CURRENT SCENARIO AND REGULATORY APROVAL PROCESS OF AI/ML BASED MEDICAL DEVICES

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Running title: AI/ML based medical devices regulatory approval process

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ABSTRACT

Medical devices based on artificial intelligence and machine learning (AI/ML) have become more popular. In the modern days of healthcare, the role of AI, an emerging technology, in healthcare institutions is on the rise. AI technology is employed to diagnose diseases, the choice of therapies, and the education of healthcare professionals. It has the ability to solve a variety of issues in the healthcare system. AI offers great potential for countries now struggling with overcrowded healthcare systems and a physician shortage. AI offers great potential for countries now struggling with overcrowded healthcare systems and a physician shortage. Modern healthcare institutions rely heavily on technology. Machine learning (ML)-based medical devices are being employed more often in the healthcare industry as a result of the rapid advancements in artificial intelligence (AI) during the past ten years. Applications of machine learning (ML) are significantly altering the healthcare industry. The main objective of ML, is to increase the efficiency and precision of medical practise. An ILD-panel constituting pathologists, radiologists and pulmonologists in some hospitals now makes the diagnosis of interstitial lung disease (ILD). Machine-learning algorithms are an example of how AI may be applied in healthcare.

Key words: AI, Machine Learning, Technology, Health Care, ILD

INTRODUCTION

AI technology is employed in the disease diagnosis, the choice of therapies, and the education of healthcare professionals. It has the ability to solve a variety of issues in the healthcare system. The market size for healthcare related AI technology is estimated to be worth 11 bn $ in 2021, anticipated to grow to 188 bn $ by 2030 globally[1]. The modern healthcare system is heavily reliant on AI technology, which is constantly developing and offering effective and efficient medical support. The method that diagnoses and treats patients has changed because of AI technologies. Artificial intelligence (AI) has exploded in radiology during the past twenty years. The phrase "Machine Learning (ML)" refers to numerous statistical techniques that permit computers to understand from experiences without being explicitly programmed[2]. By looking at a collection of images including diverse people, an ML system may be able to identify faces. The two main sub fields of ML are unsupervised learning and supervised learning. One of the greatest sectors of the global economy that this technology may help is healthcare. Machine learning is the main strategy used when applying AI to the study of medical pictures. Artificial neural networks are a type of deep learning, which is a subset of machine learning. The differences between these two technologies are given in Table 1. Computer systems called artificial neural networks are made up of synthetic neurons that can learn parametric functions. They can do parallel calculations and are used to find patterns in the given data. The advantages and disadvantages of AI and ML are depicted in Figure 1 and 2. The working of AI is depicted in Figure 3.

Table 1: Difference between Artificial intelligence and Machine learning[3]

S.No	AI	ML
i.	AI stands for artificial intelligence, and intelligence is the capacity for information acquisition and application.	Machine learning, or ML, is the term for the process of acquiring information or skills.
ii.	Instead of precision, the goal is to maximize the likelihood of success.	The objective is to enhance accuracy, although success is unimportant.
iii.	The goal of AI is to create an intelligent machine that can handle a range of challenging tasks.	Machine learning is to create tools that can only do the tasks for which they have been programmed.

iv.	There are three major types of AI: i. Artificial General Intelligence ii. Narrow Artificial iii. Intelligence Artificial Super Intelligence	Three broad categories of ML are i. Unsupervised Learning ii. Supervised Learning iii. Reinforcement Learning
v.	To tackle complicated issues, it is intended to emulate natural intelligence.	The objective is to maximize performance on a given task by learning from data about that task.

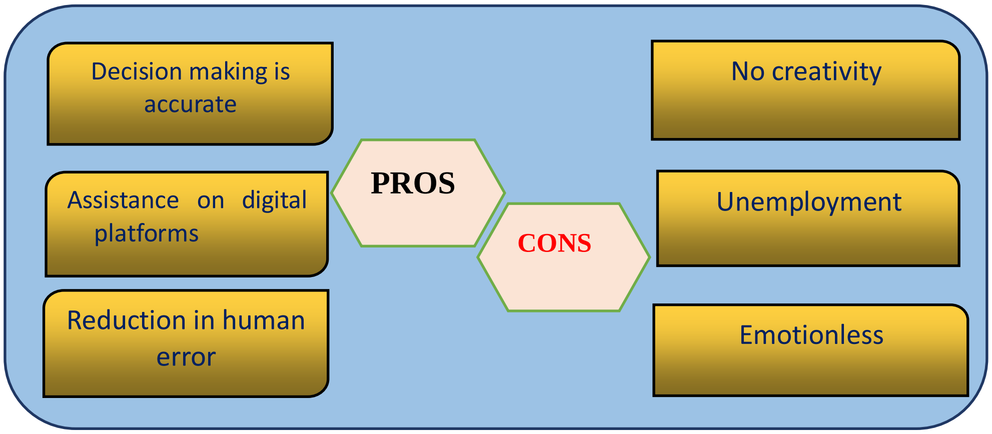

Figure 1: Pros and cons of artificial intelligence

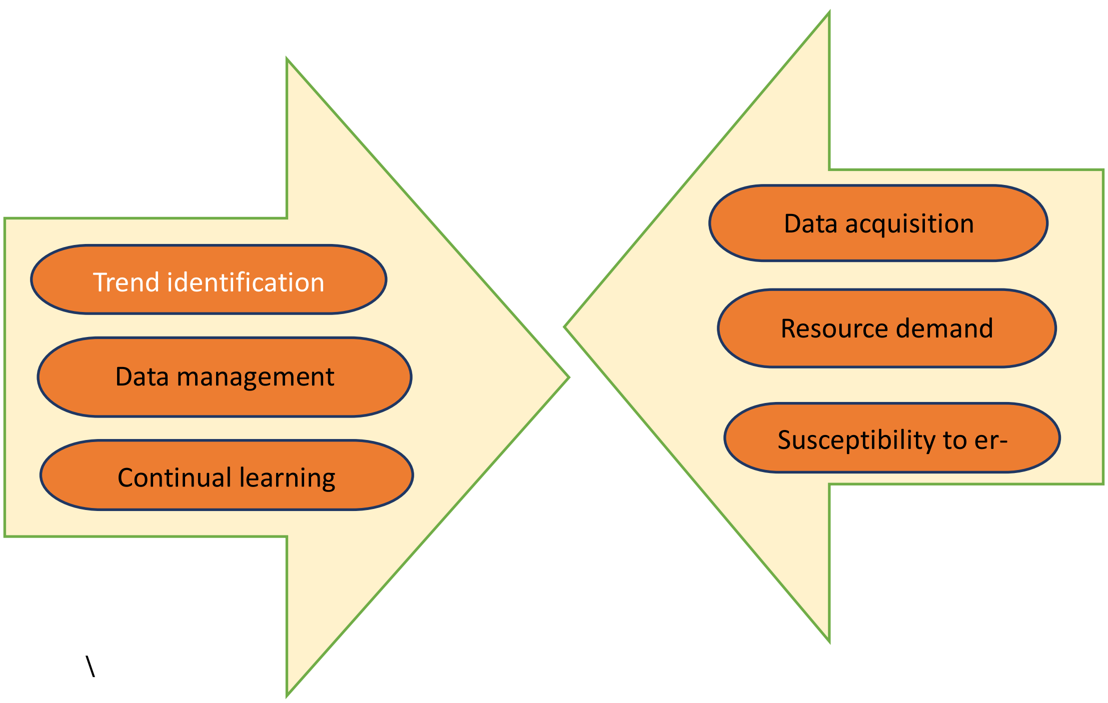

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Figure 2: Advantages and disadvantages of Machine learning

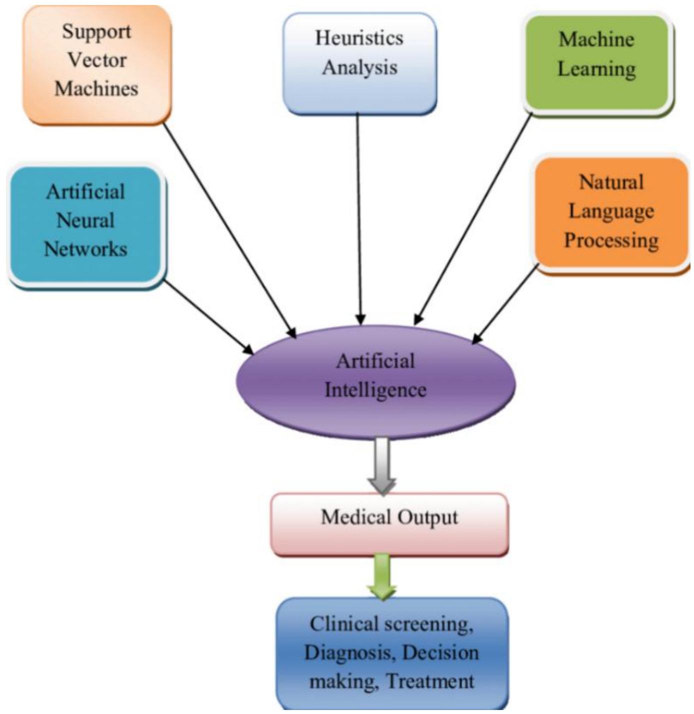

Figure 3: Working of artificial intelligence

Regulations of AI/ML based medical devices

There is no particular regulatory process for AI/ML-based medical products in the USA or Europe, distinct approaches are applied to regulate them. The premarket approval pathway, (which requires the most thorough examination for high-risk devices), the de-novo premarket review, (for low and moderate-risk devices), and the 510(k) pathway are instead used by the central FDA to approve medical devices. For the sake of simplicity, they refer to the clearance of such devices as approval. In Europe, unlike the USA, there is no one agency that approves medical equipment. However, the manufacturer is solely responsible for ensuring that items in risk class I medical devices (i.e., class I) conform the requirements without going through an approval procedure. Medical devices of the highest risk classes (IIa, IIb, and III) are handled by private entities known as "Notified Bodies," which are entities authorised to conduct a conformity assessment and issue a Conformité Européenne (CE)[4] label. The similar method may be used with in vitro (IVD)[5] medical devices. In USA, a total of 422 AI/ML based medical devices were approved during the period 2010-2022. . Here are the FDA approved AI/ML based medical devices number annually. In 2010, one device was approved and gradually it started increasing. From 2011 to 2015, a total of 19 AI/ML based medical devices approved by FDA. From 2016 to 2020, the number of devices approved were 286. In 2021, 115 and in 2022, 91 AIML based medical devices were approved by FDA. The graphical representation is given below Figure 4.

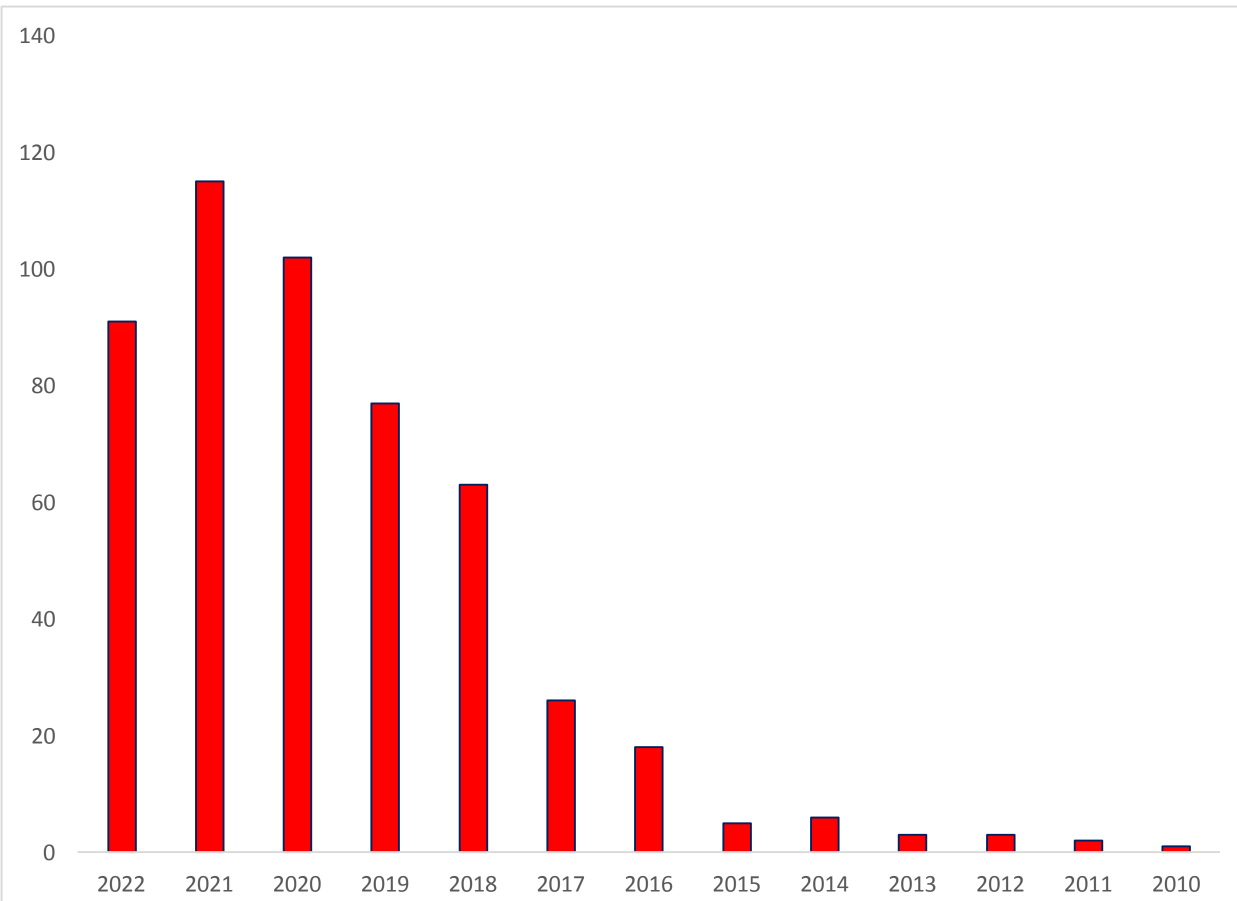

Figure 4: FDA approved AI/ML based medical devices from 2010 to 2022

Approved AI/ML based medical devices by category

In radiology, 392 and in cardiovascular, 57 AI/ML based medical devices were approved. Out of which, 79 (radiology devices) and 8 (cardiovascular devices) were approved in 2022, 97 and 13 were approved in 2021, 90 and 6 were approved in 2020, 51 and 12 were approved in 2019, 39 and 9 were approved in 2018, 15 and 6 were approved in 2017, 11 and 4 were approved in 2016, no radiology device was approved and one cardiovascular device was approved in 2015, 5 radiology devices were approved and no cardiovascular device was approved in 2014[6]. The list is given in the Table 2.

Table 2: FDA approved AI/ML based medical devices in various categories

Year	Radiology	Cardiovascular	Haemotology	Neurology	Opthalmic	Gastroenterology and Urology
2022	79	8	1	1	1	0
2021	97	13	0	2	1	3
2020	90	6	3	0	1	0
2019	51	12	1	4	1	1
2018	39	9	2	4	2	1
2017	15	6	2	1	0	1
2016	11	4	0	1	0	0
2015	0	1	0	0	0	0
2014	5	0	0	1	0	0

Total number of AI/ML based medical devices approved by FDA

The total number of AI/ML based medical devices approved by FDA in medical speciality are: In Radiology-392 devices, in Cardiovascular-57 devices, in Haematology-15 devices, in Neurology-14 devices, in Opthalmic-7 devices, in Gastroenterology and urology-6 devices, in Clinical chemistry-6 devices, in Microbiology-5 devices, in General and plastic surgery-5 devices, in Pathology-4 devices, in Anaesthesiology-4 devices, in General hospital-3 devices, in Orthopaedic-1 device, in Obsteric and gynaecology-1 device, in Dental-1 device were approved[7]. The data was depicted in Figure 5.

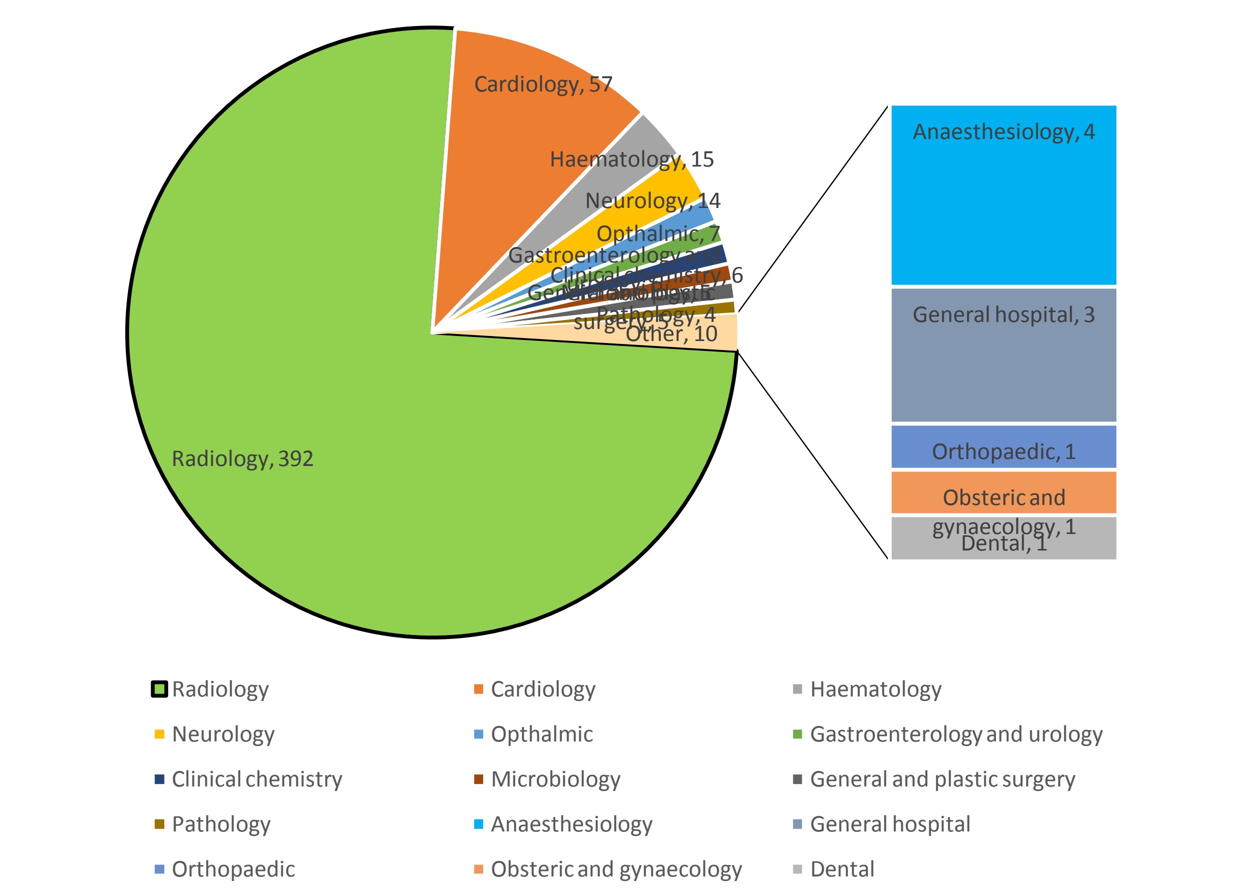

Figure 4: Categories of AI/ML based medical devices approved by FDA

Risk classifications and regulatory pathways

Only three AI/ML-based medical devices have received premarket clearance in the United States. Two are radiological tools for assisting with breast cancer and breast abnormalities diagnosis. Only two AI/ML-based medical devices were designated as risk class III in Europe. Both are radiological instruments that enable the post-processing processes for cardiac MRI and CT. The radiology device MammoScreen (Therapixel, Valbonne, France) for breast cancer detection support and Cardio AI (Arterys, San Francisco, CA, USA) as part of the Arterys MICA device for cardiac MRI post-processing workflows are two examples of devices for similar intended uses that were approved through relatively lenient approval processes. The size of the manufacturers, the planned use by patients vs health care professionals, or the place of origin of the manufacturer of the devices were not shown to be statistically associated with the FDA regulatory processes. An association between the intended use by the health-care professional application and direct patient use would have been expected from a regulatory standpoint because professional applications include tools that assist health-care professionals in making critical medical decisions, such as the monitoring and analytics of acute blood loss (e.g., Early Bird Bleed Monitoring System (Saranas, Houston, TX, USA) or pulmonary nodule detection from CT scans (e.g., syn). Only a statistically significant correlation between the FDA regulatory process and the field of molecular genetics was found. In Europe, statistically significant correlations between risk class I of CE-marked AI/ML-based medical devices and the nation of origin of the manufacturer (Israel and England), as well as between the risk classes and the size of the firms, have been found. The nations and Notified Bodies where the medical devices are evaluated might be able to explain these findings. The CE marking of a medical device in Europe does not have to be done in the nation where the maker is headquartered or where the medical device was invented; this practise is known as "forum shopping".Different standards are also used by the Notified Bodies for classifying risks.

Healthcare facility

Healthcare facility is an establishment that treats or tends to people's physical, mental, psychological, and emotional illnesses. Facilities for healthcare are those whose primary goal is to treat persons who are physically and psychologically ill[8]. Healthcare facilities also cover methods for diagnosing and preventing certain diseases. Healthcare facilities involve a variety of elements including hospitals, nursing homes, physicians, nurses, medical labs, and other diagnostic tools[9]. The three main illness fields that make use of AI techniques are cardiology, neurology, and cancer. Healthcare organizations throughout the world use a variety of cutting-edge technology to change and enhance services to patients. Through thorough analysis, AI aids healthcare practitioners in understanding the patterns and needs of their patients. The capacity to examine data enhances the diagnosing process and aids medical professionals in creating efficient patient treatment programmes. It is useful in radiological image analysis viz., EEG and ECG.

FDA approved AI-enabled products[10]:

- **Guardian Connect System: Method for constantly monitoring glucose -** Using a sensor placed beneath the skin on the arm or the belly, this device measures the levels of glucose in a diabetic patient's tissues. This data is processed by a transmitter and wirelessly sent to a mobile application. The programme allows users to check whether their blood glucose levels are too low or excessive.

- **OsteoDetect: Identifies and treats wrist fractures -**This programme examines X-rays for indications of a distal radius fracture and pinpoints its position to help with discovery and diagnosis.
- **ContactCT: detects a potential stroke and alerts a professional -** This software scans CT scans of the brain for signs typically linked to strokes and texts a specialist right once if it suspects a big vascular blockage, possibly involving the specialist earlier than is customary in normal treatment.
- **FibriCheck: Atrial fibrillation detection app for mobile -** This programme analyses and records cardiac rhythms using the camera on a smartphone or the sensors in a wearable. This data is combined with the symptoms the patient is asked to list, and a report is created with any required recommendations for the patient's next steps.
- **Embrace: seizure-monitoring wearable technology -** Through a wristband, this gadget detects physiological signs. The system will send a command to a linked wireless device set up to notify the patient's authorised carer if it detects activity that may be a seizure. Additionally, the device will capture and save sensor data for later examination by a medical expert.

Machine learning for healthcare

It has been suggested that the idea of ML and its flexible capabilities can benefit the healthcare industry in a number of ways. Some of the mainly enhanced quality pillars are the maintaining records of patient data, behavioural adjustments, outbreak prediction capabilities, medical imaging diagnostics, etc. While there is a demand for these services in healthcare practises, the efficacy and superior performance of these ML features give all the fundamental underpinnings.

Using data and an algorithm, ML trains computers to spot patterns. Manual illness detection is challenging; ML is crucial in identifying the patient's condition, keeping track of his health, and advising necessary preventative measures. It might include everything from simple ailments to serious conditions like cancer that are challenging to discover early. This helps mental healthcare professionals identify the groups of people who are more vulnerable to stresses like pandemics or natural disasters.

Salient Features of Associated Machine Learning in Healthcare

It displays a range of traits connecting the ML culture to a broad variety of healthcare services. It also involves assistance from a variety of clever and digital tools, like cloud data performance and AI. The creation of electronic medical records, even at a low cost, further remarkably benefits the healthcare industry. ML systems are being used by healthcare organisations to track and foresee future epidemic outbreaks throughout the globe. Healthcare institutions can use ML to forecast global issues that have not yet affected the patient. This makes it possible for doctors to provide therapies that either completely eliminate the issue before it arises or greatly lessen its severity. Early diagnosis is crucial for the treatment of cancer, hence it is extremely crucial. There is a wealth of information regarding the patient's health, much like in the healthcare industry. As a result, humans are unable to digest it. As a result, ML offers a method to identify patterns from the vast amounts of data and utilise algorithms to forecast the patients' future outcomes. Utilising machine learning (ML) in healthcare enables users to perceive information about the effectiveness of existing programmes and discover the therapy that offers patients the greatest results based on their situation.

Artificial intelligence in Interstitial lung diseases

Binary or multiclass classification can be utilised by artificial intelligence to diagnose a variety of medical disorders. This graphic shows an example of the construction of an AI model for diagnosis, albeit it does not reflect all conceivable pathways.

A typical AI-based medical diagnostic model's process. Data from various clinical/laboratory data, patient demographics and medical imaging modalities are collected in the first step. To be prepared for the creation of an AI model, this will require substantial processing. The models created need to be verified by human professionals and assessed against empirical data.

AI Techniques for ILD Diagnosis and Prognosis

It may eventually be possible to diagnose diseases based on clinical characteristics and baseline imaging. But existing models frequently depend primarily on data from radiological imaging. The most effective strategy could therefore be to create brand-new multivariate models that include information on the patient's background, medications, lung function test, and laboratory findings. ILD analysis revolves on these concerns:

- **Pattern Detection, Segmentation, and Distribution -** Given the wide variations in each ILD's prognosis and course of therapy, it is essential to establish the right ILD diagnosis. IPF generally has a poorer prognosis than ILDs without IPF[11]. As a gauge of lung function, doctors frequently track changes in forced vital capacity (FVC) and lung carbon monoxide diffusing capacity (DLCO). This is standard procedure, however the readings (FVC and

DLCO)[12] are erratic and inconsistent. Studies have shown the significance of imaging characteristics in high resolution CT (HRCT) scans[13] in contrast to this unreliable component. Monitoring FVC and HRCT pictures at set, routine intervals may be a novel way to track the development of IPF. There are many steps to the analysis of ILDs. Segmenting the various anatomical structures comes first, then utilising deep and radiomic characteristics, detecting, characterising, and quantifying abnormal patterns. The most useful characteristics are determined and examined in relation to clinical outcomes, such as illness progression and diagnosis.

- **Diagnosis -** In the 1950s, the idea of computer-aided diagnostic (CAD) systems was initially developed[14]. These systems can be characterised as computer programmes that can mimic the diagnostic skills of human professionals. A thorough analysis of the use of deep learning in ILDs, with an emphasis on CAD systems, was published by Trusculescu et al[15]. We will concentrate on two retrospective research that produced effective CAD tools for ILD classification using AI. Walsh et al.[16] used deep learning in 2018 to classify fibrotic lung illnesses using HRCT data. The study includes data augmentation, producing a final training set of 420,096 original montages from a data bank of 1,157 anonymized HRCT images with fibrotic lung disease. Thoracic radiologists with experience divided the information into three groups: The terms "UIP," "possible UIP," or "inconsistent with UIP" are all used. The creation of a neural network that could forecast one of the three classes was made possible by this supervised learning arrangement. The method was examined by 91 thoracic radiologists for validation. The algorithm's accuracy was 73.3%, compared to the radiologists' median accuracy of 70.7%. The research's strength is how few resources are needed after the algorithm has been taught to produce outcomes for specific patients. The paper's biggest flaw is the possibility that data was lost during dataset generation; these issues might be resolved in the future with more advanced machines.

- **Pattern Quantification and Follow-up -** The measurement of the diseased pattern in radiological imaging is a crucial component in the monitoring and forecasting of fibrosing ILDs. In general, a higher degree of fibrosis on a chest CT is associated with a higher death rate. There is a relationship between certain patterns, including honeycombing and bronchiectasis, and a poorer prognosis. The interrater variability for the observed patterns, however, has only been found to be mild[17]. Humphries recent study shown that data-driven texture analysis can offer reliable estimates of disease severity [18]. When compared to lung function tests, comparisons may reveal the threshold for clinically significant disease development.

- **Longitudinal Evaluation and Disease Prognosis -** AI technologies that incorporate imaging data, clinical data, lung function test results, and laboratory values may be used to estimate the progression of clinical illness and may outperform human specialists. The output variables used to classify existing AI techniques for illness prediction and progression are the major criterion. With inferring the amount of specificity with which other research have approached the prediction of ILDs, AI tools may be categorised according to their desired outcomes and use the target variable as a categorising characteristic [19].

CONCLUSION

AI technology has a significant impact on the development of medical devices and the detection of various diseases. The number of AI/ML-based medical devices that have been authorised has significantly grown. Radiology is the field in which AI/ML-Enabled Medical Devices are used most frequently. Large datasets may be utilised for research purposes by scientists as well as for manufacturing medical equipment by manufacturers since radiological imaging is requested by physicians during ordinary clinical practises and follow-up visits. Modern healthcare facilities are dependent on cutting-edge technology, and integrating AI technology into medical equipment is one way to enhance technology. Different pharmaceutical firms may manage their inventory and supply of medications using appropriate AI technology. The companies can also use AI technology to aid in the creation and research of new medications. A stress-free and healthy lifestyle will be advantageous for people. In the hands of any doctor, scientist, or researcher, ML has the potential to be a potent tool. Doctors and surgeons are using ML ideas in order to save lives, identify illnesses and other issues even before they manifest, improve management of patients, and do a lot more. By utilising AI-driven technologies and machine learning models, enterprises throughout the world enhance healthcare delivery.

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