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Artificial intelligence in medicine: its working, potentials and challenges

Rajeev Goel*

Department of Biophysics, Dr. R. P. Govt. Medical College, Kangra at Tanda, Himachal Pradesh, India

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***Correspondence:**
Dr. Rajeev Goel,
E-mail: rgoel302@yahoo.com

ABSTRACT

Artificial intelligence (AI) is the science and engineering of making intelligent machines to think and learn. The interest and involvement of AI in health care has expanded fast during the last decade. The use of AI based technologies has been integrated into medicine to raise the standard of patient care by accelerating processes and achieving greater accuracy in different clinical settings. The patient's electronic records, pathology slides and different radiological images are nowadays assessed by AI technologies such as machine learning (ML) and deep learning (DL). This, in turn, has aided in the process of diagnosis and treatment of patients and increased physicians' capabilities. AI is poised to transform medical practice in future. AI can aid clinicians to make accurate remedy choices, minimize needless surgeries, benefit oncologists to enhance patient's chemotherapy regimen etc. The aim of this review is to primarily develop fundamental knowledge and awareness of AI among the healthcare professionals. The article mainly deals with the basic mechanism of AI, the recent scientific developments and applications of AI along with its risks and challenges in clinical setup.

Keywords: Artificial intelligence, Neural networks, Machine learning, Deep learning, Biomedicine, Future of medicine

INTRODUCTION

Artificial intelligence (AI) makes use of computers and technology to simulate intelligent behavior and critical thinking broadly comparable to a human being.[1] The term AI was formulated by John McCarthy in 1956 who described it as the science and engineering of making intelligent machines.[2] However, Alan Turing in 1950 who evolved the Turing test to differentiate humans from machines was the first one to raise the possibility of machines ability to replicate human behavior and thinking.[3]

The 1980s and 1990s saw a burst in the interest in AI. AI began to expand, resulting in developments in expert systems, evolutionary computing, machine learning (ML), deep learning (DL), natural language processing, computer vision and other data processing technologies. Today, AI is intermixed into our daily lives in varied ways, such as personal assistants (Google Assistant, Alexa, Siri etc.), computer gaming, telecom, e-commerce, automated mass transportation, aviation, supply chains, marketing etc.[4]

The recent advances in technology, computing, data accessibility, and technical talent have expedited the amalgamation of AI (artificial intelligence) into healthcare. The core idea of AI is the predictive and accurate diagnosis and treatment analysis from the digitized health records and clinical methodologies by using AI based computer programs and algorithms. It is postulated that AI based smart machines-led predictive tech can put forward wide range of advantages over human analytics and clinical decision-making methods.[5]

MEDICAL ARTIFICIAL INTELLIGENCE

It is well known that the evidence-based medicine is based on the clinical decision making through observation of the past data. This task is usually made simple by distinguishing the patterns within data as mathematical equations, e.g., linear regression implies a 'line of best fit'. AI, whereas, provides solutions that unfolds multiplex associations difficult to be reduced to any single equation. For instance, neural networks in AI exhibit data through huge numbers of interconnected artificial neurons or nodes in a manner nearly corresponding to the human brain. This enables AI systems to address complex problem solving by carefully considering evidences to reach systematic and methodological decisions equitable to a clinician.[6,7]

Understanding the difference between AI, ML and DL

AI is an umbrella discipline that covers everything related to making machines smarter. It is a broad discipline of computer science and empowers machines to think without any human intervention. AI enables the devices to execute tasks based on algorithms. ML and DL are frequently used along with AI but ML is a subset of AI whereas DL is a subset of ML (Figure 1).[8,9] ML focuses on machines' ability to abstract and generalize the data as they modify the algorithm based on the data it is processing. ML thus makes use of many statistical learning algorithms to fabricate smart systems. These systems can learn on their own and become proficient without explicitly being programmed. The examples to understand ML, in daily life, are the personalized recommendation systems of music and video streaming on mobile/social apps. DL, whereas, is a ML algorithm that uses deep neural networks to analyze data to predict and classify information as an output. It processes data broadly akin to human brain. DL can be called as the next evolution of ML and is one of the ways to implement ML. Self driving cars make use of DL technology.[10-12] The learning algorithms are categorized as supervised, unsupervised and semi supervised which are discussed in the following section.

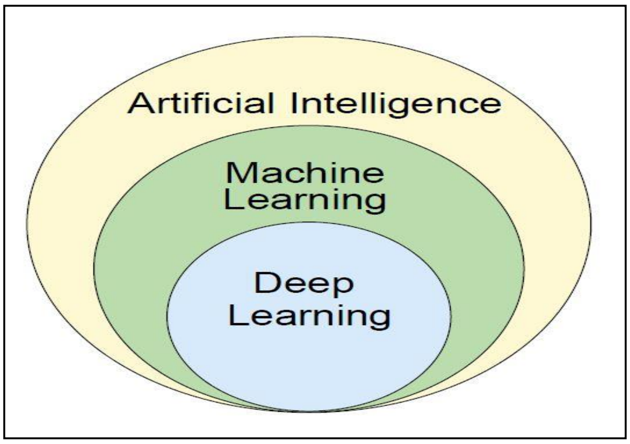

Figure 1: AI versus ML versus DL.[57]

Neural networks in AI

Neural networks are computing systems that draw inspiration from biological neural networks in terms of neuronal connectivity and activation threshold. These neural networks to a certain extent are analogous to the functioning of neurons in the human brain to recognize and establish the underlying relationships in a set of data (scans, X-ray images, patient's test reports etc.) to arrive at some meaningful output. The domain of AI which is primarily based on the concept of neural networks has far ranging applications in health care particularly in visually oriented specialties such as pathology, radiology, ophthalmology, dermatology etc.[13]

General structure and functioning of an artificial neural network

The general structure of a neural network consists of a connected series of layers of neurons i.e., input layer, output layer and hidden layers sandwiched between the input and output layer (Figure 2).[14] Each layer consists of a group of neurons. The neurons in the input layer receive a set of inputs (in terms of clinical data) which are transmitted to the neurons in the hidden layer for processing. The output of the neurons in a hidden layer automatically becomes the input of the neurons of the successive hidden layer for processing. This goes on till the neurons in the output layer finally produce a specific result, meaningful to the health care professional.[15] The connection and activation methods of neurons in the neural circuits are, however, regulated by certain complex interplay of mathematical functions to improve the training effect of these neural networks.[16,17]

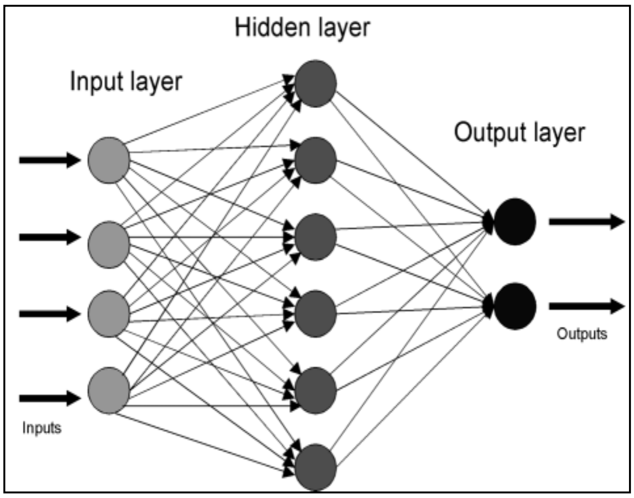

Figure 2: Schematic representation of a neural network.[30]

Supervised, unsupervised and semi supervised learning

The neurons in the neural circuits in AI are complex computer algorithms developed by the data scientists by using tools of mathematical computing. These algorithms in neural circuits when trained to learn by using the known clinical data (already labeled or diagnosed) to produce the desired clinical outcome on an unknown/test data (unlabeled or non-diagnosed) is called as supervised learning. The outcome for example can be a diagnosis, outlining of a polyp in an image, etc. The training data set must represent the problem it is being asked to solve, to ensure accurate results. Thus, both the input and output values of the data are known in supervised learning (Figure 3A).[18]

In case of unsupervised model, input data fed to the model is known, but not the corresponding output data. (Figure 3B).[19] The algorithms in the neural circuits in unsupervised learning self learn or infer patterns from the unlabeled input data and produce an output data with certain novel findings or useful insights which a clinician otherwise may not be able to capture or comprehend due to its hidden nature.

Semi supervised learning additionally takes an intermediate approach. It is a combination of supervised and unsupervised ML methods and can also be called as partially supervised and partially unsupervised. It employs the use of a relatively small set of labeled training data and a bulk of unlabeled data. Thus, in semi-supervised learning one has input data, and only some of the input data are labeled as the output. The algorithm is then directed to extrapolate what it learns from the labeled data to the unlabeled data and draw conclusions from the set as a whole (Figure 3C).[20] One can apply semi-supervised techniques to increase the size of one's training data in case sufficient labeled data and the resource to get more data to produce an accurate AI model is not available.

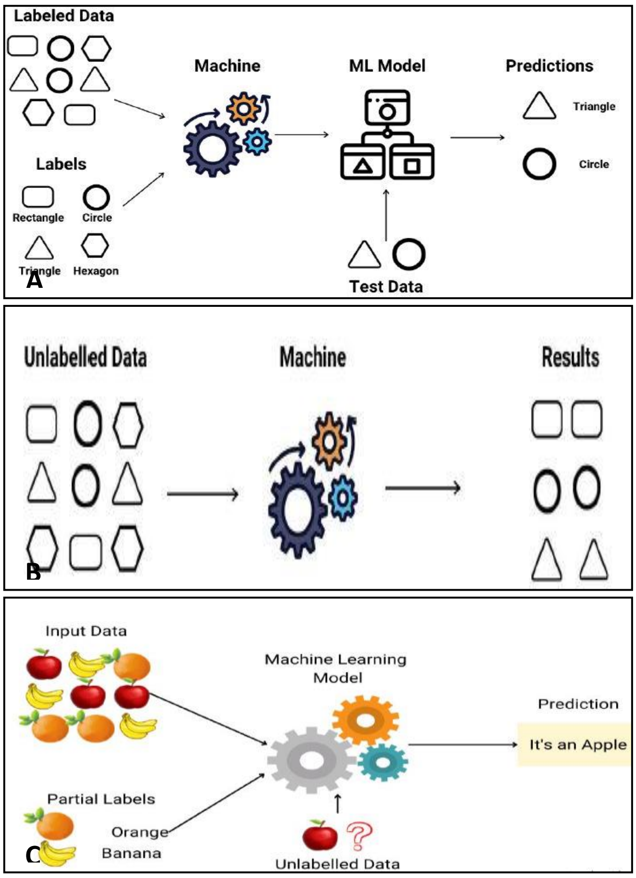

Figure 3 (A-C): Schematic representation of supervised; unsupervised; and semi-supervised learning.[58]

WORKING OF AN AI BASED ALGORITHM

The medical professionals are not required to have an in-depth understanding of these complex algorithms, but it is still useful to have a general idea of how AI-based healthcare tools work. To elucidate an AI based algorithm, let us break down the components of one specific algorithm that flags patients in the early stages of the sepsis and see how it works.[21] Sepsis is a common target for AI based tools as it can be difficult to establish sepsis in early stages because the signs are elusive. This particular tool uses mathematical techniques that are typical of medical algorithms. The algorithm supports a program called Sepsiswatch developed at Duke University, North Carolina, U.S.A. in the year 2018 and keeps an eye on patients when he/she is hospitalized.[22]

Many factors merit a person's risk of developing sepsis including age, immune-compromising health conditions and time duration of hospital stay. The varied signs from all over the body including parameters like biomarkers, blood pressure, heart rate, respiratory rate, body temperature etc. can guide a clinician when sepsis may be happening. The Sepsiswatch program needs consistent data about a patient on all such parameters to make out a prognosis.

Let's consider a hypothetical 60 years old male patient hospitalized with an infection. A part of the patient data, like age, pre-existing diseases (say thyroid disease) or earlier medications (say antihypertensive medication) is easy to record and enters into the program and that won't change while the patient is under hospital admission. The patient's other dynamic parameters like blood pressure, oxygen levels, respiration rate, heart rate or glucose etc. can change through the course of the day. The AI based program needs this dynamic data recorded at different intervals to fill in the gaps on these inconsistent metrics. The program uses a method called a Gaussian process (used for prediction and parameters estimation) to fill the gaps by making out the best path to draw a line through all the available data points, and adds in any missing numbers along that line.[23] It can now predict with a smooth line of evenly spaced data points in place, for example, what patient's glucose level should have been at regular intervals throughout the day if we already know the glucose level at certain intervals. All that data can now be packaged, and fed into the neural network underpinning the Sepsiswatch.[22]

The neural network in Sepsiswatch is a complex series of algorithms that look for patterns in the clutter data. It comprises a series of neurons that each take in data (blood pressure, glucose level, oxygen saturation etc), process it, and pass it on to the next neuron before finally reporting an outcome (Figure 4). It has initially been trained with hundreds of examples of data from patients with and without sepsis. The network automatically refines the way it works with the data each time it receives the new data until it could positively pick out what patterns and combinations of data associate or relate to sepsis. The neural network also simultaneously stores in its memory all the information it learns from previous times the program ran. This all is passed on to the next layer, with its own neurons and memory banks. The neural network after processing the data through complex sequence of algorithms finally gives a score between 0 and 1, signifying the probability of the event that a patient has developed sepsis at that particular moment in time. The closer the score is to 1, the more likely the patient has sepsis. This is how, one simple number as an outcome of AI based program can help clinicians and paramedics to care for the patient.[22]

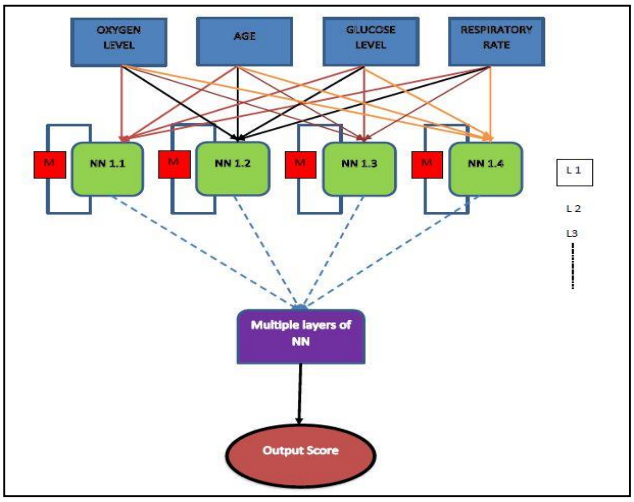

Figure 4: Schematic representation of neural network in Sepsiswatch (NN: Neural node; L1: Layer1; M: Memory; L1.1: layer1, node1; L1.2: layer 1, node 2).

CLINICAL APPLICATIONS OF AI

The use of AI in healthcare can prevent the onset of disease and promote a holistic approach to wellness and cure. This can be achieved by subjecting narrative, diagnostic data, and clinical findings to AI based software in order to promptly identify, minimize and reduce risks by tapping into early actionable points. Clinical decision-making can also have advantage by applying AI algorithms, to minimize delays due to traditional processes, diagnostic inefficiencies, resulting in better options and outcomes on a real-time basis.[24] AI-enabled robotics surgeries can diminish the risks of complex surgical procedures and complications if any with precision surgeries.[25,26]

The AI systems can concurrently perceive and swiftly undertake an almost limitless number of inputs which is not possible by a single clinician. For example, an AI-based smart phone app now adequately and effectively handles the task of triaging or prioritizing millions of people in certain European countries to accident and emergency department.[27,28] Furthermore, these AI systems are inherently built in a way having ability to automatically learn from each incremental case and can be laid open, within minutes, to more cases than a treating physician could see in many lifetimes.

The fuel behind AI's expansion is the availability of large digital datasets which is used by the AI algorithms to train themselves to perform a specific task, such as identifying a lesion in an image. The application of AI based algorithms can acquire much greater experience in a remarkably shorter amount of time than human subjects can gain in their lifetime. A radiologist will examine approximately 225,000 MRI/CT scans over 40 productive career years.[29] The AI, whereas, can start off with this number and within a short period of time reach into the millions of scans, thus further enhancing its accuracy. This is the reason that an AI-driven application is capable of out-performing dermatologists at precisely classifying suspicious skin lesions or performing radiologist-level accuracy in figuring out breast cancer in ultrasound images or the AI is being credited with tasks where experts often differ, such as diagnosing pulmonary tuberculosis on chest radiographs. The AI can therefore be expected to be more accurate and much faster than the average human in reading and diagnosing the scans.[30]

The specialist diagnostic expertise can be achieved at the primary care level by incorporating AI based systems. The images such as radiographs, ultrasound, scans or skin lesions can be directly transmitted by a general practitioner via a computer to specialist AI systems for immediate interpretation. The high risk identified patients through such a system can be referred instantly to the tertiary care which will lower the referral waiting times for such patients and specialists would consequently be evaluating selected patients only.[31]

The problem of missing secondary diagnosis which can worsen patient outcomes and precipitate costly readmissions can be resolved by the use of AI driven computer assisted physician documentation (CAPD) systems. The AI based CAPD enables clinicians to document and mark all secondary diagnosis while still focused on the primary clinical problem. This also eliminates staff burn out, to go through every patient's chart for any additional diagnosis besides augmenting documentation integrity and lowering readmissions and costs. AI driven CAPD solutions have helped healthcare organizations to analyze pertinent notes to pinpoint undocumented diagnosis and co- morbidities and document them to withstand audit scrutiny. It reduces severity of illness score by 41%, risk of mortality score by 49% and reduce retrospective severity queries to clinicians by 63%.[32,33]

The Kempegowda International Airport, Bengaluru, India, has recently installed an AI and chest X-ray based real time scanner called CHOCO to detect communicable diseases among international travelers which can deliver results within seconds. Its multiple trials across the country have shown promising results. This technology has jointly been developed by the Indian Radiological and Imaging

Association (IRIA) in collaboration with Chennai-based Corporeal Health Solutions (CHS).[34]

Philips Foundation, South Africa has successfully implemented in eleven South African hospitals an AI software named CAD4COVID, developed by Delft imaging, Netherland, to help triage and monitor COVID-19 patients via X-ray imaging in resource-constrained settings and high-prevalence areas. The CAD4COVID evaluates the severity and progression of COVID-19 disease based on routinely available chest X-rays.[35] The technology is based on the same technical core of Delft Imaging's CAD4TB tuberculosis (TB) detection software. CAD4TB is a CE (Conformité Européenne)- certified and WHO approved cost effective AI software to support data driven fast, easy, highly accurate automated TB screening and detection. CAD4TB is available for online and offline use to analyze images from adults and children from four years age. The software has been trained in the detection of TB-related abnormalities by applying DL and has screened over 10 million people globally.[36]

Yang et.al from Massachusetts Institute of Technology, Cambridge, have very recently, devised an AI model for an early detection (before clinical motor symptoms) of Parkinson's disease (PD) and to follow disease progression over a period of time using nocturnal breathing signals which acts as a diagnostic and progressional digital biomarker for PD.[37,38]

A unique DL strategy has been developed for individuals with ischemic heart disease to predict arrhythmia-related sudden cardiac death (SCDA) risk. This novel DL technique is named as survival study of cardiac arrhythmia risk (SSCAR) methodology. SSCAR combines the survival analysis and neural networks to estimate individualized survival curves in coronary artery disease using clinical variables and contrast-enhanced cardiac magnetic resonance (CMR) imaging. SSCAR visualizes individual patient times to SCDA (TSCDA) in split seconds.[39]

Deep longevity, a biotechnology company aims to revolutionize longevity R and D by developing ML based biomarkers of aging by making use of clinical blood tests, transcriptomic, proteomic, epigenetic, microbiome, imaging, wearable, behavioral, and multiple other data types. Its "Young AI App" is a future friendly AI medium to keep track of the aging processes. Deep longevity, in collaboration with Harvard Medical School, has developed a DL approach to human psychology and mental health as well. Its deep neural network model predicts individual's chronological age and psychological well-being. This model of human psychology offers superior personalization which can be used in self-help digital applications and during therapist sessions.[40]

A supervised learning based AI tool, 'PIVOT', that can predict cancer-causing genes in an individual has been developed by the Indian Institute of Technology (IIT), Madras, India, by making use of information on mutations, expression of genes, and copy number variation in genes and disruptions in the biological network because of an altered gene expression. This AI tool has been developed for predicting lower grade glioma, breast carcinoma, colon adenocarcinoma and lung adenocarcinoma.[41]

AI IN BIOMEDICINE RESEARCH

AI is promoting researches in genetics and molecular medicine by providing ML algorithms and knowledge management. A fairly large number of AI companies are developing and making use of their in- house built tools like AI platforms and algorithms to be used in drug discovery. These proprietary products are equipped with such important functionalities (to assist, steer, empower and supplement experts belonging to different health or medical fields) as insights in clinical trial studies, drug discovery, diagnosis through medical imaging etc. Few companies have also shown their openness to work jointly with major pharma companies like GKS, Pfizer, Novratis, AstraZeneca, Roche etc. and a few are using their copyright products for generating vision for their own team, involved in drug discovery, medical imaging and clinical trials.[42,43]

The unsupervised protein-protein interaction algorithms have led to the discovery of novel therapeutic targets.[44] The DNA variants such as single nucleotide polymorphisms (SNPs) as predictors of diseases or traits have also recently been identified using novel evolutionary embedded AI algorithms that are more powerful and less inclined to over-fitting issues.[45] The DL models with varying magnitude of success can nowadays predict that how genetic variations modulate cellular processes responsible for pathogenesis and to know which small molecules will alter the activity of therapeutically appropriate proteins. The AI based software based on ML has recently been developed that analyzes and draws inferences with high accuracy from patterns in the "whole exome sequencing" data to predict the risk of embryonic aneuploidy in female IVF patients. The three genes namely MCM5, FGGY, and DDX60L have also been identified that when mutated are highly correlated with aneuploidy.[46] DeepMind Technologies, a subsidiary of Alphabet Inc, Google parent company introduced Alphafold, an AI system, which consists of neural network named "Evoformer", that can predicts proteins 3D structure from the respective primary amino acid sequences with an accuracy score comparable to lab techniques. AlphaFold last year has completed the prediction of nearly every protein in human body which may now help to understand diseases better, develop new drugs and vaccines.[47]

THE COMPANIES FABRICATING AI BASED HEALTHCARE TOOLS

The few AI companies that are revolutionizing the healthcare industry for the information of readers are namely 1) Arterys in medical images which was the first to receive FDA approval for a cloud-based product with AI; 2) Caption Health known for additional care settings through AI technology platform coupling AI and ultrasound technologies for an early disease detection particularly the heart diseases; 3) Butterfly Network for better clinical decisions through better information and insight at the point of care through the delivery of high-quality, affordable, easy-to-use, intelligently connected AI based ultrasound technology; 4) Enlitic Inc, a leader in medical DL that leverages proprietary algorithms to quickly and accurately improve healthcare diagnosis; 5) Owkin to identify new drug candidates, de-risk and accelerate clinical trials and build diagnostic tools by using AI algorithms for right treatment and improved patient outcomes; 6) Corti offers digital assistants for patients interview to save time and reduce costs; 7) CloudMedX Health unifies all data sources and other systems together for a complete picture to simplify health care through AI; 8) Google Health/Deep Mind for AI applications for health care to empower people with the information they need to act on their health. Deep Mind developed an app "Streams" that sends alerts to the physician about patients at risk of acute risk injury and is in the process of building AI technology for eye scans for early detection of signs of blindness; 9) Aspirus health previously known as IBM Watson health have initiated digital tools that helps facilitate medical research, clinical research, and healthcare services, through the use of AI, data, analytics, cloud computing, and other advanced information technology for community-directed AI based health system and 10) Komodo Health delivers patient-level insights by dynamically analyzing the broadest array of data across patients, practitioners, and health systems through innovative AI based platforms.[48]

THE SAFETY AND CHALLENGES OF MEDICAL AI

It seems that AI in future will dramatically transform the overall healthcare system keeping in view the ongoing advancements in AI technology. However, there are certain technical and non-technical apprehensions about the use of AI technology in clinical settings. Health care is a dynamic and multifarious system which demands highest safety standards. The technical lapse, if any, on the part of AI may prove fatal to patients. It is difficult for an AI software to achieve in its technical design, the requirements of all clinical settings which by itself are complex and ever-changing phenomenon. There are also concerns on the working of AI based soft wares and their final clinical outcome or decision which is known as black box problem of the DL algorithms of AI.[49] The black box problem is the inability of certain DL algorithms to exhibit how they arrive at their conclusions. This is beyond the control of health safety engineers and clinicians alike which raises ethical constraints and safety regulations as compared to standard clinical practice. The attempts have, however, been made to overcome the black box problem in selected cases.[50] Further, many AI models are tutored and authenticated in the same patient cohort which needs validation of its generality to other populations for which the AI models require future testing to prove their efficacy in clinical or other outcomes.

The other technical issue is over fitting of AI algorithms which arises when an algorithm trained on one dataset, have limited applicability to other datasets. Over fitting occurs when an AI model acquires the detail and noise in the training data to the extent that it negatively impacts the performance of the model on new or unseen data. The salient factor of over fitting is the overtraining of an algorithm on a specific dataset. For example, an AI model may be over fitted if, the training and testing data sets differs significantly in respect of prevalence and incidence of disease. The algorithms, after training, therefore should be studied for over fitting by evaluating them on multiple different datasets.[51] The solution lies in training the AI model with large volume and high-quality data to avert over fitting. The regulatory approval of the medical AI algorithms is another challenge. The medical AI like drugs and clinical devices will be regulated by the regulatory agencies of respective countries such as FDA, EMA, CDSCO etc. One needs to have considerable documentation from non- clinical and clinical studies along with stringent assessment by the pre-market approval mechanism to prove that the new AI based diagnostic tool is safe and effectual enough.[52] It becomes all the more pertinent if the consequences of a misdiagnosis are extremely harmful.

Apart from these, the use of medical AI raises a medico legal issue that "who is responsible for the diagnosis" particularly if it turns out to be wrong. Will the treating physicians still be liable when they are no longer the main stakeholder for the clinical decision/ diagnosis made by the AI? Furthermore, the intellectual property rights also come into play when patient data are used to build AI products, finally generating profit which too requires due consideration.[53] The use of AI thus, brings issues of accountability, transparency, permission and privacy. The introduction of medical AI algorithms in patient care raises concerns about the nature of the relationship between physicians and patients which otherwise is considered to be a core element in the ethical principles of medicine and is based on deep trust.[54] The implementation of AI in clinical practice will also require that trainees learn how to best integrate AI in practice, and therefore a specific AI and informatics module will have to be included in the future medical training curricula. The another pitfall of medical AI could be lack of interpretation and other clinical skills among the medical trainees once the AI technology becomes part of the health system.[55] There are also risks of intended hacking of an AI algorithm to harm people at a large scale which will have its own fatal consequences.[56]

CONCLUSION

AI has several potential applications in medicine. The field is definitely high on promise. It remains to be seen that how it unfolds. However, the safety issues and other challenges discussed in the article need to be addressed properly for ensuring the safe adoption of AI in daily clinical practice. The onus lies on the researchers active in this field to produce evidences that AI technology genuinely works with precision on a practical level, to make AI acceptable to all stakeholders in health care without any qualm. The more randomized controlled studies to prove the efficacy of the AI systems in medicine are needed. The medical AI models for earlier adoption should be methodologically approved by the regulating agencies, integrated with electronic health record systems, standardized to a sufficient extent that similar models work in a similar fashion, taught to clinicians and updated over time as per the advancements in the field. The integration of the AI systems into clinical practice will demand building a symbiotic relationship between AI and clinician. This will only be possible when the AI will supplement clinicians greater efficiency/ cost-effectiveness and clinicians, in turn, will offer AI the requisite volume of clinical data which AI requires to learn complex clinical case management. Last but not the least, it will be imperative to ensure that AI does not eclipse the human face of medicine because the main hindrance to AI's overall adoption will be the public's mistrust to accept an increasingly controversial technology. Nonetheless, there is compelling evidence that medical AI can play a vital role in assisting the clinicians to efficiently deliver health care in the 21st century.

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