

Original Article

Diagnostic efficiency of artificial intelligence for pulmonary nodules based on CT scans

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Abstract: Purpose: To explore the accuracy of artificial intelligence (AI) for the diagnosis of pulmonary nodules (PNs) on computerized tomography (CT) scans. Methods: In this study, 360 PNs (251 malignant nodules and 109 benign nodules) were retrospectively analyzed in 309 participants examined for PNs, and CT images were reviewed both by radiologists and using AI technology. With postoperative pathologic results as the gold standard, the accuracy, misdiagnosis, missed diagnosis, and true negative rates of CT results (human and AI) were calculated by using 2×2 crosstabs. Data confirmed to be normally distributed by the Shapiro-Wilk test were compared by the independent sample t-test, and the reading time of AI and human radiologists was compared. Results: 1) The accuracy rate of AI for diagnosing PNs was 81.94% (295/360), the missed diagnosis rate was 15.14% (38/251), the misdiagnosis rate was 24.77% (27/109), and the true negative rate was 75.23% (82/109). 2) The accuracy, missed diagnosis, misdiagnosis, and true negative rates of human radiologists in the diagnosis of PNs were 83.06% (299/360), 22.31% (56/251), 4.59% (5/109), and 95.41% (104/109), respectively. 3) The accuracy and missed diagnosis rates were comparable between AI and radiologists, but AI had a significantly higher misdiagnosis rate and a markedly lower true negative rate. 4) The image reading time required for AI (195.4±65.2 s) was statistically shorter than that required for manual examination (581.1±116.8 s). 5) The accuracy of AI for detecting low, moderately, and highly malignant PNs was 13.64% (9/66), 25.33% (19/75), and 48.61% (35/72), respectively. Conclusions: AI demonstrates favorable accuracy for CT diagnosis of lung cancer and requires a shorter time for film reading. However, its diagnostic efficiency in identifying low- and moderate-grade PNs is relatively low, indicating a need for expansion of machine learning samples to improve its accuracy in identifying lower grade cancer nodules.

Keywords: CT of lung cancer, pulmonary nodules, artificial intelligence

Introduction

Lung cancer (LC) is one of the most common malignancies worldwide, with the latest global cancer statistics indicating it is the second most prevalent cancer, accounting for 11.4% of the total cancer population with approximately 2.2 million patients worldwide [1]. It is also one of the main causes of cancer-related death, with about 17,600 associated deaths each year [2]. In addition to smoking, the greatest risk factors for LC, age, weight, nodule size, and upper lobe position have been shown to increase the risk of LC and mortality [3]. LC can be classified into central and peripheral types according to the lesion location, and as small or non-small cell LC based on the histopatho-

logic characteristics [4]. The pathogenesis of LC is heterogeneous and complex, and its onset and progression have been linked to epidermal growth factor receptor (EGFR), killer activation receptor, and other gene profile diseases [5].

Early diagnosis improves the prognosis and therapeutic efficacy for LC patients [6, 7]. Pulmonary nodules (PNs) produced by the lung parenchyma are believed to be the histopathologic basis of LC [8]. Therefore, early evaluation of suspected patients is carried out by screening for PNs. Computerized tomography (CT) is a powerful means to screen PNs and plays an important role in early diagnosis of LC. However, the large amount of image information generated by CT may reduce the evaluation efficiency

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of radiologists [9]. Machine learning-based artificial intelligence (AI) is expected to be applied to imaging diagnosis as a supplemental method to manual review, to aid PN identification and segmentation [10, 11]. A clinical study on the application of AI in screening PNs found that this approach was more accurate and sensitive for diagnosing PNs than manual review [12]. In addition, a multi-cohort study involving 18,232 patients demonstrated the value of an automatic AI system for detecting EGFR mutation phenotypes based on CT images, suggesting that AI techniques can be used to analyze EGFR genotypes from lung information displayed in CT images [13]. It can thus be seen that AI technique has great application potential for improving the diagnostic efficiency and accuracy of LC. This study explored the feasibility and diagnostic efficiency of AI in PN screening in LC patients. This can help optimize the early diagnosis and treatment of LC. However, there are only a few relevant studies on the value and efficiency of AI versus manual film reading for LC screening in patients undergoing PN examination, as well as for the determination of the degree of malignancy of PNs using AI. The novelty of this study is that it not only fills these gaps, but also provides robust scientific evidence for the application of AI for CT diagnosis of PNs.

In order to explore the diagnostic efficacy of AI-assisted CT in diagnosing PNs, this study retrospectively included 309 participants who underwent PN examination, and calculated the accuracy, missed diagnosis, misdiagnosis, and true negative rates of AI, with postoperative pathologic results of PNs serving as the gold standard.

Methods

Participants

360 PNs from 309 participants who underwent PN examination, with low-, moderate-, and high-grade nodules accounting for 59 (23.50%), 97 (38.65%), and 95 (37.85%), respectively, were retrospectively analyzed. The research population comprised 186 (60.19%) males and 123 (39.81%) females, with a mean age of (52.32±17.17) years old. The included patients, aged ≥18, all underwent low-dose chest CT scans, with available postoperative histopathologic staining results and the CT images were

evaluated by two radiologists. Excluded patients were those with other malignancies, PNs confirmed to be above 5 cm ×5 cm in size, or the presence of a large area of lung shadow. This research was approved by the Hospital Ethics Committee of The 904th Hospital of Joint Logistic Support Force of PLA.

CT imaging and film reading

Patients were lying supine for Chest CT scanning using the third-generation dual source spiral CT (Siemens, Germany), with the scan parameters set as follows: 120 kVp tube voltage and 70 eff mAs for patients with a body mass index (BMI) >30, and 110 kVp tube voltage and 40 eff mAs for those with a BMI<30; thickness/interslice spacing: 5 mm, thin-film layer thickness/interslice spacing: 1 mm, gantry rotation time: 0.5 s, and spacing: 0.7. For manual film reading, two radiologists made independent judgments on the CT images, and reached a consensus through consultation in case of disagreement. In terms of AI diagnosis, the CT AI diagnostic system for LC was used to analyze and evaluate the CT images and obtain PN detection results.

Image segmentation: 1) The boundaries of both lungs were identified, that is, the whole lung tissue was extracted from other tissues and the surrounding environment through lung parenchyma segmentation; 2) PN images were used, and the contrast between pixel values of PNs and those of other anatomic parts was enhanced to extract candidate nodules; 3) The gray-scale histogram was plotted. Gray-scale features were extracted to construct gray-scale level co-occurrence matrices. After extracting the texture features, the areas and edges of the PNs were analyzed by using the edge orientation histogram method and the geometric parameter method to extract morphologic features; 4) PN segmentation and diagnosis were performed according to the gray-scale features, texture features, and morphologic characteristics.

Outcome measures

The primary outcome measures of this study were accuracy, missed diagnosis rate, misdiagnosis rate, true negative rate, and average film reading time, while the secondary outcome measures were the accuracy of AI for detecting low, moderate, and high malignancy PNs.

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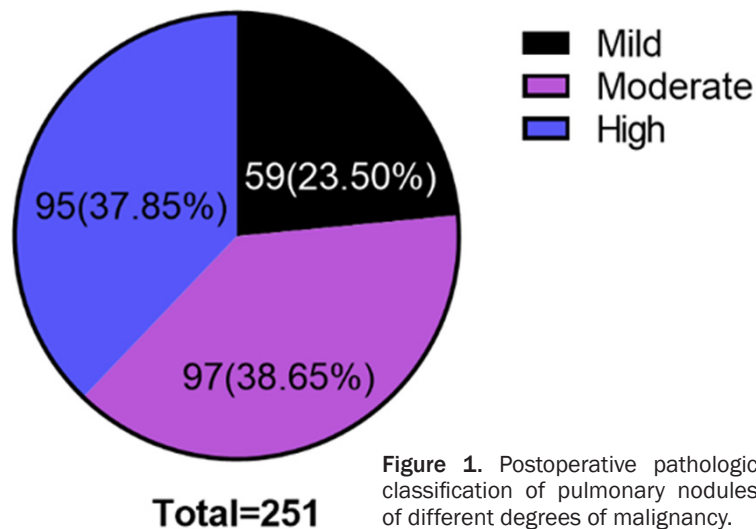


Figure 1. Postoperative pathologic classification of pulmonary nodules of different degrees of malignancy.

On this basis, the accuracy rate was calculated as the ratio of the number of accurately diagnosed PNs among the total number of PNs; the missed diagnosis rate was the ratio of patients who tested positive by the gold standard diagnosis but were judged to be negative by the diagnostic method to the number of positives identified by the gold standard diagnosis; the misdiagnosis rate was the ratio of patients diagnosed negative by the gold standard but judged to be positive by the diagnostic method in the negatives identified by the gold standard diagnosis; the true negative rate was 1 - misdiagnosis rate.

Statistical analyses

The pathologic and CT diagnosis results (including manual review and AI) of 309 patients were collected. With postoperative pathologic results as the gold standard, the accuracy, misdiagnosis, and missed diagnosis rates of the CT diagnosis results were calculated by using 2×2 crosstabs. The accuracy, misdiagnosis rate, missed diagnosis rate, and true negative rate of PNs detected by manual review and AI were compared by the Chi-square test, and data differences were identified using the paired Chi-square test. Data that were confirmed to be normally distributed by the Shapiro-Wilk test were compared using the independent sample t-test. The reading times required for AI and manual review were comparatively analyzed. Values of $P < 0.05$ were considered significant at 95% confidence interval (95% CI). The mean and standard deviation were calculated by the

SPSS software, and data visualization was performed by GraphPad.

Results

LC pathology

Among the 309 patients undergoing PN examination in this study, 209 patients were pathologically diagnosed with LC after surgery, with 360 PNs (251 malignant nodules and 109 benign nodules) detected. Of the 251 malignant nodules, low-, moderate, and high-grade nodules accounted for 59

(23.50%), 97 (38.65%), and 95 (37.85%), respectively (**Figure 1**).

Diagnostic efficiency of AI for PNs

Based on the CT images, the AI technique detected 240 malignant PNs and 120 benign PNs. Taking postoperative pathologic results as the gold standard, the accuracy, missed diagnosis, misdiagnosis, and true negative rates of AI for diagnosing PNs were calculated to be 81.94% (295/360), 15.14% (38/251), 24.77% (27/109), and 75.23% (82/109), respectively (**Table 1**).

Diagnostic efficiency of manual review for PNs

Two radiologists reviewed the CT images and identified 200 malignant PNs and 160 benign PNs. Taking postoperative pathologic results as the gold standard, it was found that the accuracy of manual review in the diagnosis of PNs was 83.06% (299/360), the missed diagnosis rate was 22.31% (56/251), the misdiagnosis rate was 4.59% (5/109), and the true negative rate was 95.41% (104/109). See **Table 2** for details.

Comparison of efficiency between manual review and AI diagnosis

The Chi-square test was used to compare the efficiency between manual review and AI for diagnosing PNs. The two diagnostic modalities were not statistically different for accuracy or missed diagnosis ($P > 0.05$), while AI had a higher misdiagnosis rate and a lower true negative

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Table 1. Efficiency of AI for diagnosing pulmonary nodules based on CT images

	Pathologically positive	Pathologically negative	Total
AI positive	213	27	240
AI negative	38	82	120
Total	251	109	360

Note: CT, computerized tomography; AI, artificial intelligence.

rate than manual review ($P < 0.05$). See **Table 3** for details.

Comparison of film reading time between AI and manual review

The average reading time was calculated to be (195.4 ± 65.2 s) for AI and (581.1 ± 116.8 s) for manual review. According to statistical analysis (**Figure 2**), the film reading time required for AI was shorter than that required for manual review ($P < 0.0001$, $t = 41.68$).

Diagnostic efficiency of AI for screening PNs of different degrees

Postoperative pathologic results excluded 27 suspected PNs. Of the 66 low-grade nodules detected by AI, 9 were confirmed by postoperative pathology; AI detected 75 moderate-grade nodules, of which 19 were pathologically diagnosed after surgery; and 35 of the 72 AI-detected high-grade nodules were confirmed by postoperative pathology (**Figure 3**). The accuracy of AI for detecting low-, moderate-, and high-grade malignant nodules was 13.64% (9/66), 25.33% (19/75), and 48.61% (35/72), respectively.

Typical cases

Case 1 was a 53-year-old man. Histologic staining of tumor biopsies was performed using hematoxylin eosin (H&E) staining. As shown in **Figure 4A**, the nucleus was blue-purple and highly stained, while the cytoplasm was cherry-red; meanwhile, tissue and cell structural damage as well as cytoplasm sparsity were observed. PNs were found on CT imaging (**Figure 4B**).

The H&E staining results of Case 2, a 61-year-old female patient, showed that there was mucus in the tumor tissue with a sieve-like structure, which was suspected to be invasive

Table 2. Diagnostic efficiency of manual review for pulmonary nodules

	Pathologically positive	Pathologically negative	Total
Positive	195	5	200
Negative	56	104	160
Total	251	109	360

alveolar adenocarcinoma of the lung (**Figure 5A**). CT imaging revealed PNs (**Figure 5B**).

Discussion

Accurate staging is crucial to the treatment and management of lung cancer (LC, especially non-small cell LC), and CT screening is the most widely used basis for diagnosis and staging at present [14]. However, the large amount of imaging information affects the review efficiency of radiologists [15]. AI technique based on deep learning and machine learning is expected to address these problems [16]. In this study, the clinical data of 309 participants undergoing PN examination in our hospital were retrospectively analyzed to discuss the value of AI in diagnosing PNs with postoperative pathology as the gold standard. The AI technique was identified to have a high discrimination power of PNs (accuracy rate $> 80\%$) and contribute to effectively shortened film reading time. Therefore, this study supports that AI techniques can be used as an auxiliary means to assist manual review.

The manual screening for LC used to be based on the interpretation of chest radiographs, but the manual opinions vary greatly and is neither specific nor sensitive [17]. It has been reported that manual review of chest radiographs may miss 19-26% of lung tumors on first reading [18]. Therefore, CT is increasingly used for diagnosis and screening. However, manual review based on CT is still not optimal, and this may lead to large differences in diagnosis. The application mechanism of AI technology in tumor pathologic identification is related to the development of image analysis methods, which accomplish the digitization of pathology through image segmentation, enhanced contrast, morphologic feature extraction and segmentation diagnosis, with reliability, stability, reproducibility and accuracy that may not be inferior to pathologists [19]. Machine learning, one of its underlying mechanisms, is based on the

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Table 3. Comparison of PN diagnosis efficiency between manual review and AI

	Manual review	AI	χ^2	P
Accuracy	83.06% (299/360)	81.94% (295/360)	0.154	0.695
Missed diagnosis rate	22.31% (56/251)	15.14% (38/251)	4.241	0.040
Misdiagnosis rate	4.59% (5/109)	24.77% (27/109)	17.727	<0.001
True negative rate	95.41% (104/109)	75.23% (82/109)	17.727	<0.001

Note: PN, pulmonary nodule; AI, artificial intelligence.

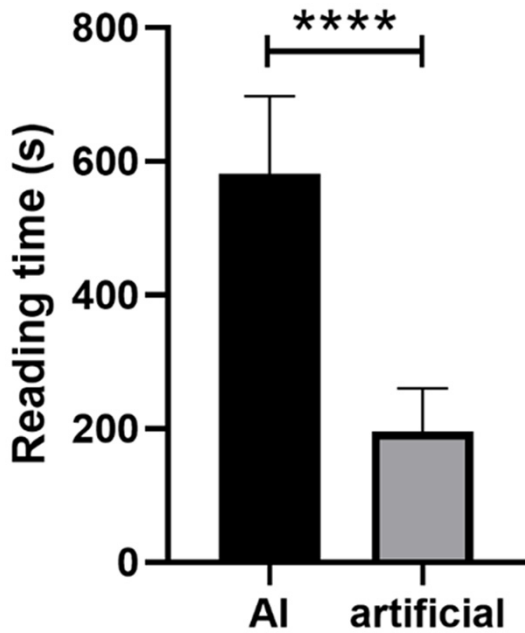


Figure 2. Comparison of film reading time between AI and manual review (**** $P < 0.0001$). AI, artificial intelligence.

learning of data input by machines, while deep learning is a special machine learning method implemented through artificial neural networks [20]. First of all, slightly lower diagnostic accuracy of AI techniques versus manual review for identifying PNs was determined in this study. AI techniques have been indicated to play a vital role in identifying PNs, which utilize machine learning to construct digital features about PNs and then automatically extract features and data labeling for diagnostic images to classify the nature, malignancy, or tumor grade of PNs [21]. According to a retrospective analysis of 652 patients, the accuracy rates of AI system-based convolution and recurrent neural networks for identifying malignant and benign PNs were 92.3% and 82.8%, respectively, suggesting that AI has high efficiency and great value in the diagnosis of PNs [22]. Zhou et al. [23]

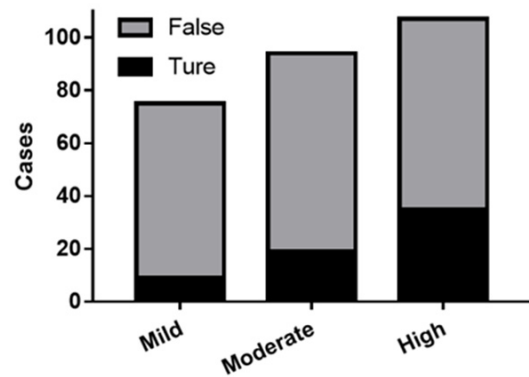


Figure 3. Detection results of different degrees of malignancy of pulmonary nodules by AI. AI, artificial intelligence.

reported that the accuracy of AI-assisted CT review with support vector machine training as the classifier and optimization by the mesh optimization model was as high as 98% for PN classification. This study found a similar identification rate between AI techniques and manual review. Herein, a total of 240 malignant PNs were detected by the AI technique, of which 27 suspected PNs were excluded and 213 were pathologically confirmed after surgery. The manual review achieved an accuracy rate of 83.06 percent. Notably, we confirmed that AI had a lower rate of missed diagnosis and true negative diagnosis and a higher rate of misdiagnosis than manual review, suggesting that the efficiency of AI diagnosis is still limited in clinical practice. The high misdiagnosis rate and low true negative rate of AI are closely related to its learning depth and sample quality [24-26]. In other words, the identification of PNs by AI technique depends on a large number of samples. In this process, the sample quantity, quality, and sample distribution may lead to a certain degree of sampling error, which limits the identification rate of AI [27]. Nasrullah et al. [28] pointed that incorporating clinical factors into the deep learning model

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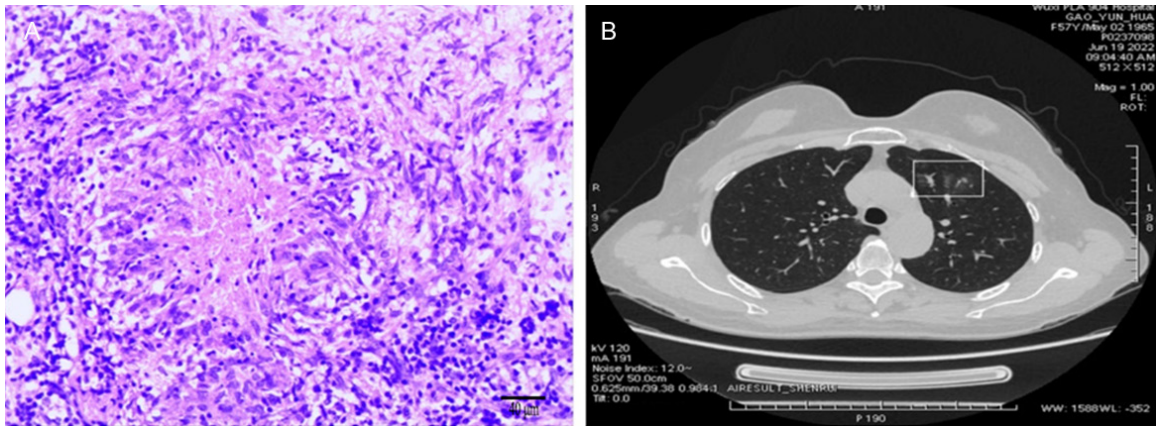


Figure 4. Tumor histopathologic staining ($\times 200$) (A) and CT image (B) of Case 1. CT, computerized tomography.

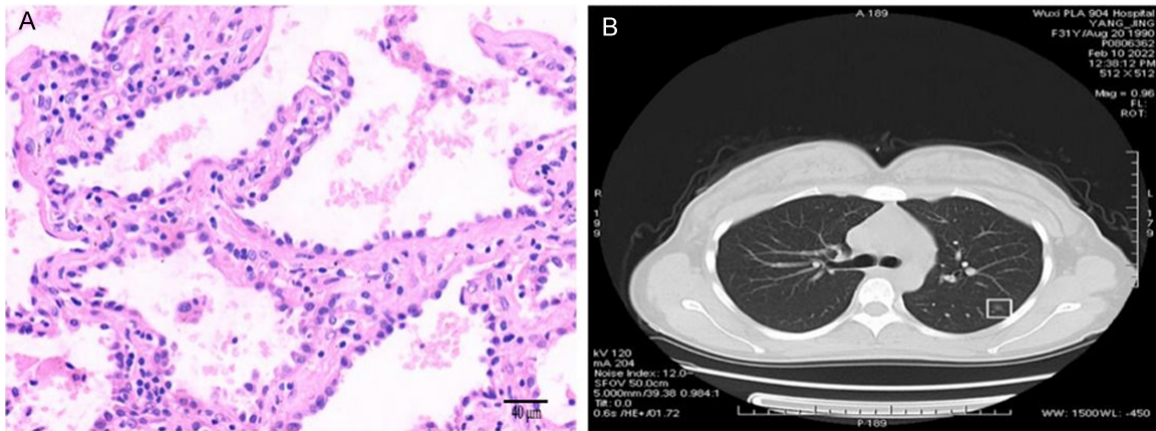


Figure 5. Tumor histopathologic staining ($\times 200$) (A) and CT image (B) of Case 2. CT, computerized tomography.

used in AI technology for nodular detection and classification would be beneficial, as it might reduce the misdiagnosis rate in the diagnosis of LC. The advantage of low missed diagnosis rate of AI may be attributed to its precise capture of nodules, whereas manual review, which involves a high workload, may lead to fatigue among radiologists and the possibility of overlooking small lesions [29].

Subsequently, this study determined that AI techniques could greatly shorten the film reading time. This study found that the time required by AI (195.4 ± 65.2 s) for film reading was statistically shorter than that of manual review (581.1 ± 116.8 s), suggesting that AI can shorten the diagnostic time and waiting time of patients. The efficiency of AI techniques benefits from their own characteristics. AI saves identification time by simplifying CT images

through multiparameter clustering [30, 31]. In the study of Huang et al. [32], 73.62% of doctors supported the use of AI-assisted CT diagnosis for the classification of benign and malignant PNs, and such a high support rate is associated with a reduction of the workload of radiologists with the help of AI while taking into account the high diagnostic efficiency. Hsu et al. [33] reported that a concurrent-reading mode in which junior and senior readers used AI-powered computer-aided detection further shortened the reading time to (124 ± 25 s) in CT-based PN screening, providing a more efficient option for PN screening in clinical practice. However, the accuracy rates of AI for detecting low-, moderate- and high-grade malignant nodules were found to be 13.64% (9/66), 25.33% (19/75), and 48.61% (35/72), respectively. Previous studies have shown that the AI identification rate may be related to the

uneven edges of nodules [34]. Improving AI algorithms and optimizing accurate segmentation should be the focus of future AI technique-related research.

To sum up, AI techniques can significantly shorten the film reading time, but given its low diagnostic efficiency for moderate- and low-grade nodules, a large number of machine learning samples are needed to improve its accuracy in identifying lower-grade cancer nodules. AI techniques are expected to be widely used in CT examination of PNs and have the potential to play a potent supporting role in assisting radiologists in the diagnosis of LC.

Disclosure of conflict of interest

None.

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