Artificial Intelligence and Lung Cancer

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Lung cancer is the second most common cancer in both males and females, with the highest mortality worldwide, causing 21% of total cancer-related deaths. The notion of artificial intelligence (AI) was initially proposed by John McCarthy in 1956. It involves using computer systems and technology to replicate human-like intelligent behavior and critical thinking abilities. In the realm of medicine, AI is divided into two main categories: virtual and physical. The virtual branch is further categorized into machine learning (ML) and deep learning (DL).

lung cancer artificial intelligence machine learning deep learning radiomics screening diagnosis treatment

1. Artificial Intelligence in Lung Cancer Screening

The National Lung Screening Trial (NLST) has revealed that early diagnosis among the high-risk population has been shown to reduce the lung cancer death rate by 20% [1]. These compelling statistics underscore the urgent need for the development of highly accurate screening methods and extensive patient education to promote early diagnosis and ultimately improve the prognosis for those affected by this devastating disease. As of March 2021, according to the U.S. Preventive Services Task Force (USPSTF), individuals aged 50 to 80 who have a history of smoking at least 20 packs of cigarettes and either smoke currently or have quit within the past 15 years are advised to undergo yearly low-dose computed tomography (LDCT) screenings for the detection of lung cancer. It is advised to stop the screening process if a person has not smoked for 15 years or has a health issue that significantly shortens their life expectancy or prevents them from having curative lung surgery [2][3].

Artificial intelligence (AI) models have become an integral part of the lung cancer screening process and can offer a range of benefits. These include minimizing the radiation exposure, accurately detecting and categorizing lung nodules, personalizing screening schedules, and providing LDCT interpretation in regions with a shortage of skilled radiologists [4]. Convolutional neural networks (CNNs), a class of deep-learning artificial neural networks, has shown promising results in predicting lung cancer risk by using visual imagery and clinical information retrieved from electronic medical records (EMRs).

Numerous experimental studies have been undertaken to identify high-risk populations that can be explored further. Based on non-imaging data, CNNs have successfully identified high-risk patients and predicted a 1-year lung cancer rate with excellent accuracy, demonstrated by an overall AUC—0.90 [5]. Among the models that used imaging data, CXR-LC identified high-risk patients by relying solely on CXR findings and limited clinical data with an accuracy (AUC–0.755) comparable to the previous models like PLCO(AUC–0.751) [6], whereas Sybil (a validated model) predicted a 6-year lung cancer risk using a single LDCT scan data [7]. Another deep-learning CNN, LUMAS, predicted the 1-year lung cancer risk using previous and recent CT scans with AUC—0.94 and successfully outperformed radiologists [8]. These findings exhibit potential for large-scale screening based on EMR data, and a path toward efficient screening strategies.

2. Artificial Intelligence in Lung Cancer Diagnosis

Lung cancer diagnosis primarily relies on a CT scan and tissue biopsy, which can lead to misdiagnosis and omissions [9]. Enhancing the sensitivity and specificity of non-invasive biomarkers is crucial. Factors like tumor location, pathology type, metastasis presence, and complications make diagnosis challenging [10]. AI models have become an effective tool in lung cancer diagnosis, improving the accuracy, stability, and efficiency [9][11]. This research covers the applications of AI models in diagnostic imaging, pathology tests, and biomarkers (**Table 1**).

Table 1. Studies showing the Diagnosis of lung cancer using AI models.

Author, Year	Dataset	AI Algorithm	Outcomes	Results
Ardila et al., 2019 [7]	Low-dose CT scan	Deep learning algorithm	Diagnosis of lung cancer	AUC = 0.94
Delzell et al., 2019 [11]	CT scan of 200 lung nodules	Radiomics	Verify nodules as benign or malignant	AUC = 0.72
Schwyzer et al., 2018 [12]	FDG-PET imaging	Deep machine learning	Diagnosis of lung cancer using ultra-low-dose PET scans	Sensitivity = 95.9% Specificity = 98.1%
Liu et al., 2023 [13]	Images and radiological features of 5251 patients from 14 studies	ANN SVM	Diagnosis of lung cancer	Sensitivity = 87% Specificity = 87%
Zheng et al., 2022 [14]	CT images of 9 NSCLC studies	Radiomics Deep learning	To diagnose whether patient had NSCLC	AUROC = 0.78
Sun et al., 2020 [15]	Pure ground glass nodules of 385 patients	Radiomics	Invasiveness prediction	AUC = 0.77
Feng et al., 2019 [16]	Sub-solid nodules of 100 patients	Radiomics	Differentiate minimally invasive and invasive adenocarcinoma	AUC = 0.912

Author, Year	Dataset	AI Algorithm	Outcomes	Results
Avanzo et al., 2020 [17]	Nodules of low-dose CT scan	SVM	Differentiate adenocarcinoma from focal pneumonia	Accuracy = 87.6%
Aydin et al., 2021 [18]	301 lung cancer CT scans	CNN	Differentiate into squamous cell, adenocarcinoma, and small cell carcinoma	Sensitivity = 90% Specificity = 44%
Chen et al., 2020 [19]	CT radiomics of 69 lung cancer patients	Radiomics	Differentiate NSCLC from SCLC	AUC = 0.93
Yu et al., 2016 [20]	2480 histopathological images of lung adenocarcinoma	SVM Random forest	Distinguish malignant tumors from healthy tissue	AUC = 0.81
Teramoto et al., 2017 [21]	298 histopathological images	Conventional deep neural networks	Classified adenocarcinoma, squamous cell carcinoma, and small cell carcinoma	Accuracy = 89%, 60%, 70% respectively
Coudray et al., 2018 [22]	Pathological images of adenocarcinoma	Conventional deep neural networks	Predicted 10 most prevalent genes in adenocarcinoma	Accuracy = 73.3%–85.6%
Flores-Fernandez et al., 2012 [23]	Serum biomarkers of 63 lung cancer patients	Artificial neural network modeling	Correctly classifying lung cancer patients based on biomarker panel	Correct classification rate = 93.3%

SVM—support vector machine, ANN—artificial neural network, CNN—conventional neural networks, NSCLC—non small cell lung cancer, SCLC—small cell lung cancer.

[9] to find an between people. With the growing popularity of AI, the medical field has recognized its impact in assisting the use of diagnostic imaging [9]. Ardila et al. [7] developed a deep learning algorithm for detecting lung cancer by low-dose CT scan and achieved a striking AUC of 94.4%. Another study examined the CT scans of 200 lung nodules with an AUC of 0.72 [12]. Additionally, a study investigated the use of ML for detecting lung cancer by FDG-PET imaging and achieved a sensitivity of 95.9% and 91.5% and a specificity of 98.1% and 94.2% with standard dose and ultralow dose, respectively. These findings indicate that ML modules may help detect lung cancer even at a very low radiation exposure of 0.11 mSv [15]. In a meta-analysis by Liu, the combined sensitivity, specificity, and sum of area under the combined subject operating characteristic (SROC) curve of the AI-aided diagnosis system for lung cancer diagnosis by using CT images were 87%, 87%, and 93%, respectively [13]. In another meta-analysis, which included nine NSCLC studies, the pooled sensitivity and specificity were 78% and 71%, respectively, and the AUROC of radiomics was 0.78 (95% CI 0.73–0.83) [15].

A study by Sun [15] included 395 pure ground glass nodules (pGGNs) from 385 patients who were randomly assigned to a training set (n = 277) and a validation set (n = 118). Based on the radiomics, a nomogram was developed on the RAD score, margin, speculation, and nodule size. The combined radiographic–radiomics model (AUC 0.77; 95% CI, 0.69–0.86) predicted the invasiveness better than the radiographic model (AUC 0.71; 95% CI, 0.62–0.81) in the validation set. This model may be used to evaluate invasive prediction in patients with pGGNs [16]. To validate the efficiency of radiomics, another Chinese retrospective study evaluated 100 patients with solitary sub-solid nodules confirmed pathologically with either minimally invasive (MIA) or invasive adenocarcinoma (IAC).

They constructed an integrated model using CT-based findings like nodule size, shape, margins, and radiomic signatures. This model showed good differentiation in the training set (AUC 0.943) and validation set (AUC 0.912) [18]. From these findings, researchers conclude that machine-learning features can be integrated with CT-based subjective findings to improve the accuracy of tumor differentiation and their invasiveness.

Another study, which included 301 lung carcinoma images from CT scans, correctly detected lung cancer using convolutional deep neural network methods with 0.93 sensitivity, 0.82 precision, and a 0.87 F1 score. This CNN model further differentiated small cell lung carcinoma, adenocarcinoma, and squamous cell lung carcinoma, with sensitivity, specificity, and F1 scores of 0.90, 0.44, and 0.59, respectively [19]. Lastly, Saad et al. achieved an AUC of 0.93 in differentiating NSCLC and peripherally located small cell lung cancer (SCLC) by using radiomics [24]. Physicians rely on pathological analysis to reveal these phenotypic variations, which require invasive methods such as biopsy and resection samples [20]. But AI-mediated imaging can help detect subtypes, which is non-invasive and can assist in starting early treatment.

2.2. Histopathological Diagnosis

This often refers to histological examination through bronchoscopy or percutaneous puncture biopsy, the gold standard for lung cancer diagnosis. Manual reading is difficult when assessing the pathological type of lung cancer because of the many subtypes. In a study by Yu, they used 2480 histopathological images from squamous cell carcinoma and adenocarcinoma of the lung and successfully differentiated malignant tumors from healthy tissues with an AUC of 0.81 [20]. Teramoto et al. examined 298 images using deep CNNs and classified adenocarcinoma, squamous cell carcinoma, and small cell lung cancer with an accuracy of 89%, 60%, and 70%, respectively, which was higher than the accuracy of cytotechnologists and pathologists [21]. In another prospective study, the prediction model that included clinical information (age and smoking history), radiological features of lung nodules (nodule diameter, nodule count, upper lobe location, malignant sign at the nodule edge, and sub-solid status), and LDCT data from AI analysis and liquid biopsy gave the best detection results in the training group (a sensitivity of 89.53%, specificity of 81.31%, the area under the curve [AUC] = 0.880). This can be applied to improve early lung cancer diagnosis while sparing patients with benign features from harmful surgery [25]. AI-mediated histopathological diagnosis will increase pathologists’ productivity and will significantly decrease misdiagnosis [10].

2.3. Biomarkers

The most common biomarkers predicting lung cancer are Rb, K-RAS, EGFR, c-MET, TP53, ALK, and PDL1 [22][26]. Though several potential biomarkers have been identified, their clinical utility remains limited because of a lack of consistency in diagnosis and predicting prognosis. Now, AI-mediated proteomics is trying multiple biomarker panels for the better detection of different types of lung cancer. Coudray et al. [22] anticipated that specific gene mutations would modify the framework of lung cancer cells in the section images; they predicted the ten most common mutant genes in adenocarcinoma by training neural networks. Pathological images predicted six of them (KRAS, STK11, TP53, EGFR, SETBP1, and FAT1) with an accuracy of 73.3–85.6% [27]. In another study, Zhong et al. [27] measured the five most predictive antibody markers, tentatively, paxillin, SEC15L2, BAC clone RP11-499F19, XRCC5, and MALAT1 in 23 stage 1 NSCLC patients and 23 risk-matched control samples. All 46 samples were used as a training set and were combined in a logistic regression model, yielding an AUC of 0.99, a 91.3% sensitivity, and a 91.3% specificity [23]. A study tested a biomarker panel composed of Cyfra 21.1, CEA, CA125, and CRP in 63 patients with lung cancer and 87 noncancer patients. This panel correctly classified 135/150 subjects. In the training, validation, and testing phases, the accurate classification rate of the lung cancer patients was 88.9%, 93.3%, and 90%, respectively [27]. Furthermore, research has shown that using a diagnostic model on lung cancer that includes human epidermis secreting protein 4 (HE4), secreting vascular cell adhesion molecule-1 (sVCAM-1), sarcosine (TTR), apolipoprotein A2 (ApoA2), sarcosine (TTR), in conjunction with the carcinogenic antigen CEA can greatly improve lung cancer detection accuracy. With a sensitivity of 93.33% and a specificity of 92.00%, this model achieved an AUC value of 0.988, suggesting a strong prediction accuracy [10]. As there is no universal biomarker panel for lung cancer, optimized panels must be tested and validated in each population before being applied in the clinical setting [28]. These results imply that deep learning algorithms may help pathologists detect cancer subtypes and genetic mutations [27]. As a result, based on available data from various studies, AI recognition technology may aid clinicians in screening and diagnosing early lung cancer [9].

3. Artificial Intelligence in Predicting Treatment Outcomes

AI has been shown to have the capacity to play a role in medical decisions by predicting treatment responses, including survival and adverse events, and helping to choose a group of patients to receive a specific treatment [26]. Dercle et al. reported that an AI model based on the CT-based radiomic characteristics and random forest algorithm accurately predicted the treatment response of various therapies like nivolumab, docetaxel, and gefitinib [29].

DL models have shown promising ability in identifying therapy response and prognosis. Specifically, these models have successfully predicted the EGFR mutation probability and patient response to EGFR-tyrosine kinase inhibitors (TKIs) and CPIs. By accurately identifying patients at different risks of progression, these AI models could aid in treatment decision-making and improve patient outcomes [30][31][32].

Additionally, by identifying specific radiomic features associated with local failure, tumor recurrence, and chemotherapy response, radiomics-based models can guide treatment decisions and predict treatment outcomes [33]. Furthermore, integrating multi-omics data through AI in precision medicine holds great promise. Radiomics-based AI models have demonstrated the ability to predict PD-L1 expression levels by combining radiomic images with clinical data. These models have also shown prognostic performance in predicting progression-free survival and clinical benefit in immunotherapy candidates [34].

ML applications have also been used to predict early death following curative intent chemoradiation and failure in early stage NSCLC patients treated with stereotactic body radiation therapy, and this can be used to educate patients about possible treatments and optimize care [35]. AI has also shown potential for incorporating serial imaging data to track tumor changes over time. By leveraging DL methods and recurrent neural networks (RNN), AI can analyze longitudinal data from post-treatment CT scans and provide valuable insights into phenotypic characteristics and treatment response [36].

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