

CHAPTER 13

ARTIFICIAL INTELLIGENCE IN PULMONARY DISEASES

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INTRODUCTION

As in numerous sectors, a new era of artificial intelligence (AI) and machine learning (ML) is currently transforming healthcare with processing big data collected from medical imaging, genomics and electronic records. This dramatic breakthrough of AI has brought together new horizons and opportunities to deploy in clinical practice. It is projected that AI in the healthcare market will grow from 6.9 billion USD in 2021 to 67.4 billion USD in 2027. More interestingly, the advent of 'Metaverse' at the end of 2021 seems to change the 'play' completely all over again. We will all see how this will affect and be integrated in the field of medicine.

There is a reciprocal interaction between AI algorithms and medical big data, mainly patient records. As the data accumulate, new applications of AI are being introduced and vice versa. Without doubt, one of the medical domains that use AI commonly is pulmonology, mainly due to interpretation of imaging and histopathological outcomes. AI has found several areas of usage in the diagnosis and management of pulmonary diseases with a continuous expansion. In this chapter, a brief definition of AI and MŞ is described, followed by the use of AI in the medical field. Then the chapter focuses on applications of AI in pulmonary diseases with examples of the most common implementations.

ARTIFICIAL INTELLIGENCE (AI) AND MACHINE LEARNING (MI)

The term artificial intelligence (AI) was coined for the first time for the Dartmouth Summer Workshop in 1956 and was broadly defined as "thinking machines" (1). (AI) is a strong technological revolution that flatten the world by granting a machine the ability to perform cognitive functions including perceiving, reasoning, learning and implementing. Although there is no a universal definition agreed on it, AI is generally defined as "machines that respond to stimuli consistently with

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response from humans, based on the ability of humans for contemplation, judgment and intention”. AI had rapidly entered our daily lives by solving problems through advanced algorithms, big data and increasing computational power at lower costs (2). Although the projections are changing on daily basis, it has been estimated that AI will increase the global average revenues by more than ten trillion dollars and to transform many sectors including healthcare.

AI focuses on a specific functionality to find intelligence patterns. This process is realized with three steps: (1) intelligence requires algorithm that mimics the human brain, (2) first, we must learn intelligence patterns in order to find them and this requires the use of data, and (3) we must make computations as the brain makes (3). Unlike past experiences, today accumulated big data and lower costs of computations with the advancements of information technologies have facilitated the integration of these three steps.

Machine Learning (ML) is the basic component and a subset of AI. The majority of AI advancements and implementations are categorized as ML. ML algorithms are statistical instruments used to find patterns through the big data and then to make predictions using these data (4). The patterns are the association between the inputs and outputs. ML is defined as a set of techniques that enable machines to learn from data without being programmed to do this task. AI and ML are not a futuristic vision, but rather they are something that is here today, integrated and deployed into a variety of sectors (5). A schematic illustration of AI and ML is given in Figure 1.

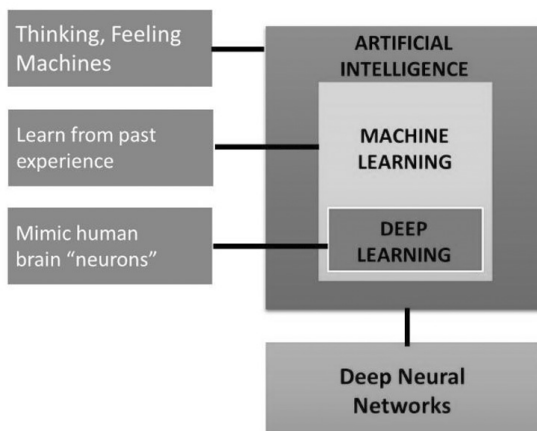


Figure 1. Relationship between AI and ML

ARTIFICIAL INTELLIGENCE APPLICATIONS IN MEDICINE

ML algorithms based on neural networks (NN) have been already introduced in several fields of medicine. The medical areas that most commonly use AI include medical diagnosis and prognosis, decision making, treatment, drug development, gene studies and individualized medicine. AI research has shown that the input/output ratio is more promising in medicine compared to that of other fields (6). The combination of AI and medicine, termed as AI plus, changes the conventional medical model and makes an evolutionary progression. In addition, AI plus medicine is promising for potential future applications.

AI has revolutionized medical techniques and can be considered as the part of computer science with the ability to deal with complex problems using numerous applications with big data but little theory (7). This development has caused the raising of a new field in medicine: augmented medicine, which refers to the use of medical technologies aimed at improvement of different aspects of clinical practice. Augmented medicine based on AI applications enabled efficient computer assisted surgical operations, virtual reality tools for surgery, pain management etc. (8). Some current AI applications in the field of medicine are shown in Figure 2.

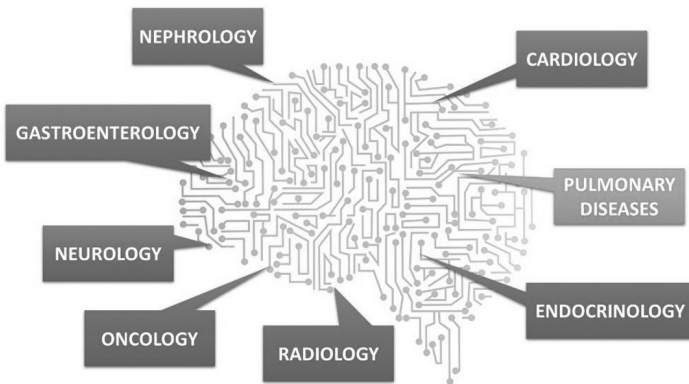


Figure 2. AI application in clinical practice

AI in Medical Diagnosis

Diagnosis of a patient utilizing AI results provides significant time saving and diagnostic efficiency increases considerably. AI can analyze data from radiology departments such as X-ray, CT and MRI outcomes, and from pathological, endoscopic, ultrasonographic and biochemical examinations, and output the results quickly, making a change in traditional medical models, particularly in complicated cases.

AI in Radiology

Radiology is involved in almost all diseases as a scientific basis for medical diagnosis. The demand for a radiological diagnosis is steadily increasing at a high rate; however, the number of physicians experienced in radiation medicine is increasing slowly, leading to a gap between supply and demand balance and causing occupational pressure and likelihood of misdiagnosis. Radiology is one of the leading fields of medicine where AI is involved with various applications. Numerous AI applications have been introduced in radiological diagnosis in recent years. Among these, a new algorithm was found with a high sensitivity for early screening, rapid diagnosis and grading of retinal diseases (9). Another example is the use of AI in MRI. An AI algorithm has been shown to be superior to human observers in early detection of inflammation in patients with rheumatoid arthritis (10).

AI in Pathology

Whole-slide imaging technique has become a standard diagnostic method in pathological investigations with the advancements in pathological scanning modalities. However, it is still challenging to automatically analyze pathological images to achieve an accurate diagnosis as soon as possible. AI has been used successfully in pathological diagnosis with promising results (11, 12). AI algorithms have been used in pathological segmentation, tumor identification and determining metastasis in a shorter duration and higher quality (13). Even in some cases, AI algorithms outperformed pathologists for diagnosis based on pathological images (14). Deep learning model has been confirmed to predict six genetic mutations associated with cancer to assist doctors for detection of subtype and gene mutation in cancer cases with an accuracy of 97% (15). AI algorithms have been used in the diagnosis of lung cancer, epithelial tumors and basal cell carcinoma (16, 17).

AI in Endoscopy

AI technology has been proven to effectively detect lesions, colorectal polyps, gastric and esophageal cancers through endoscopy (18). It has been reported that AI can significantly enhance the diagnosis of intestinal and gastric diseases such as Barrett's esophagus, gastric cancer and squamous carcinoma by increasing diagnostic accuracy and shortening detection time (19). Obviously there is a bright future for this new AI technology as more research confirms the utility of AI plus endoscopy in the diagnosis and classification of various diseases.

AI in Medical Treatment

AI in Surgery

The concept of AI plus the surgical system has been raised with the advent of AI technology. With the use of AI algorithms, surgical systems have shifted to an “intelligent” form from a “non-intelligent” form. The development of the Da Vinci surgical system has been the most groundbreaking advancement in the use of AI in surgery. Da Vinci system has three components including a surgeon console, manipulator operating system and imaging system. This method has been approved by the Federal Drug and Food Administration (FDA) in 2000 for use in clinical surgery. This new AI system has revolutionized conventional surgery systems. Using the Da Vinci system, for instance thyroid surgery can be performed by preserving postoperative cosmesis and the patient’s voice (20), lung cancer surgery has become beneficial to patients in terms of postoperative outcomes (21).

Augmented Reality (AR) and Virtual Reality (VR)

AR and VR, are new forms of digital holographic imaging modalities that partly employ AI technologies in order to reconstruct clinical data. VR involves virtual digital images generated by an intelligent AI algorithm that enable surgeons to make practice without any serious consequences of surgery, permitting them to enhance their surgical practice skills on 3D holograms (22). However, they can not be adapted to the real surgery because of the lack of real-world experience. In order to overcome this issue, AR is utilized to assist surgery pre – and intraoperatively through conversion of patient data and addition of VR to the real world. AR technology recognizes complex anatomical structures and navigates the operation accordingly (23, 24). Because of these advantages, this new mixed reality (MR) technique has been used successfully in a wide spectrum of medical procedures including skull, spine, orthopedic, kidney and liver surgeries (25-27).

AI in Anesthesiology

Anesthesia is an important part of surgical operations supporting a smooth procedure, although there are numerous risks and complications during anesthesia. Perioperative anesthesia is a long process involving pre-, intra – and postoperative periods. This is one of the medical fields where AI is used widely. The use of AI in anesthesiology practice include deep monitoring, anesthesia control, prediction of adverse events, ultrasonography assistance, pain control and the management of operating theatre (28). AI has been used successfully in anesthesia practice with promising outcomes (29).

AI in Pulmonary Diseases

The primary application areas of AI in pulmonary medicine include decision support systems to assist pulmonologists by processing physiological data from physical exam and imaging studies to achieve a diagnosis. First use of AI in respiratory medicine has been interpretation of thoracic CT scans, which has been successfully performed with a high rate of accuracy. Another domain of AI in pulmonology practice is the assessment of lung physiology and detection of abnormal respiratory function to help physicians in the decision making process. Pulmonary function test interpretation is based on numerical values of different variables and can be performed readily by AI algorithms (30). AI has also been used to predict 3-year risk of developing lung cancer and guide clinical management accordingly. The use of AI algorithms, ML, deep learning and neural networks in pulmonary diseases is being expanded every passing day. Among the numerous applications of AI in pulmonary medicine, here we will give the examples of most commonly used implementations due to limited space.

AI in Diagnosis of COPD and Asthma

The diagnosis of COPD and asthma is mainly based on imaging and it involves historyü physical exam, pulmonary function tests and imaging investigations such as X-ray, Ct scans and bronchoscopy. Because both COPD and asthma are heterogenous diseases and their management strategies differ (31, 32), the challenges in the diagnosis of COPD and asthma and potential risks of mistreating or not treating these diseases underline the importance of any new assisting technique including AI. In a study with 120 pulmonologists from 16 European countries, the physicians and AI algorithm evaluated 50 cases of pulmonary diseases with limited clinical information such as smoking, history, sputum etc. In that study, both sensitivity and positive predictive value of the AI algorithm was superior over those of the pulmonologists (30). It was concluded that AI-based software provided more accurate interpretations and could serve as a potent decision support tool to improve clinical practice (30).

AI in Pulmonary Function Testing

Pulmonary function tests (PFTs) are the primary tools used by pulmonologists to evaluate the function of the respiratory system (33). To establish a definitive diagnosis, interpretation of PFTs are combined with history, symptoms, and results of other tests including imaging, blood analysis and biopsies (34). Since PFTs are used worldwide in a standard way, they are suitable to be interpreted by AI algorithms because of their ability to process big amounts of data unlimitedly. In a study by Topalovic et al., more than 1500 historical cases examined and AI algo-

rithms were demonstrated to improve the clinical reading of PFTs and overcome the variable test interpretations of individual pulmonary diseases specialists (30). On the other hand, ML can be used to analyze continuous data including diffusion capacity of the lung, flow-volume loop, and nitrogen washout curves. Owing to these analyses, new markers can be discovered in the near future (35).

AI in Thoracic Imaging

Thoracic imaging plays a critical role in pulmonary medicine practice. While chest X-rays and CT scans have been intensely utilized, automated image analysis emerges as a new AI application in thoracic imaging. ML for imaging analysis uses deep learning algorithms that employ convolutional neural networks (CNN). These systems process millions of pixels on X-rays and CT scans to recognize the pattern and this process progresses in a similar way to the human brain.

An area that has attracted great interest in AI is the detection and classification of pulmonary nodules through low dose CT scans. Kao et al. developed a ML system that automatically determines abnormal chest examinations by screening the working lists of radiologists, and reduces reporting time by 44% (36). Nam JG et al. developed a new ML algorithm to detect malignant pulmonary nodules on chest X-rays and compared it with that of physicians including radiologists and pulmonologists. At the end of the study, all physicians showed improved nodule detection when using the ML system as a second reader to assist them (37).

AI in Diagnosis of Tuberculosis

Tuberculosis (TB) is an important public health problem worldwide and especially in underdeveloped countries due to lack of radiologists. Various techniques have been utilized to detect TB on chest X-rays. Automated detection is another field of research. ML approaches mainly use pattern features with and without bone suppression to interpret X-ray images. Rohmah et al. used a new approach in which statistical features were utilized to identify TB positive radiographs and obtained a 95.7% accuracy rate (38). Hwang et al. developed a new deep learning-based automatic detection (DLAD) algorithm. They used 54221 normal X-rays and 6768 X-rays with TB positive labeled by certified radiologists. The new DLAD algorithm showed a superior performance over radiologists in both classification and localization of TB (39). Combining telehealth, diagnosis of TB using AI technology and ML algorithms shows promise for future applications to identify and classify patients with TB especially those living in underdeveloped countries, where access to a quality healthcare is challenging.

AI in Other Pulmonary Diseases

CNNs that have been successfully used for evaluation of pulmonary nodules on thoracic CT are also useful to predict acute respiratory distress syndrome (ARDS) and to estimate mortality among smokers. CNNs are also used to identify infiltrative lung disease and to classify fibrotic lung disease automatically. Campo et al. used X-rays instead of CT scans in quantification of emphysema. ML techniques have been used to assist in early diagnosis of respiratory changes induced by smoking. Computerized lung sound analysis involves distinguishing normal sounds from abnormal respiratory sounds during auscultation. ML has also been used for classification of lung fibrosis disease by means of high-resolution CT scans against current guidelines (40). Liao et al. have successfully used ML approaches and algorithms for predicting acute respiratory failure, ventilator dependence and mortality from pulmonary diseases, and especially from COPD (41).

AI in Histopathology and Cytology

Using AI technology, diagnostic pathology has undergone significant changes through digitalization, which have enabled important changes in decision-making process, workflow and job description (42). Currently there is a shifting from physical storage slides system to virtual storage of virtual slides (43).

AI algorithms have been applied to histopathology in order to help improve efficiency and accuracy of definitive diagnosis and predicting prognosis of non-small cell lung carcinoma (44). Koh et al. coined a three-marker immunohistochemical panel that could be used with minimal amount of tissue and successfully differentiate adenocarcinoma from squamous cell carcinoma in 82% of patients (45). This example suggests that owing AI technology, clinicians will be able to obtain more accurate data for differential diagnosis with less tissue required. Xiong et al. developed a deep neural network to identify acid fast stain Mycobacterium tuberculosis on digital cytology slides and obtain a sensitivity of 98% (46).

AI in Telemedicine

Telemedicine is emerging as a novel important tool in monitoring and self management of obstructive pulmonary with the increasing use of smartphones. Telehealth can be used to help medical services in isolated locations and save life in the case of emergencies. Telemonitoring devices collect data from medical records to identify and recognize patterns in data sets in order to offer a way to predict clinical outcomes (47). Recent applications of AI algorithms in telemonitoring is prediction of exacerbation in COPD and asthma patients (48). Chamberlain et al. developed an interesting system consisting of an electronic stethoscope, peak flow

meter and a patient questionnaire to screen patients for COPD or asthma (49). An example of an AI algorithm in pulmonary diseases is shown in Figure 3.

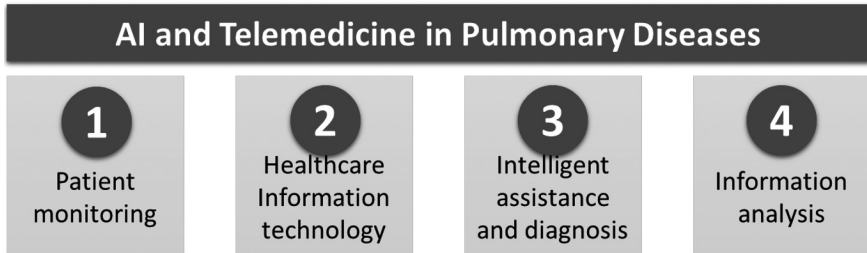


Figure 3. AI algorithm of Telemedicine in Pulmonary Diseases

AI in COVID-19

In the global race to control COVID-19 caused by the novel coronavirus 2019, AI was used to work as human intelligence for early recognition and diagnosis, treatment monitoring, tracing contacted people, prediction of mortality, development of new vaccines and drugs and disease prevention (50). Zhang et al. coined a new system based on analysis of CT images based on deep learning methods and found that the right lower lobe of the lung was the high occurrence site of COVID-19 pneumonia (51). Mashamba developed a point-of-care diagnostic service that blended radiology, pathology and AI algorithms to assist the diagnosis of COVID-19 (52). In addition, there has been much research on AI algorithm assistance that pushed quick development of COVID-19 vaccines (54, 54).

CONCLUSION

AI has rapidly entered medical practice and its applications in this field are continuing to expand rapidly. As the big medical data grows, accuracy and sensitivity of AI applications further increase. In pulmonology practice AI shows promising outcomes for future projection to use its algorithms more intensively. Rapid diagnosis with AI technology will facilitate management of pulmonary diseases and improve the outcomes. However, the future of AI has come and this new technology will bring our clinical practice into an unprecedented new era.

REFERENCES

1. Bhinder B, Gilvary C, Madhukar NS, et al. Artificial Intelligence in Cancer Research and Precision Medicine. *Cancer Discov.* 2021;11(4):900-915. doi:10.1158/2159-8290.CD-21-0090.
2. Ergen M. What is Artificial Intelligence? Technical Considerations and Future Perception. *Anatol J Cardiol.* 2019 Oct;22(Suppl 2):5-7. doi: 10.14744/AnatolJCardiol.2019.79091.

3. Friston K, Moran RJ, Nagai Y, et al. World model learning and inference. *Neural Netw.* 2021 Dec;144:573-590. doi: 10.1016/j.neunet.2021.09.011.
4. Raita Y, Camargo CA Jr, Liang L, et al. Big Data, Data Science, and Causal Inference: A Primer for Clinicians. *Front Med (Lausanne).* 2021 Jul 6;8:678047. doi: 10.3389/fmed.2021.678047.
5. Gupta R, Srivastava D, Sahu M, et al. Artificial intelligence to deep learning: machine intelligence approach for drug discovery. *Mol Divers.* 2021 Aug;25(3):1315-1360. doi: 10.1007/s11030-021-10217-3.
6. Patel VL, Shortliffe EH, Stefanelli M, Szolovits P, et al. The coming of age of artificial intelligence in medicine. *Artif Intell Med.* 2009 May;46(1):5-17. doi: 10.1016/j.artmed.2008.07.017.
7. Peng Y, Zhang Y, Wang L. Artificial intelligence in biomedical engineering and informatics: an introduction and review. *Artif Intell Med.* (2010) 48:71-3. doi: 10.1016/j.artmed.2009.07.007.
8. Overlay SC, Cho SK, Mehta AI, et al. Navigation and robotics in spinal surgery: where are we now? *Neurosurgery.* (2017) 80:S86-99. doi: 10.1093/neuros/nyw077.
9. Sorrentino FS, Jurman G, De Nadai K, et al. Application of Artificial Intelligence in Targeting Retinal Diseases. *Curr Drug Targets.* 2020;21(12):1208-1215. doi: 10.2174/1389450121666200708120646.
10. Stoel BC. Artificial intelligence in detecting early RA. *Semin Arthritis Rheum.* 2019 Dec;49(3S):S25-S28. doi: 10.1016/j.semarthrit.2019.09.020.
11. Acs B, Rantalainen M, Hartman J. Artificial intelligence as the next step towards precision pathology. *J Intern Med.* 2020;288(1):62-81.
12. Allen TC. Regulating Artificial Intelligence for a Successful Pathology Future. *Arch Pathol Lab Med.* 2019;143(10):1175-1179.
13. Wang S, Yang DM, Rong R, et al. Pathology Image Analysis Using Segmentation Deep Learning Algorithms. *Am J Pathol.* 2019;189(9):1686-1698
14. Komura D, Ishikawa S. Machine learning approaches for pathologic diagnosis. *Virchows Arch.* 2019;475(2):131 - 138.
15. Coudray N, Ocampo PS, Sakellaropoulos T, et al. Classification and mutation prediction from non-small cell lung cancer histopathology images using deep learning. *Nat Med.* 2018;24(10):1559-1566.
16. Iizuka O, Kanavati F, Kato K, et al. Deep Learning Models for Histopathological Classification of Gastric and Colonic Epithelial Tumours. *Sci Rep.* 2020;10(1): 1504.
17. Kanavati F, Toyokawa G, Momosaki S, et al. Weaklysupervised learning for lung carcinoma classification using deep learning. *Sci Rep.* 2020;10(1):9297.
18. Namikawa K, Hirasawa T, Yoshio T, et al. Utilizing artificial intelligence in endoscopy: a clinician's guide. *Expert Rev Gastroenterol Hepatol.* 2020;1-18.
19. Gulati S, Emmanuel A, Patel M, et al. Artificial intelligence in luminal endoscopy. *Ther Adv Gastrointest Endosc.* 2020;13:2631774520935220.
20. Tae K. Robotic thyroid surgery. *Auris Nasus Larynx.* 2020;48(3):331-338.
21. Stefanelli LV, Mandelaris GA, Franchina A, et al. Accuracy Evaluation of 14 Maxillary Full Arch Implant Treatments Performed with Da Vinci Bridge: A Case Series. *Materials (Basel).* 2020;13(12):2806.
22. Mirchi N, Bissonnette V, Ledwos N, et al. Artificial Neural Networks to Assess Virtual Reality Anterior Cervical Discectomy Performance. *Oper Neurosurg (Hagerstown).* 2020;19(1):65-75.
23. Creighton FX, Unberath M, Song T, et al. Early Feasibility Studies of Augmented Reality Navigation for Lateral Skull Base Surgery. *Otol Neurotol.* 2020;41(7):883-888.
24. Gibby J, Cvetko S, Javan R, et al. Use of augmented reality for image-guided spine procedures. *Eur Spine J.* 2020;29(8):1823-1832.
25. Gu Y, Yao Q, Xu Y, et al. A Clinical Application Study of Mixed Reality Technology Assisted Lumbar Pedicle Screws Implantation. *Med Sci Monit.* 2020;26:e924982.
26. Chytas D, Chronopoulos E, Salmas M, et al. Comment on: "Intraoperative 3D Hologram Support With Mixed Reality Techniques in Liver Surgery". *Ann Surg.* 2021;274(6):e761-e762.
27. Zeiger J, Costa A, Bederson J, et al. Use of Mixed Reality Visualization in Endoscopic Endona-

- sal Skull Base Surgery. *Oper Neurosurg* (Hagerstown), 2020,19(1):43 – 52.
28. Hashimoto DA, Witkowski E, Gao L, et al. Artificial Intelligence in Anesthesiology: Current Techniques, Clinical Applications, and Limitations. *Anesthesiology*, 2020,132(2):379-394.
 29. Seger C, Cannesson M. Recent advances in the technology of anesthesia. *F1000Res*, 2020,9:F1000 Faculty Rev-375.
 30. Topalovic M, Das N, Burgel PR, et al. Artificial intelligence outperforms pulmonologists in the interpretation of pulmonary function tests. *Eur Respir J*. 2019 Apr 11;53(4):1801660. doi: 10.1183/13993003.01660-2018.
 31. Global Initiative for Asthma. GINA Report, Global Strategy for Asthma Management and Prevention; 2020. Available from: <https://ginasthma.org/ginareports/>. Accessed February 05, 2020.
 32. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for Prevention, Diagnosis and Management of COPD; 2020. Available from: <https://goldcopd.org/gold-reports/>. Accessed April 05, 2020.
 33. Crapo RO. Pulmonary-function testing. *N Engl J Med* 1994; 331: 25-30.
 34. Vogelmeier CF, Criner GJ, Martinez FJ, et al. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2017 Report: GOLD Executive Summary. *Eur Respir J* 2017; 49: 1700214.
 35. Giri PC, Chowdhury AM, Bedoya A, et al. Application of Machine Learning in Pulmonary Function Assessment Where Are We Now and Where Are We Going? *Front Physiol*. 2021 Jun 24;12:678540. doi: 10.3389/fphys.2021.678540.
 36. Kao EF, Liu GC, Lee LY, et al. Computer-aided detection system for chest radiography: reducing report turnaround times of examinations with abnormalities. *Acta Radiologica*. 2015 Jun;56(6):696-701.
 37. Nam JG, Park S, Hwang EJ, et al. Development and validation of deep learning-based automatic detection algorithm for malignant pulmonary nodules on chest radiographs. *Radiology*. 2019 Jan;290(1):218-28.
 38. Rohmah RN, Susanto A, Soesanti I. Lung tuberculosis identification based on statistical feature of thoracic X-ray, in: 2013 Int. Conf. QiR, IEEE, 2013; pp. 19–26.
 39. Hwang EJ, Park S, Jin KN. DLAD Development and Evaluation Group, Development and Validation of a Deep Learning-Based Automated Detection Algorithm for Major Thoracic Diseases on Chest Radiographs. *JAMA Netw. Open*. 2 (2019) e191095.
 40. Walsh SLE, Calandriello L, Silva M, et al. Deep learning for classifying fibrotic lung disease on high-resolution computed tomography: a case-cohort study. *Lancet Respir Med* 6(11): 837-45 (2018).
 41. Liao KM, Liu CF, Chen CJ, et al. Machine Learning Approaches for Predicting Acute Respiratory Failure, Ventilator Dependence, and Mortality in Chronic Obstructive Pulmonary Disease. *Diagnostics (Basel)*. 2021 Dec 20;11(12):2396. doi: 10.3390/diagnostics11122396.
 42. Giansanti, D.; Pochini, M.; Giovagnoli, M.R. Integration of Tablet Technologies in the e-Laboratory of Cytology: A Health Technology Assessment. *Telemed. e-Health* 2014, 20, 909–915.
 43. Giansanti, D.; Grigioni, M.; D’Avenio, G.; Morelli, S.; Maccioni, G.; Bondi, A.; Giovagnoli, M.R. Virtual microscopy and digital cytology: State of the art. *Annali dell’Istituto Superiore Sanità* 2010, 46, 115–122.
 44. Rabbani M, Kanevsky J, Kafi K, Chandelier F, Giles FJ. Role of artificial intelligence in the care of patients with nonsmall cell lung cancer. *Eur J Clin Invest*. 2018;48(4):e12901.
 45. Koh J, Go H, Kim MY, et al. A comprehensive immunohistochemistry algorithm for the histological subtyping of small biopsies obtained from non-small cell lung cancers. *Histopathology*. 2014;65(6):868–78.
 46. Xiong Y, Ba X, Hou A, et al. Automatic detection of Mycobacterium tuberculosis using artificial intelligence. *J Thorac Dis* 2018;10:1936–40.
 47. Bates DW, Saria S, Ohno-Machado L, et al. Big data in healthcare: using analytics to identify and manage high-risk and high-cost patients. *Health Aff (Millwood)* 2014; 33:1123–1131.
 48. Shah SA, Velardo C, Farmer A, et al. Exacerbations in chronic obstructive pulmonary disease:

- identification and prediction using a digital health system. *J Med Internet Res* 2017; 19:e69.
49. Chamberlin J, Kocher MR, Waltz J, et al. Automated detection of lung nodules and coronary artery calcium using artificial intelligence on low-dose CT scans for lung cancer screening: accuracy and prognostic value. *BMC Med.* 2021 Mar 4;19(1):55. doi: 10.1186/s12916-021-01928-3.
 50. Vaishya R, Javaid M, Khan IH, et al. Artificial Intelligence (AI) applications for COVID-19 pandemic. *Diabetes Metab Syndr*, 2020,14(4):337-339.
 51. Zhang HT, Zhang JS, Zhang HH, et al. Automated detection and quantification of COVID-19 pneumonia: CT imaging analysis by a deep learning-based software. *Eur J Nucl Med Mol Imaging.* 2020 Oct;47(11):2525-2532. doi: 10.1007/s00259-020-04953-1.
 52. Mashamba-Thompson TP, Crayton ED. Blockchain and Artificial Intelligence Technology for Novel Coronavirus Disease-19 Self-Testing. *Diagnostics (Basel).* 2020 Apr 1;10(4):198. doi: 10.3390/diagnostics10040198.
 53. Arash KA, Julia W, Milad S, et al. Artificial Intelligence for COVID-19 Drug Discovery and Vaccine Development. *Front Artif Intell*, 2020,3:65
 54. Elaziz MA, Hosny KM, Salah A, et al. New machine learning method for image-based diagnosis of COVID-19. *PLoS One*, 2020,15(6):e235187