ARTIFICIAL INTELLIGENCE IN CLINICAL STUDIES

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ABSTRACT

Artificial intelligence (AI) has revolutionized information technology. The new economy of information technology has shaped the way we are living. Recently, AI algorithms have attracted close attention of researchers and have also been applied successfully to solve problems in engineering. Nevertheless, for large and complex problems, AI algorithms consume considerable computation time due to stochastic feature of the search approaches. Therefore, there is a potential requirement to develop efficient algorithm to find solutions under the limited resources, time, and money in real-world applications. This special issue aims to report the latest advances in every aspect of artificial intelligence technology, including machine learning, data mining, computer vision, multiagent systems, evolutionary computation, and fuzzy logic. Artificial Intelligence is a method of making a computer, a computer-controlled robot, or a software think intelligently like the human mind. AI is accomplished by studying the patterns of the human brain and by analyzing the cognitive process. The outcome of these studies develops intelligent software and systems.

Keywords: *Artificial intelligence, data mining, machine learning.*

1. INTRODUCTION:

The theory and development of computer systems able to perform tasks normally requiring human intelligence, such as visual perception, speech recognition, decision-making, and translation between languages is called as the Artificial intelligence.

AI programming focuses on cognitive skills that include the following:

1.1. Learning: This aspect of AI programming focuses on acquiring data and creating rules for how to turn it into actionable information. The rules, which are called algorithms, provide computing devices with step-by-step instructions for how to complete a specific task.

1.2. Reasoning: This aspect of AI programming focuses on choosing the right algorithm to reach a desired outcome.

1.3. Self-correction: This aspect of AI programming is designed to continually fine-tune algorithms and ensure they provide the most accurate results possible.

1.4. Creativity: This aspect of AI uses neural networks, rules-based systems, statistical methods and other AI techniques to generate new images, new text, new music and new ideas.

Artificial intelligence (AI) refers to the simulation of the human mind in computer systems that are programmed to Think like humans and mimic their actions such as learning and Problem-solving. AI should be able to perform tasks that normally require human intelligence, such as visual perception, Decision-making, and communication. AI-based computational Pathology as an emerging discipline has recently shown great Promise to increase both the accuracy and availability of high quality health care to patients in many medical fields. The Primary forces and limitations in this field are: a shortage of Experienced pathologists and the limitation of global health Care

resources the ever increasing amount of health Data available, including digital images, omics, clinical records, And patient demographic information, being generated through the process of patient care [2]; (3) the increased complexity that is created in managing and integrating the data across different sources in order to maximize patient care; and machine learning-based algorithms need to be efficiently harnessed in order to process and understand the big data. AI technologies have the ability to handle the gigantic quantity of data created throughout the patient care lifecycle to improve pathologic diagnosis, classification, prediction, and prognostication of diseases.

2. PREDICTIVE MODELLING AI IN HEALTHCARE:

Artificial Intelligence has several applications in medicine including hospitals, clinical laboratories, and research facilities. Healthcare administration and operations; clinical decision support; predictions in healthcare; patient monitoring; and healthcare interventions are key domains where AI is applied. Predictive modeling in healthcare is a proactive step towards identifying patients at risk of disease or adverse outcomes. One of the most common AI predictive model is the patient inflow into emergency department; re-admissions into emergency departments; disease or other outcomes; and in-patient mortality.

Recently AI techniques have sent vast waves Across healthcare, even fuelling an active Discussion of whether AI doctors will eventually replace human physicians in the future. We believe that human physicians will not Be replaced by machines in the foreseeable Future, but AI can definitely assist physicians to Make better clinical decisions or even replace Human judgement in certain functional areas Of healthcare (eg, radiology). The increasing Availability of healthcare data and rapid development of big data analytic methods has Made possible the recent successful application of AI in healthcare. Guided by relevant Clinical questions, powerful AI techniques can unlock clinically relevant information hidden In the massive amount of data, which in turn Can assist clinical decision making.1–3 we survey the current status Of AI in healthcare, as well as discuss its future. We first briefly review four relevant aspects

2.1. From medical investigators' perspectives:

1. Motivations of applying AI in healthcare

2. Data types that have be analyzed by AI systems.

2.3. Early detection of disease:

AI is acting as the most important tool in the healthcare industry for identifying critical at the initial stage. Baidu research recently announced about its deep learning algorithm that can outperform even trained pathologists in recognizing breast cancer metastasis. Mammograms are not quite effective in tracking cancer, and 1 in 2 women in the USA are identified with breast cancer falsely. As a relief, AI can translate mammograms 30 times faster and give accurate results.

Not just cancer, but AI can also be used to detect early stage heart diseases and provide right treatment at the right time. AI, in the integration with consumer wearables and medical wearable devices can identify heart diseases in patients and monitor them with the right treatment.

2.3. Quick diagnosis and treatment:

Artificial intelligence can process an enormous amount of data without being interrupted, which is humanely impossible. Thus enabling improvements in the medical front with increased diagnostic accuracy. AI-assisted diagnosis is important for healthcare providers to detect diseases early and support patients in their efforts to live a healthy lifestyle. Unlike human, AI algorithms don't lose their edge while diagnosing several samples together and collecting useful patterns.

3. DIGITAL PATHOLOGY, MACHINE LEARNING & COMPUTATIONAL PATHOLOGY:

The development of bright field and fluorescent slide scanners Made possible the virtualizing and digitalizing the whole glass Slides. Digital pathology includes the process of digitizing Histopathology, immunohistochemistry or

cytology slides Using whole-slide scanners as well as the interpretation, management, and analysis of these digitized whole-slide images using computational approaches. The digital data of the slides can be stored in a central cloud-based space allowing for remote access to the information for manual review by a pathologist o which r automated review by a data algorithm. It makes AI; a branch of computational science generates the data algorithms, to be applied in pathology possible.

Machine learning is an AI process to allow a Computer system to automatically learn and improve from the Data set by itself and to solve problems without being programmed during the process. Machine learning is an Advanced branch of AGI using a large amount of initial data, Training set, to build statistic algorithms to interpret and act on New data later on. At pervious machine learning based approaches have been developed and tested in pathology to assist pathologic diagnosis using the basic morphology Pattern such as cancer cells, cell nuclei, cell divisions, ducts, Blood vessels, etc.. Deep learning (also known as deep structured learning) is a subfield of machine learning based on artificial neural networks (ANNs) in which the statistic models are established from input training data.

Computational Pathology not only facilitates a more efficient pathology Workflow, but also provides a more comprehensive and personalized view, enabling pathologists to address the Progress of complex diseases for better patient care.

4. PATHOLOGIST-CENTERED MEDICAL SYSTEM:

Although most AI research is still focused on the detection And grading of tumors in digital pathology and radiology, Computational pathology is not limited to the detection of a Morphological pattern. It can also contribute to the complex Process of analysis and judgment using demographic Information, digital pathology, -omics, and laboratory Results. Therefore, AI has the potential to contribute to nearly all aspects of the clinical workflow, from more Accurate diagnosis to prognosis, and individualized treatment. Multiple sources of clinical data [28] are incorporated Into mathematic models to generate diagnostic and predictions, to enable physicians, patients, and laboratory the best possible medical decisions.

5. ARTIFICIAL INTELLIGENCE BASED CLINICAL DATA MANAGEMENT SYSTEM:

Clinical Data Management Forms a fundamental part in the clinical trial studies. CDM is implied in All the facets of operating computers, dispensation of the clinical data, Managing the subject data and database systems to support the collection Of the data. Clinical Data Management is precisely defined as the Collection, integration and validation of the trial data. When the Clinical trials are performed, the prime duty of the investigators is to collect the data of the patient's wellbeing after a specific interval of time. Further, this data is given to the trial sponsor who quantifies and qualifies the given data by statistical means. When the approval of new drugs is to be made by the regulatory agencies it is reliant upon the clinical trial data Presented. The trust on the clinical data is usually adhered to the quality Practices and standards of the clinical trials performed. Therefore, the organizations assure that the clinical trials performed and the data obtained are in the hands of well qualified and trained staff.

The key objective of CDM is to Offer high quality data by observing the errors and missing data and Keeping it as low as possible to congregate maximum data for analysis. Various practices have been developed to ensure that the data obtained is Complete, processed correctly and reliable. This has been easily achieved by the use of applications of the software that presents effortless detection and motion of data discrepancies and is used to maintain audit trials. In clinical data management, softwares are generally required to address. The electronic data capture, preparation of the electronic FDA submission, acceleration of the clinical trial management processes.

The novel developments in the technology of computer hardware and Software have contributed in making clinical trials effective, reliable and Timely which act as the centerpiece for conducting a successful Trial. With the advancement in the computer world and the availability of Design tools, software vendors, commercial databases and security applications the management of clinical trial data is widely attainable, less Time consuming, easier, more scalable and secure than the past. Undoubtedly, these attributes give the assurance in the confidence of the Results but novel challenges have evolved with the use of these attributes which also must be kept in mind. These usually include learning curve Cost, trading with unforeseeable events and changing errands [4]. There Are good

clinical data management practices that deal with data acquisition, privacy, electronic data capturing, Case Report Form (CRF) Printing, preservation of CRF, data storage, validations and many more.

Standard operating procedures are the processes that are followed to accomplish data management activities and to support the responsibility of obeying the guidelines as per ICH GCP and 21 CFR part 11. Standard Operating procedures or SOP's are usually applied in pharmaceutical Processing and are also related for clinical studies. In clinical studies, the Main focus is on recurring application of unaffected processes and their Documentation therefore, it supports the isolation of origins, effects and Causes. Further, applications made are with respect to the priority of Patient treatments when the restricted sources get utilized according to Estimation on urgency, staffing possibilities and ranking. The quality Assurance team is responsible for monitoring that the study and test meet.

6. CASE REPORT FORMS:

A case report form (or CRF) Is a paper or electronic questionnaire specifically used in clinical trial research.[1] The case report form is the tool used by the sponsor of the clinical trial to collect data from each participating patient. All data on each patient participating in a clinical trial are held and/or documented in the CRF, including adverse events.

The sponsor of the clinical trial develops the CRF to collect the specific data they need in order to test their hypotheses or answer their research questions. The size of a CRF can range from a handwritten one-time 'snapshot' of a patient's physical condition to hundreds of pages of electronically captured data obtained over a period of weeks or months. (It can also include required check-up visits months after the patient's treatment has stopped.)

The sponsor Is responsible for designing a CRF that accurately represents the protocol of the clinical trial, as well as managing its production, monitoring the data collection and auditing the content of the filled-in CRFs.

Case report forms contain data obtained during the patient's participation in the clinical trial. Before being sent to the sponsor, this data is usually de-identified (not traceable to the patient) by removing the patient's name, medical record number, etc., and giving the patient a unique study number. The supervising Institutional Review Board (IRB) oversees the release of any personally identifiable data to the sponsor.

From the sponsor's point of view, the main logistic goal of a clinical trial is to obtain accurate CRFs. However, because of human and machine error, the data entered in CRFs is rarely completely accurate or entirely readable. To combat these errors monitors are usually hired by the sponsor to audit the CRF to make sure the CRF contains the correct data.

When the study administrators or automated mechanisms process the CRFs that were sent to the sponsor by local researchers, they make a note of queries. Queries are non-sensible or questionable data that must be explained. Examples of data that would lead to a query: a male patient being on female birth control medication or having had an abortion, or a 15-year-old participant having had hip replacement surgery. Each query has to be resolved by the individual attention of a member of each local research team, as well as an individual in the study administration. To ensure quality control, these queries are usually addressed and resolved before the CRF data is included by the sponsor in the final clinical study report. Depending on variables relating to the nature of the study, (e.g., the health of the study population), the effectiveness of the study administrators in resolving these queries can significantly impact the cost of studies.

A well organized CRF is developed in a manner that the data handling And electronic database designs can be easily cut down. It also focuses on Capturing decipherable, compelling and dependable data which minimize the freight on data entry resolution and query generation. For Developing an error free and well referenced CRF the CRF design should Be followed and for this purpose a proper header and footer must be Provided to the CRF. Widely, the header and footer contain Sponsor ID, Subject ID, protocol number, and subject initials and so on and this information uniquely identifies a CRF page [6]. It is mandatory that all the Pages in a CRF are properly arranged in a chronological order as it helps in the identification of the query and manual review. A sequence number provided to the CRF. Widely, the header and footer contain Sponsor ID, Field can be provided in the footer for the detection of the sequential Order of the photocopied pages. This number is also helpful in the salvage Field can be provided in the footer for the detection of the sequential Order of the photocopied pages. This number is also helpful in the salvage Of CRFs and developing database. Also, the sequential order is necessary as it reflects the plan of

assessments that are specified in the protocol. Responsibilities for developing an accurate CRF is usually Distributed in the organization among clinical research associates, data Manager, database development, coding, standards and research nurse. For the development of an error free CRF the developers should thoroughly obey and include all the safety and efficacy parameters that are given in the protocol using standard libraries. It is suggested that only the Data that is required by the protocol must be collected and the protocol must be worked out within the schedule and at the final stage interdisciplinary review is mandatory. Nowadays, a term called eCRFs is widely Used that stands for electronic CRFs. This technique involves the use of Remote data capturing technology. In general, the concepts for the Development of eCRFs are similar to the concepts involved in the design of paper CRFs. The major advantage is that there is no need to print and distribute the paper among the members of the organization.

6.1. CRF Designing:

A CRF is made by for the collection of data from the protocol. A CRF May be paper based or in the form of EDC. There is a proper coding given To the CRF to communicate the collection of data which is to be stored in the database. A CRF should be constructed in such a way that it must be Concise and the data must be stored in high quality. The header and the Footer given in the CRF must be made in such a way that it should give the Details about the study. During the designing of the CRF the discrepancies In the data can be avoided by making a proper layout of the CRF that Should be of basically three types that is, time dependent, non-time Dependent and cumulative layout [6]. There should be uniform use of Layouts, fonts and queries. CRF pages should be orderly arranged according to the unambiguous protocols. Proper organized data will provide simplified data analysis. A proper CRF completion manual should be provided to the personnel for accurate data entry. Thus, there will be reduced query generation and data integrity will be improved. It is suggested that a library of templates for the standard CRF module must be established in order to save time.

6.2. Data Management:

Data acquisition is usually referred to as that gadget that is used to Attain the data from the clinical trial without any omission from the set of Rules that are given to conduct the trial. The quality of the data acquires depends entirely upon the quality of the instrument used to acquire data. Therefore, the design, quality assurance and development of such an instrument must be given paramount importance. Collection or acquisition of the clinical data may be brought by using various technicalities that may include but not necessarily be limited to paper forms, interactive voice response systems, electronic or paper medical proceedings, central web based systems or electronic data capture systems. For the proper reference of these systems the ICH guidelines on good clinical practices use the term “Case Report Form” which is utilized for the eminence and uprightness of the data.

6.3. Paper Based- System:

In the paper based systems the case report forms are filled manually at The site and are then mailed to the company. The data that has been Collected is further sent to the CDMS tool that is, Clinical Data Management System through data entry. For this matter, the most common Method used is the double data entry method wherein, two diverse data Entry operators enter the data in the system separately and both the Entries made are compared by the system. In case, if there is any divergence in the entry the system sends alerts and the verification can be Done manually. Also, a single data entry method is widely used in which a Single operator enters the data in the system. The data in the CDMS are Further given for validation purposes also, during the data validation the Data explanation is done from various sites through paper forms, which Contain the problem description and are then send to the investigator site And it responds by answering them through mails.

6.4. Data collection:

Data collection is done in the CRF in the form of either a paper or an Electronic version. In the traditional method, paper CRFs were used to Collect data responses which were then translated to the database by the Means of data entry done in-house. The filling of the paper CRF is done by The investigator according to the guidelines given for the completion of CRF. In the electronic systems of CDM the designee or the investigator is Primarily logged in to the system and the data is directly entered in the Site. In this method, the probability of errors is less and the discrepancies Can be managed easily . Pharmaceutical companies need a reduction In the time for drug development processes which is achieved by Enhancing the speed of processes that are involved thus; most of the Companies opt for e-CRF.

7. CRF TRACKING:

CRF tracking stands for the checking of the entries that are made in The CRF which is monitored by Clinical Research Associate thus filled and Complete CRF are then handed over to the team of CDM. Further tracking Is done by CDM team and a record is maintained. Usually, the CRF Tracking is performed for indecipherable data and mislaid pages to assure That the data is not misplaced. In the above case, in order to resolve the Issue amplification is obtained from the investigator.

7.1. Data entry:

Data entry is done according to the guidelines provided. This is Applicable only in the case of paper CRF. Also, double entry can be Performed when the data in entered by two different operators individually. The entry entered by the second person helps in resolution and Substantiation by depicting the dictation errors and discrepancies Caused by the indecipherable data. Also, it has been found that a double Data entry helps in achieving a cleaner database than a single entry. Moreover, studies show that the double data entry ensures better uniformity with paper CRF and also there are a lesser number of errors .

7.2. Data validation:

Test of the validation of the data according to the protocol mentioned Is known as the data validation. The discrepancies embedded in the Database entry are identified to ensure data validity. The programs are Printed according to the logical circumstances mentioned in the data Validation plan. These programs are primarily checked with replica data That contain discrepancies. Discrepancies are defined as the data points That fail to pass the validation check. These discrepancies may arise due To the missing data, inconsistent data, range checks and deviations from Protocol. Data validation is done frequently in the case of e-CRF. Investigators then resolve the issues after logging into the system. During The course of CDM the quality control of the data is checked at regular Intervals. When there are discrepancies in the data they will be highlighted in the system and in the Data Clarification Forms.

7.3. Discrepancy management:

This is also termed as query resolution. In the discrepancy management the steps involved are reviewing the discrepancies, investigating the reasons and further resolving them with the documentary proof and finally announcing them as irresolvable. The main function of the Discrepancy management is cleaning of the data and gathering evidences For the deviations determined in the data. All the softwares of the CDM Have a discrepancy database in which all the discrepancies are stored and recorded with the audit trials. Based on the basis of types of discrepancies, they are either flagged to the investigator for illumination purposes or they are clogged in-house by Self Evident Corrections (SEC). The commonly encountered SECs are spelling errors. When the resolution is given by the investigator, the same will be restructured in the database. If talking about e-CRFs the investigators can access the flagged discrepancies and will be resolved online.

7.4. Database locking:

The final data validation is done after a proper quality check and Assurance. If there are no discrepancies found the datasets are finalized With the statistician. Before locking the database all the management of Data activities should be completed. This is ensured as the database Cannot be altered in any manner after locking. Once the stakeholders Approve the database locking, the data is locked and the clean data Is extracted.

8. ADVATAGES OF ARTIFICIAL INTELLIGENCE:

8.1. Reduction in Human Error:

One of the biggest advantages of Artificial Intelligence is that it can significantly reduce errors and increase accuracy and precision. The decisions taken by AI in every step is decided by information previously gathered and a certain set of algorithms. When programmed properly, these errors can be reduced to null.

8.2. Zero Risks:

Another big advantage of AI is that humans can overcome many risks by letting AI robots do them for us. Whether it be defusing a bomb, going to space, exploring the deepest parts of oceans, machines with metal bodies are resistant in nature and can survive unfriendly atmospheres. Moreover, they can provide accurate work with greater responsibility and not wear out easily.

8.3. 24x7 Availability:

There are many studies that show humans are productive only about 3 to 4 hours in a day. Humans also need breaks and time offs to balance their work life and personal life. But AI can work endlessly without breaks. They think much faster than humans and perform multiple tasks at a time with accurate results. They can even handle tedious repetitive jobs easily with the help of AI algorithms.

8.4. Digital Assistance:

Some of the most technologically advanced companies engage with users using digital assistants, which eliminates the need for human personnel. Many websites utilize digital assistants to deliver user-requested content. We can discuss our search with them in conversation. Some chatbots are built in a way that makes it difficult to tell whether we are conversing with a human or a chatbot.

8.5. New Inventions:

In practically every field, AI is the driving force behind numerous innovations that will aid humans in resolving the majority of challenging issues. For instance, recent advances in AI-based technologies have allowed doctors to detect breast cancer in a woman at an earlier stage

8.6. Unbiased Decisions:

Human beings are driven by emotions, whether we like it or not. AI on the other hand, is devoid of emotions and highly practical and rational in its approach. A huge advantage of Artificial Intelligence is that it doesn't have any biased views, which ensures more accurate decision-making.

8.7. Perform Repetitive Jobs:

We will be doing a lot of repetitive tasks as part of our daily work, such as checking documents for flaws and mailing thank-you notes, among other things. We may use artificial intelligence to efficiently automate these menial chores and even eliminate "boring" tasks for people, allowing them to focus on being more creative.

8.8. Daily Applications:

Today, our everyday lives are entirely dependent on mobile devices and the internet. We utilize a variety of apps, including Google Maps, Alexa, Siri, Cortana on Windows, OK Google, taking selfies, making calls, responding to emails, etc. With the use of various AI-based techniques, we can also anticipate today's weather and the days ahead.

8.9. AI in Risky Situations:

One of the main benefits of artificial intelligence is this. By creating an AI robot that can perform perilous tasks on our behalf, we can get beyond many of the dangerous restrictions that humans face. It can be utilized effectively in any type of natural or man-made calamity, whether it be going to Mars, defusing a bomb, exploring the deepest regions of the oceans, or mining for coal and oil.

8.10. Faster Decision-making:

Faster decision-making is another benefit of AI. By automating certain tasks and providing real-time insights, AI can help organizations make faster and more informed decisions. This can be particularly valuable in high-stakes environments, where decisions must be made quickly and accurately to prevent costly errors or save lives.

8.11. Pattern Identification:

Pattern identification is another area where AI excels. With its ability to analyze vast amounts of data and identify patterns and trends, AI can help businesses and organizations better understand customer behavior, market trends, and other important factors. This information can be used to make better decisions and improve business outcomes.

8.12. Medical Applications

AI has also made significant contributions to the field of medicine, with applications ranging from diagnosis and treatment to drug discovery and clinical trials. AI-powered tools can help doctors and researchers analyze patient data, identify potential health risks, and develop personalized treatment plans. This can lead to better health outcomes for patients and help accelerate the development of new medical treatments and technologies.

9. DISADVANTAGES OF ARTIFICIAL INTELLIGENCE:

9.1. High Costs:

The ability to create a machine that can simulate human intelligence is no small feat. It requires plenty of time and resources and can cost a huge deal of money. AI also needs to operate on the latest hardware and software to stay updated and meet the latest requirements, thus making it quite costly.

9.2. S0 Creativity:

A big disadvantage of AI is that it cannot learn to think outside the box. AI is capable of learning over time with pre-fed data and past experiences, but cannot be creative in its approach. A classic example is the bot Quill who can write Forbes earning reports. These reports only contain data and facts already provided to the bot. Although it is impressive that a bot can write an article on its own, it lacks the human touch present in other Forbes articles.

9.3. Unemployment:

One application of artificial intelligence is a robot, which is displacing occupations and increasing unemployment (in a few cases). Therefore, some claim that there is always a chance of unemployment as a result of chatbots and robots replacing humans.

For instance, robots are frequently utilized to replace human resources in manufacturing businesses in some more technologically advanced nations like Japan. This is not always the case, though, as it creates additional opportunities for humans to work while also replacing humans in order to increase efficiency.

9.4. Make Humans Lazy:

AI applications automate the majority of tedious and repetitive tasks. Since we do not have to memorize things or solve puzzles to get the job done, we tend to use our brains less and less. This addiction to AI can cause problems to future generations.

9.5. No Ethics:

Ethics and morality are important human features that can be difficult to incorporate into an AI. The rapid progress of AI has raised a number of concerns that one day, AI will grow uncontrollably, and eventually wipe out humanity. This moment is referred to as the AI singularity.

9.6. Emotionless:

Since early childhood, we have been taught that neither computers nor other machines have feelings. Humans function as a team, and team management is essential for achieving goals. However, there is no denying that robots are superior to humans when functioning effectively, but it is also true that human connections, which form the basis of teams, cannot be replaced by computers.

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