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Artificial Intelligence in Pulmonary Medicine: Future Perspective

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Abstract

Artificial intelligence (AI) is transforming healthcare, with a staggering increase in data interwoven with genomics, medical imaging, and electronic health records. Pulmonary research is no such exception in the field of healthcare, to date several studies have been published exploring the role of AI in pulmonary medicine. The present review broadly categorized its application in pulmonary medicine into A) Thoracic imaging. B). Histopathology or cytology. C) Physiological measurements and biosignals. We have also emphasized its application in developing countries like India and its application in combination with telehealth.

***Keywords**: Pulmonary Research, Deep Learning, Machine Learning, telehealth.*

Introduction

A new era of artificial intelligence (AI) is transforming healthcare, with a staggering increase in data interwoven with genomics, medical imaging, and electronic health records. Such colossal growth has fuelled the development of an escalating number of AI-based applications that can be deployed in clinical practice. [1]

Artificial intelligence in the healthcare market is projected to grow from USD 6.9 billion in 2021 to USD 67.4 billion by 2027; it is expected to grow at a compound annual growth rate of 46.2% from 2021 to 2027. The rising demand to reduce healthcare costs, improving computing power, decreasing hardware costs, and growing partnerships and collaborations among different domains are the key factors fueling this market. [2]

Pulmonary research is no such exception in the field of healthcare, till date several studies have been published exploring the role of AI in pulmonary medicine. [3,4]

AI has been primarily used in image analysis wherein it evaluates CT scans of the chest for any abnormalities. In a recent systematic review exploring the diagnostic accuracy of artificial intelligence-based software for identification of pulmonary radiologic abnormalities from 4712 articles screened. It was found that the Areas under the receiver operating characteristic curve were significantly higher: in preclinical studies AUC: 0.88 [0.82–0.90]) versus Clinical studies (0.75 [0.66–0.87]; and with deep-learning (0.91 [0.88–0.99]) versus machine-learning (0.82 [0.75–0.89] .Thereby showing the promising outcome of AI in Pulmonary imaging. [5]

This review will focus on the advances that have been made in AI and machine learning as applied to pulmonary medicine in the past years. The inputs that have been subjected to machine learning techniques may be broadly categorized into A) Thoracic imaging. B). Histopathology or cytology. C) Physiological measurements and biosignals.

Methodology

Search Strategy

The string "((pulmonary) OR respiratory)) AND ((artificial intelligence) OR machine learning)" was used in PubMed as a search strategy. The intercepts from these studies were represented in this review to explore the role of artificial intelligence in the field of pulmonary medicine.

Working Mechanism of AI

Machine learning is the brain of an AI machine. The core of machine learning is to create algorithms that learn from input data to automatically perform a targeted task like decision making or prediction.

In machine learning, inputs are numerical features (raw data or derived features). Given a pre-selected type of machine learning model, a type of input data and a targeted task, the data scientist trains the algorithm on a cohort of example cases (data record) to perform the task as "accurately" as possible.

Inside the algorithm, a variety of data manipulation, comparison and aggregation techniques are deployed and optimized, to transform the input numerical values into a final instruction or decision (the "task").

The distinction is made between supervised and unsupervised learning. While the former within healthcare can alleviate a diagnostic task and lead to an extended understanding of key informative factors of a given pathology, the latter opens the way to discovering new phenotypes.

Deep learning (DL) is currently the most powerful machine learning algorithm. DL algorithms can learn from raw (or with little pre-processing) input data and build by themselves sophisticated abstract feature representations (useful patterns) that enable very accurate task decision-making. This is a major revolution, from traditional machine learning which relied on the explicit formulation of decision-making processes and rules.

DL is particularly performed in handling complex input data (large size, large number of variables, large variability) for categorizing, finding patterns, and extracting discriminating information. The inherent limitation of any machine learning is the dependence on the "training" data and the risk of making errors with any future "unseen" cases if the training cohort did not include "similar" cases. Testing the reproducibility of the task performance quality on an independent cohort is therefore essential.

Current Application of AI in Healthcare system of Developed countries

Developed countries with abundant resources have evolved AI technology to sophisticate the entire patient journey. The eight such application categories are shown in brief (Figure-1).

A.	Wearables	D.	Physiological monitoring
1	Prediction of falls	1	Medication adherence
2	Prediction of heart failure	2	Prediction seizures and early detections health abnormalities
3	Continuous glucose monitoring	3	Retinal scan for monitoring Multiple Sclerosis
4	Remote monitoring with arm straps	4	Screening of diabetic retinopathy
5	Pre/post-surgery monitoring with activity trackers	E.	Real world data
6	Patient's recovery monitoring in neurology	1	Patient recruitment and retention for clinical trials
7	Pill-cam	2	Prediction of drug effectiveness
B.	Imaging	3	Automation of pharmacovigilance
1	Detection of pulmonary pathologies with chest X-rays	F.	Virtual health assistance
2	Detection of coronary artery diseases	1	Automation of medical records transcription
3	Detection of breast cancer	2	Extraction of information to answer patients questions
4	Image acquisition and reconstruction	3	Administrative timesaving
5	Detection of COVID-19	G.	Personalised apps
6	Diagnosis of dermatological conditions	1	Behavioural counselling for metabolism pathologies
7	Preparation time for radiation	2	Personalized monitoring by a virtual nurse assistant
8	Skin cancer self-scanning solutions	H.	Robotics
C.	Labs	1	Robot-assisted surgeries
1	Detection of pathogens	2	Auxiliary robot assisting nurses
2	Automation of data workflows in laboratory	3	Sleep assistant
3.	Characterisation of genomic sequencing		

Figure 1 .Current application of AI in Healthcare system open access Available from: https://www.intechopen.com/chapters/70446

Application in Pulmonary Medicine

Thoracic Imaging

In the world of pulmonary medicine, thoracic imaging plays an integral role in diagnosis and long-term management. Chest radiographs and chest CTs have been intensely studied, with start-up companies now offering automated image analysis.

Much of the ML for image analysis, including that of chest radiographs and CTs, involves a type of deep learning that employs convolutional neural networks (CNN). All images contain millions of pixels that need to be processed by these systems to be able to recognize patterns, and CNN's make this process more efficient by segmenting an image and avoiding the need to process each pixel separately. Like the hierarchical structure of the visual system in the human brain, the network of CNNs is layered in units that detect specific features. The output of these units is iteratively fine-tuned (changing the 'weights' assigned to particular inputs) to reduce the error as closely as possible based on the data used for training. **[**8**]** (Fig.2)

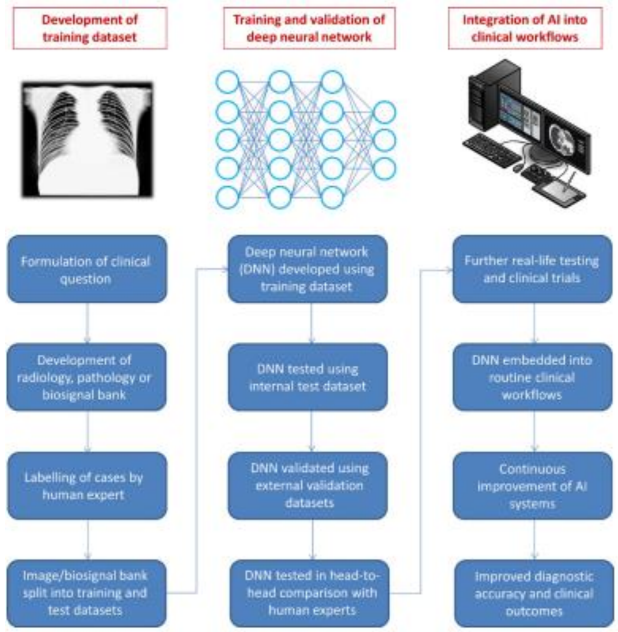

Figure 2. The typical path for the development of a machine learning model and its incorporation into clinical practice (Adapted from Gonem S, et al. Thorax 2020; 0:1–7. doi:10.1136/thoraxjnl-2020-214556)

The area that received great interest of AI in pulmonary medicine is the detection and classification of pulmonary nodules for Lung Cancer Screening via low dose CT scan. Some algorithms assist with the detection, per se, of nodules (computer-aided detection or CAD), and those that assist with specific diagnosis (computer-aided diagnosis or CADx).9 The earliest study was carried out by Kao EF et al. **[**10**]** who developed a computer-aided diagnosis (CAD) system to automatically determine abnormal chest examinations in the worklist of radiologists interpreting chest examinations. The turnaround time for reporting abnormal CXR was reduced by 44 %.

The extent of the work in CAD is reflected in the 2019 systematic review by Pehrson et al., **[**11**]** which presented 41 papers on ML models for automated nodule detection applied to the Lung Image Database Consortium Image Collection. These studies are heterogeneous in their approach to modeling, with some using CNN or other “deep learning” methods, while others use more “feature-based” approaches. The feature-based approaches require that the images already have structured annotations to describe the nodules, whereas the deep learning algorithms do not require this step, making the latter more generalizable. In the Pehrson review, five of the feature-based and two of the deep learning methods had an accuracy of more than 95% for nodule detection.

There has also been extensive research into CADx, where the usual goal is to develop models that can distinguish between benign and malignant lesions based on imaging. Uthoff et al. **[**12**]** captured specific perinodular parenchymal features in a model which showed significant improvement compared to a model using only nodular features. This was the first study to report a comparison to the Fleischner pulmonary nodule follow-up guidelines and suggested a reduction in repeat imaging and biopsy is possible with the use of the algorithm.

Recently Nam JG et al. [13] developed a deep learning-based detection algorithm for malignant pulmonary nodules on chest radiographs and compared its performance with that of physicians, with half of them being radiologists. They used a dataset of 43,292 chest radiographs with a normal to the diseased ratio of 3.67. Using an external validation dataset, they found AUC of the developed algorithm was higher than that of 17 of the 18 physicians (range of 0.92-0.99). All physicians showed improved nodule detection when using the algorithm as a second reader.

Tuberculosis Diagnosis

Automated detection of tuberculosis on chest radiographs is another important field of research. Tuberculosis is an important cause of death worldwide, with a high prevalence in underdeveloped areas where radiologists are lacking. Several approaches have been used to detect tuberculosis manifestations in CXRs. Traditional machine learning approaches mainly used textural features, with or without applying bone suppression as a pre-treatment of CXR images. Rohmah et al. [14] used statistical features in the image histogram to identify TB positive radiographs and reached an accuracy of 95.7 %. EJ Hwang et al. [15] introduced a deep-learning-based automatic detection (DLAD) algorithm using 54c221 normal CRs and 6768 CRs with active pulmonary tuberculosis that was labeled and annotated by board-certified radiologists. Their algorithm showed significantly higher performance in both classification (0.993 vs 0.746-0.971) and localization (0.993 vs 0.664-0.925) compared to all groups of physicians. Lakhani & Sundaram (2018) used deep learning with CNNs and achieved accurately classified tuberculosis from the CXR with an area under the curve of 0.99. [16]

Other Lung Diseases

The use of CNN for thoracic CT is not restricted to nodule evaluation but can also be applied to diagnose and stage COPD and predict acute respiratory distress (ARD) and mortality in smokers. [18] Training a CNN on the CT scans of 7,983 COPD Gene participants, AUC for the detection of COPD was 0.856 in a non-overlapping cohort of 1000 other COPD Gene participants. AUCs for ARD events were 0.64 and 0.55 in COPD Gene and ECLIPSE participants, respectively. CNNs can also be used for the detection and quantification of infiltrative lung diseases (ILD) or automated classification of fibrotic lung diseases.

Anthimopoulos M et al [19] proposed and evaluated a CNN for the classification of Interstitial Lung Disease (ILD) patterns. This method used the texture classification scheme of the ROI for the generation of an ILD quantization map of the whole lung by sliding a fixed proportion classifier on the pre-segmented lung field. Then, the quantified results were used in the final diagnosis of the CAD system.

Campo MI et al. [20] used X-rays to quantify the emphysema instead of CT scans. Their model was able to calculate emphysema percentage with an ow-attenuation lung area percent mean error of 3.96, and it obtained an AUC accuracy of 90.73% for an emphysema definition of ≥10%, with a mean sensitivity of 85.68%, significantly improving X-ray-based emphysema diagnosis.

Pulmonary Image Database

The Pulmonary Image Databases have been developed by various academic institutions around the globe as a publicly available database of thoracic computed tomography scans or Chest X-rays as a medical imaging research resource to promote the development of computer-aided detection or characterization of pulmonary diseases. Few such databases were highlighted below.

i) The Lung Image Database Consortium image collection (LIDC-IDRI) (Armato III SG, 2011) consists of chest medical image files (such as CT and X-ray) and the corresponding pathological markers of the diagnostic results. The data were collected by the National Cancer Institute to study early cancer detection in high-risk populations. The dataset contains 1018 research cases, and the nodule diameter in the LIDC-IDRI dataset ranged from 3 mm to 30 mm. Their procedure aims to identify all pulmonary nodules in each CT scan as completely as possible without compulsory consistency. [21]

ii)LUNA16 dataset, a subset of LIDC-IDRI which includes 1018 low-dose lung CT images, while LUNA excludes CT images with slices thicker than 3 mm and pulmonary nodules smaller than 3 mm. The database is very heterogeneous. It is clinically collected from seven different academic institutions for dose and low-dose CT scans, and it has a wide range of scanner models and acquisition parameters. [22]

iii)The dataset released by the National Institutes of Health includes 112 120 frontal-view X-ray images of 30 805 unique patients. The database contains more than 100 000 X-ray front views (about 42 g) of 14 lung diseases (atelectasis, consolidation, infiltration, pneumothorax, edema, emphysema, fibrosis, effusion, pneumonia, pleural thickening, cardiac hypertrophy, nodules, masses, and hernia). [23]

iv) The Montgomery County X-ray dataset consists of 138 frontal chest X-rays from the TB screening program in the Department of Health and Human Services, Montgomery County, Maryland, USA. In addition, 80 patients were in normal condition and 58 patients had imaging symptoms of tuberculosis. All pictures were captured using the conventional X-ray machine (cr) to store 12-bit gray levels in the form of PNG images. They can also be used in the form of DICOM as required. The size of the X-ray is 4020 X 4892 or 4892 X 4020 pixels. [24]

v) Geneva database was collected by the University Hospitals of Geneva, Geneva, Switzerland. (https://medgift.hevs.ch/wordpress/databases/ild-database).The dataset consists of chest CT scans of 1266 patients between 2003 and 2008 in the University Hospitals of Geneva. Based on the EHR information, only cases with HRCT (without contrast agent, 1 mm slice thickness) were included. Up until now, more than 700 cases were revised and 128 were stored in the database that affected one of the 13 histological diagnoses of ILDs. The database is available for research on request and after the signature of a license agreement. [25]

Histopathology and cytology

AI has also been applied to histopathology to help improve the accuracy and efficiency of diagnosis and prognostication of non-small cell lung cancer (NSCLC). [26] Koh et al. developed a three-marker immunohistochemistry panel (TTF-1, Napsin A, and p40) that could be used with minimal tissue samples of ambiguous morphology, and succeeded in differentiating adenocarcinoma from squamous cell carcinoma in 82% of cases. In those cases where the initial panel was non-diagnostic, the use of two additional markers (p63 and CK5/6) provided the ability to further subtype 72% of the cases. [27] This is just one of the many examples of the work in this field, and as more high-throughput technologies are developed for slide analysis, the expectation is that clinicians will be able to get more accurate data more efficiently with less tissue required .16 Xiong et al [28] trained a DNN to recognize acid fast-stained Mycobacterium tuberculosis bacilli on digital cytology slides. The small size of the bacilli (20×4 pixels) and the loss of resolution when scanning the digital images resulted in some technical challenges. Although good sensitivity of 98% was achieved following modifications to the algorithm, there were several false-positive results due to contaminant bacilli and slide artifacts, resulting in a specificity of 84%.

Physiological measurements and biosignals

Interpretation of pulmonary function tests including spirometry, body plethysmography and measurement of diffusing capacity has traditionally been considered an important aspect of the expertise of respiratory physicians.

The earliest of this study was carried out in the pacific medical center, California, 1983 they have developed a PUFF system consisting set of 64 production rules dealing with the interpretation of pulmonary function tests and 59 clinical parameters. The system showed an overall rate of agreement between the two physiologists on the diagnoses of disease was 92%. The agreement between PUFF and the physician who served as the expert to develop the PUFF knowledge base was 96% and 89% agreement between those who were not the part of the knowledge base. [29]

Machine learning approaches (including ANNs and support vector machines) have been applied to classify adventitious sounds associated with asthma, [30] COPD [31] and interstitial lung disease [32] and to detect common respiratory disorders in children using cough sounds. [33] Bardou et al [34] found that DNNs outperformed traditional machine learning techniques in the classification of lung sounds into seven categories (normal, coarse crackle, fine crackle, monophonic wheeze, polyphonic wheeze, squawk and stridor).

Analysis of biosignals using machine learning may permit a superior understanding of the dynamics of physiological regulation in health and disease. Examples of biosignal monitoring in the respiratory sphere include Polysomnography, which is used to diagnose obstructive sleep apnoea and other sleep disorders. Nikkonen et al [35] developed an ANN that accurately determined the oxygen desaturation index (ODI) and apnoea–hypopnoea index (AHI) using only the oxygen saturation signal as input.

Moving in synergy with Radiologists

Missed lung cancer is a source of concern among radiologists and continues to pose an important medicolegal challenge. In 90% of cases, errors in diagnosis occur on chest radiographs. Observer error can be divided into scanning error, recognition error, decision-making error, and satisfaction of search. Tumor characteristics such as lesion size, conspicuity, and location independently contribute to sources of error. Image quality, patient positioning, inspiratory effort and motion also contribute to failure to identify lung nodules. Radiologists have studied eye movements and attempted to overcome limitations to lung nodule visibility through bone suppression, dual-energy subtraction, and other strategies. [36]

Sim et al [37] present an international multicenter observer study evaluating the detection of lung nodules from chest radiographs obtained on a very wide variety of equipment in very different populations and found improved the average sensitivity of radiologists and decreased the number of false-positive marks per radiograph (0.2 marks per image).

An increase incorrect attribution of an abnormality as lung cancer using the strategy employed in this study will be even more valuable in clinical practice, where the prevalence of lung cancer is significantly lower than in this study. Twenty-first-century improvements in diagnostic capability also require AI to assist in integrating treatment and outcomes data that cannot be managed by the radiologist alone.

Through perceptual research, radiologists will remain central to the development and application of AI to medicine. Much as an airplane requires a pilot, despite all technology and AI, radiology will continue to require radiologists. Improved identification of early lung cancer from chest radiographs is a future direction of CAD as we enter a new golden age for radiology in which AI will allow consistent rather than anecdotal identification of early lung cancer from chest radiographs.

AI and Telehealth in Pulmonary Medicine.

Pacis et.al. [38] summarized the potential impact of AI in telehealth around four emergent trends based on distinctive health care purposes i.e. patient monitoring, healthcare information technology, intelligent assistance and diagnosis, and information analysis collaboration.

Mokhtar MS et al [39] proposed a classification and regression tree (CART) based validated its application using telehealth measurement data recorded from patients with moderate/severe COPD living at home. The said algorithm was able to classify home telehealth measurement data based on three types of physiological measurements; forced expiratory volume in 1s (FEV1), arterial oxygen saturation (SPO2) and weight into either a 'low risk' or 'high risk' category with 71.8% accuracy, 80.4% specificity and 61.1% sensitivity. The authors have emphasizes the potential usefulness of automated analysis of home telehealth data in the early detection of exacerbation events among COPD patients.

Limitations

AI provides opportunities to improve the quality of care and accelerate the evolution of precision medicine. However, its limitations have nurtured the field of AI ethics and the study of the impact of AI on technology, individual lives, economics and social transformation

Bias against patients of a particular ethnicity or socioeconomic status, which might widen the gap in health outcomes. Combined with concerns for exacerbating pre-existing inequities, the potential for embedding bias by excluding minorities from datasets is a real hazard. Embedded prejudice must be mitigated, and massive datasets should provide a true representative cross-section of all populations.

Lack of prospective validation studies and difficulty improving an algorithm's performance. Many investigations are validated *in silico* by dividing a single pre-existing dataset into a training and testing dataset. However, external validation using an independent dataset is critical before implementation in a real-world environment, and inherently opaque machine-learning algorithm black-box models should be avoided as much as possible.

Finally, the future of AI-related medical applications depends on how well safety, confidentiality and data security can be assured.

In light of hacking and data breaches, there will be little interest in using algorithms that risk revealing the patient identity and of course, adverse effects on clinician workloads may arise from an overdependence on automated machine-learning systems or increases in medical errors.

Challenges in Resource-poor settings

A major lesson from the experience of those working on AI in resource-poor settings is that 'AI should build intelligence into existing systems and institutions rather than starting from scratch or hoping to replace existing systems, however, broken'. The success of AI applications requires knowledge of local markets, clear usability requirements and access to adequate training data via field testing. Examples of how AI is currently being deployed are noted below. While many of these interventions have not yet been robustly evaluated, they do provide insight into how AI subfields are being applied and their potential beyond current pilots.

In resource-poor settings, expert systems can be used to support health programs in several ways. First, medical expert systems can support physicians in diagnosing patients and choosing treatment plans as is done in high-income countries. For some conditions, they can act in place of a human expert if one is not readily available, which is often the case in poor communities.

The prioritization of AI for healthcare has created an impetus for greater collaboration between the government, technology companies and traditional healthcare providers in India. For example, NITI Aayog, the government's official policy think-tank, is working with Microsoft and the medical technology start-up Forus Health to develop a pilot for early detection of Diabetic Retinopathy. The Maharashtra state government has also signed a memorandum of understanding with NITI Aayog and the Wadhwani AI group4 to launch the International Centre for Transformational Artificial Intelligence (ICTAI), focusing on rural healthcare. **[**40**]** Similarly, the Telangana state government has adopted the Microsoft Intelligent Network for Eyecare, which was developed in partnership with Hyderabad-based LV Prasad Eye Institute .**[**41**]**

Conclusion

AI and machine learning have the power to transform many aspects of pulmonary medicine. The emergence of deep neural networks developed using big training datasets has resulted in several novel applications, particularly in the field of thoracic imaging. The countries with good resources have attempted to unlock the full potential of AI in healthcare made improvements in several areas, including the ways such technologies are evaluated and reimbursed, workforce skills and training, and data interoperability, whereas, in countries with fewer resources, the technology holds tremendous promise for transforming the provision of healthcare services.

Many of the health systems hurdles in such environments could be addressed and overcome using AI supported by other technological developments and emerging fields. The ubiquitous use of smartphones, combined with growing investments in supporting technologies (e.g., mHealth, EMR and cloud computing), provide ample opportunities to use AI applications to improve public health outcomes in low-income country settings.

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