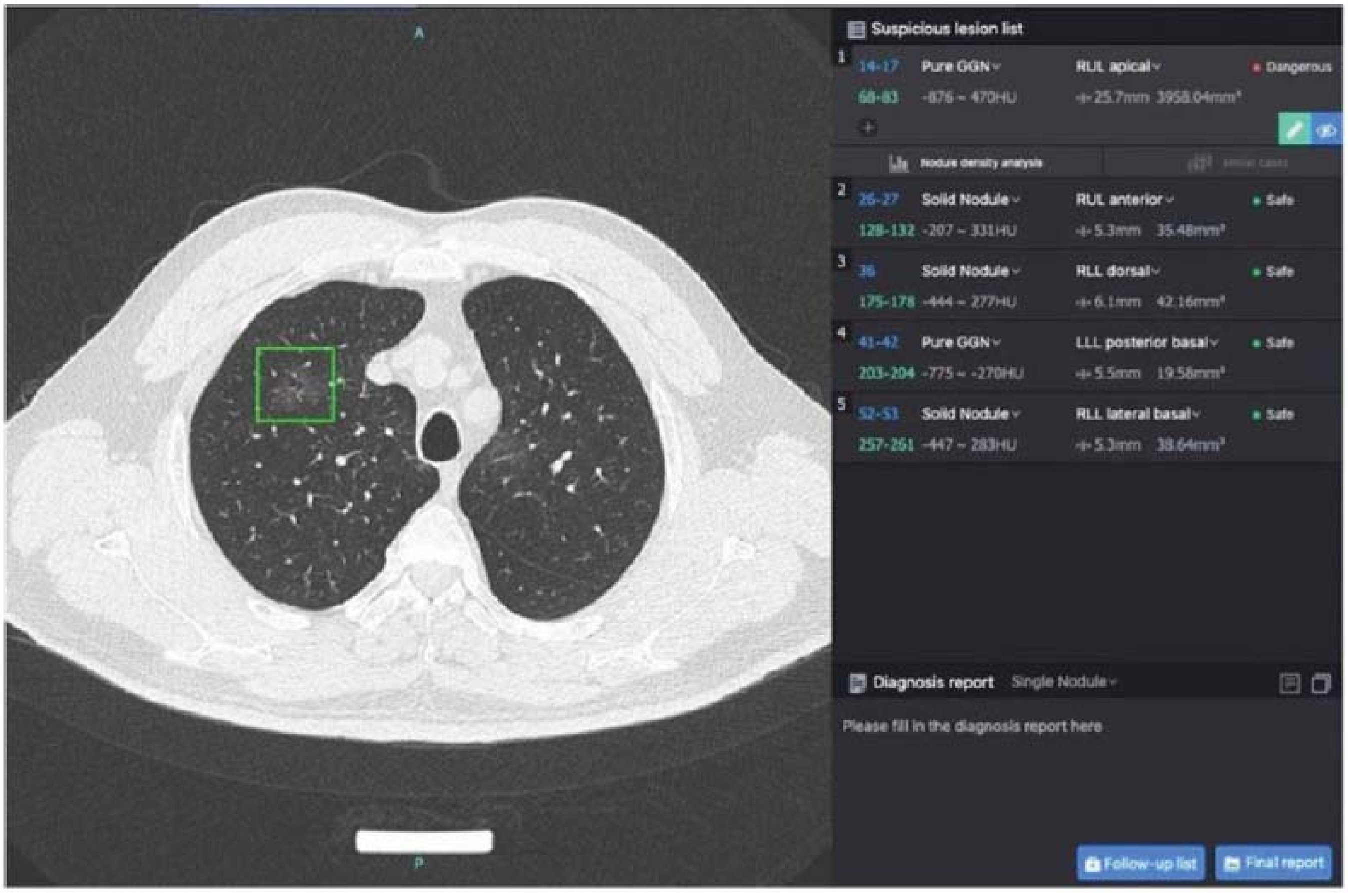

Fig. (1). The terminal interface of artificial intelligence (AI)-assisted lung nodule evaluation system (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

images of 11,625 adults (5,777 males) from multiple academic hospitals were retrospectively included to establish the AI system. The inclusion criterion was thin-slice chest CT. The exclusion criteria were as follows: incomplete coverage of all lung fields; image artifacts caused by cardiac or respiratory motion; and insufficient image quality to meet the requirements of image labeling. To generate the ground truth of nodule location for the entire dataset, each CT scan was reviewed and annotated by two radiologists with approximately 10 years of experience. The detected nodule was marked by a square bounding box for training CNN, and the nodule was located in the center.

In short, the deep learning architecture of the AI system consists of two CNN models: a faster R-CNN model as the detector and a DenseNet model as the feature map extractor. The original implementation of the fast R-CNN needs to input an image and then feeds back the extracted features to a regional proposed network to identify the potential regions of interest and further process them to classify the potential objects and generates their bounding boxes [25, 26]. To handle non-isotropic continuous CT images as input, the fast R-CNN has been improved to a multichannel 2.5D CNN. In this case, 2.5D means that the model can take continuous images as input but does not rely on 3D convolution.

The DenseNet model was used for feature extraction and backpropagation in this AI system. Although large and deep CNN is helpful to most classification tasks, computational efficiency and low parameter count are still the key factors in practice. With DenseNet structure, the convolution network can be deeper, the training efficiency is higher, and the connection between the near input layer and the near output layer is shorter [27]. DenseNet structure connects each layer to every other layer in a feedforward manner. The traditional L-layer convolutional network has L connections, and there is one connection between each layer and its subsequent layer, while DenseNet has L(L+1)/2 direct connections. As a result, DenseNet reduces the vanishing-gradient problem in CNN model training and enhances the feature propagation.

2.6. Nodule Categorization

The National Comprehensive Cancer Network (NCCN) guideline [21] categorizes lung nodules into three component types: solid, part-solid, and non-solid nodules, and defines different management workflow for each type. According to the nodule diameter, solid nodules are further stratified into ≤5 mm, 6 to 7 mm, 8 to 14 mm, and ≥15 mm; part-solid nodules into ≤5 mm and ≥6 mm; and non-solid

Table 1. Nodule detectability at the subject level between radiologist observation and artificial intelligence (AI)-assisted reading.

Nodule Component Category	Radiologist Observation		AI-assisted Reading		Panel Reading, *n*
	Detected subject, *n*	Missed subject, *n*	Detected subject, *n*	Missed subject, *n*	
Solid	131 (52.4%)	119 (47.6%)	247 (98.8%)	3 (1.2%)	250
Part-solid	3 (23.1%)	10 (76.9%)	13 (100%)	0	13
Non-solid	28 (25.2%)	83 (74.8%)	110 (99.1%)	1 (0.9%)	111

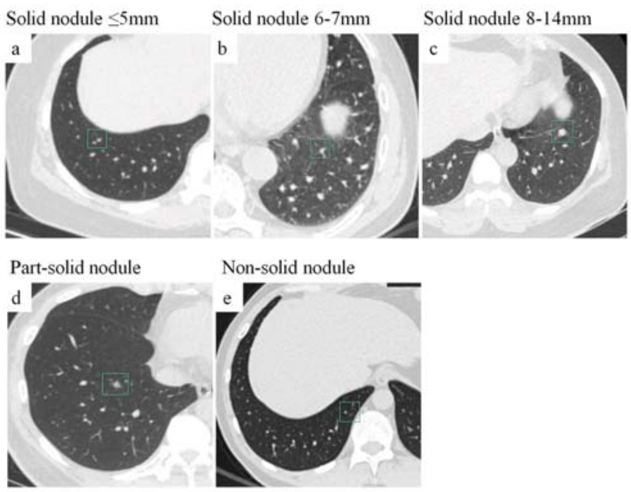

Fig. (2). Representative images of nodules that have been missed by radiologist observation but detected by artificial intelligence (AI)-assisted reading.

nodules into ≤19 mm and ≥20 mm. Since the management workflow of a screening participant depends on the largest nodule in each component category, we stratified the subjects according to the size of the largest nodule in multiple nodules.

2.7. Panel Evaluation

To determine the reference criteria for the presence of nodules, a reading panel consisting of two radiologists with 20 and 31 years of experience in thoracic radiology evaluated the results of the radiologists' observations and AI-assisted reading to confirm the detected or missed nodules. The number of true positives, true negatives, false positives, and false negatives in the radiologists' observation and AI-assisted reading was thereafter determined according to the results of the reading panel. If a lung nodule was reported by radiologist observation or by AI-assisted reading but not confirmed by the reading panel, it was considered a false-positive nodule. If a lung nodule was not reported either by radiologist observation or by AI-assisted reading but confirmed by the reading panel, it was considered a missed nodule.

2.8. Statistics

Numerical data are presented as the mean ± standard deviation for normally distributed data. Normality was tested by Kolmogorov-Smirnov test. The *Chi*-square test was used to compare the nodule detection rates between radiologists' observation and AI-assisted reading. The Confidence Interval (CI) for the predictive value was given by the standard logit confidence interval [28]. A p-value <0.05 was considered statistically significant. A software package (SPSS version 20.0, IBM) was used for statistical analysis.

3. RESULTS

An exhaustive search revealed 874 candidates, of which 860 participants (mean age 57±7 years) were eligible for this study, including 486 males and 374 females. Nine were excluded because of a history of lung surgery, and 5 were excluded because of no or incomplete diagnostic reports.

3.1. Nodule Detectability at the Subject Level

Nodule detectability at the subject level by radiologist observation and AI-assisted reading is shown in Table **1**. For solid nodules, the reading panel confirmed that 250 individuals had at least one solid nodule. In these nodules, radiologist observation detected 131/250 (52.4%), significantly lower than 247/250 (98.8%) detected by AI-assisted reading ($p<0.001$). For part-solid nodules, the reading panel confirmed 13 individuals with at least one. Among these nodules, radiologist observation detected 3/13 (23.1%), significantly lower than 13/13 (100%) by AI-assisted reading ($p<0.001$). For the non-solid nodules, the reading panel confirmed 111 subjects with at least one. Among these nodules, radiologist observation detected 28/111 (25.2%), significantly lower than 110/111 (99.1%) by AI-assisted reading ($p<0.001$).

On the other hand, radiologist observation missed at least one solid, part-solid and non-solid nodule in 119/250 (47.6%), 10/13 (76.9%), and 83/111 (74.8%) screening participants, respectively. AI-assisted reading missed only 3/250 (1.2%), 0/13 (0%), and 1/111 (0.9%) cases, respectively. The most easily missed nodules by radiologist observation were non-solid. Several representative CT images of the missed lung nodules by radiologist observation but detected by AI-assisted reading are shown in Fig. (**2**).

3.2. Nodule Detectability Stratified by Nodule Size

Table **2** presents the nodule detectability stratified by nodule size. For solid nodules, radiologist observation detected 106, 16, and 8 individuals to have at least one solid nodule of ≤5 mm, 6 mm to 7 mm, and 8 mm to 14 mm in diameter, respectively, lower than the 186, 41, and 19 individuals detected by AI-assisted reading (all $p<0.001$). For part-solid nodules, radiologist observation detected 3 and 0 cases to have at least one part-solid nodule of ≤5 mm and ≥ 6 mm, respectively, less than the 8 and 5 detected by AI-assisted reading (all $p<0.001$). For non-solid nodules, radiologist observation

Table 2. Nodule detectability stratified by nodule size between radiologist observation and artificial intelligence (AI)-assisted reading.

Nodule Component Category	Nodule Diameter Category	Subjects with ≥1 Nodule, *n*		Panel Reading, *n*
		Radiologist observation	AI-assisted reading	
Solid	≤5 mm	106	186*	188
	6 to 7 mm	16	41*	42
	8 to 14 mm	8	19*	19
	≥15 mm	1	1	1
	All	131	247*	250
Part-solid	≤5 mm	3	8*	8
	≥6 mm	0	5*	5
	All	3	13*	13
Non-solid	≤19 mm	28	110*	111
	≥20 mm	0	0	0
	All	28	110*	111

* indicates significantly different (p<0.001) by the Chi-square test between radiologist observation and AI-assisted reading.

Table 3. Diagnostic accuracy, sensitivity, and specificity of nodule detection by radiologist observation and by artificial intelligence (AI)-assisted reading using panel reading as ground truth.

Nodule Component Category	Accuracy (95% CI)		Sensitivity (95% CI)		Specificity (95% CI)	
	Radiologist observation	AI-assisted reading	Radiologist observation	AI-assisted reading	Radiologist observation	AI-assisted reading
Solid	86.2% (83.7-88.4%)	99.1% (98.2-99.6%)	52.4% (46.0-58.7%)	98.8% (96.5-99.8%)	100.0% (99.4-100%)	99.2% (98.1-99.7%)
Part-solid	98.8% (97.9-99.4%)	100.0% (99.6-100%)	23.1% (5.0-53.8%)	100.0% (75.3-100%)	100.0% (99.6-100%)	100.0% (99.6-100%)
Non-solid	90.4% (88.2-92.2%)	98.8% (97.9-99.4%)	25.2% (17.5-34.4%)	99.1% (95.1-99.9%)	100.0% (99.5-100%)	98.8% (97.7-99.5%)

CI= Confidence Interval.

detected 28 individuals to have at least one non-solid nodule of ≤ 19 mm, lower than the 110 detected by AI-assisted reading (p<0.001).

3.3. Performance of Detecting Lung Nodules between Radiologist Observation and AI-assisted Reading

The detailed diagnostic performance of nodule detection is presented in Table **3**. For solid nodules, the accuracy and sensitivity of radiologist observation were 86.2% (95%CI: 83.7% to 88.4%) and 52.4% (46.0% to 58.7%), using the panel reading as the reference, much lower than 99.1% (98.2% to 99.6%) and 98.8% (96.5% to 99.8%) detected by AI-assisted reading. For part-solid nodules, the sensitivity of radiologist observation was 23.1% (5.0-53.8%), much lower than 100.0% (75.3-100%) by AI-assisted reading. For non-solid nodules, the sensitivity of radiologist observation was 25.2% (17.5-34.4%), much lower than the 99.1% (95.1-99.9%) by AI-assisted reading. AI-assisted reading greatly increased the detection sensitivity of non-solid nodules by 74% compared with the radiologists' observation.

4. DISCUSSION

In the clinical setting, many radiologists are involved in the detection of lung nodules in a general screening population, and AI-assisted reading improved the sensitivity of nodule detection compared with real-world radiologists' observation. Importantly, AI-assisted reading greatly increased the sensitivity of detection of non-solid nodules, which were easily missed by radiologist observation before using the AI assisting system, by 74%.

Due to the advancements in CT technology, an increasing number of lung nodules have been detected. Currently, CT is widely used for lung cancer screening, and many large-sample studies have shown significant reductions in lung cancer-related mortality [2-4]. The Dutch-Belgian lung cancer screening trial (NELSON) enrolled 6,583 and 6,612 participants in the CT examination arm and the control arm, respectively, and observed lower lung cancer mortality in the CT examination arm [5]. Encouraged by the results of these lung cancer screening trials, the National Comprehensive Cancer Network (NCCN) guidelines recommend the use of CT as a first-line screening tool to detect early-phase lung cancer [21]. However, in the real-world setting, CT examinations may be performed by different types of CT equipment and be read by multiple radiologists with variable clinical experience, which greatly increases the uncertainty of nodule detection.

In lung cancer screening programmes, more than 20% of the participants with one or more lung nodules on their baseline scan require a follow-up scan [4, 29-31]. However, the heterogeneous experience of observers may affect the nodule detection and diagnosis, which might increase the possibility of missed and misdiagnosed lung nodules. Some researchers have pointed out that up to 90% of missed cancerous nodules can be found when the baseline images are re-examined [32]. The factors leading to misdiagnosis of lung cancer can be classified as those related to lesion characteristics, technical considerations, or observer performance [33]. The size of lung nodules also plays an important role in the nonperfect sensitivity of CT for nodule detection [34]. Observer error is probably the most important factor in overlooking a lesion. Awareness of the possible causes of overlooking a lung nodule can give radiologists a chance to reduce the occurrence of this eventuality [35].

According to the NCCN guideline, lung nodules are categorized into solid, part-solid, and non-solid nodules. In our study, the reading panel confirmed that AI-assisted reading missed only 1.2% and 0.9% of the patients with solid and non-solid nodules, respectively. Unfortunately, radiologist observation missed 47.6% and 74.8% of the patients with solid and non-solid nodules, respectively. Since the NCCN guideline recommends follow-up scans for participants with an indeterminate lung nodule, the detection of lung nodules would definitely change the clinical pathway and improve nodule assessment for many individuals, especially those with non-solid nodules.

As early as the 1980s, Computer-aided Detection (CAD) schemes were developed to detect lung nodules on CT images, with detection sensitivities from 68.9–100% [36, 37]. As a potential auxiliary tool in clinical practice, CAD can avoid subjective factors and reduce labour burden; thereby, CAD is helpful to improve the accuracy of early diagnosis of lung cancer [38]. Nevertheless, it is still necessary to improve the sensitivity of the algorithm, reduce the false positive rate, improve and optimize the detection algorithm of pulmonary nodules of different sizes and shapes [39]. Most of the previous CAD studies for pulmonary nodule detection were retrospective based on public datasets, such as the Lung Image Database Consortium Image Collection-Image Database Resource Initiative (LIDC-IDRI) [40], the Lung Nodule Analysis 2016 (LUNA16) [41], and the National Lung Screening Trial (NLST) [42]. However, validation on public datasets hardly represents the general population. Recently, Liu *et al.* retrospectively collected and reread 1,129 CT scans and found a CNN-based nodule detection system can improve the nodule detection rate [23]. Hsu *et al.* retrospectively collected and reread 340 nodules ≤ 10 mm in diameter and also found AI-powered system improved nodule detection sensitivity [43]. Different from these studies performing image rereading, we collected the actual reading results from the original radiology reports and compared the actual reading with AI-assisted reading. Our study provides solid evidence for the clinical application of AI-assisted reading in lung cancer screening. Comparing the AI-assisted nodule detection with the actual radiology reports is very important to evaluate the clinical value of the AI system.

The main advantage of deep learning is its ability to learn from the training data to maximize classification with limited direct supervision [44]. CNN-based algorithms have made great progress in the detection and classification of lung nodules [13, 14, 23, 37, 45], differentiation of the diagnosis between malignant and benign nodules [46], and staging of lung cancer [47]. With the popularity of AI technology in clinical work, AI systems have been integrated with RIS and PACS to improve the level of automation in the evaluation of lung nodules. Although AI offers many potential opportunities to improve lung cancer screening, pitfalls and multiple challenges have to be overcome before routine clinical application. Our study reported the real-world results of this integrated AI-assisted image reading procedure and thus provided prospects of changing the working pattern in clinical practice.

This study has limitations. First, this is a single-centre study. The utilization of AI at other institutes may vary depending on their own practice. Second, the prognostic and histologic values of AI were not investigated in this study. Extended studies on these topics will shed further light on the implementation benefits of AI-assisted image reading.

CONCLUSION

In the chest CT screening population, AI-assisted reading exhibited a significantly higher detection sensitivity for lung nodules than radiologist observation, especially for the detection of non-solid nodules. An AI-powered lung nodule evaluation system can be used as a routine assistant tool in clinical practice. The combination of radiologist expertise and AI assistance may lead to the development of a new working pattern that promises to detect lung nodules and inspires the implementation of AI in lung cancer screening.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This retrospective study was approved by the local medical ethics committee of Shanghai General Hospital (approval no. SGH-2018-56).

HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All human research procedures were followed in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

The need for written informed consent was waived.

STANDARDS OF REPORTING

The study conforms to STROBE guidelines.

AVAILABILITY OF DATA AND MATERIALS

The data of the related manuscript were not deposited in any web-based depository and will not be shared.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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