

Case Report

Malays. j. med. biol. res.



Impact of Machine Learning in Neurosurgery: A Systematic Review of Related Literature

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ABSTRACT

Machine learning is a domain within artificial intelligence that allows for computer algorithms to be learned from experience without them having being programmed. The objective of this study is to summarize the neurosurgical applications of machine learning when compared to clinical expertise. This study uses a systematic search to review articles from the PubMed and Embase databases in comparing various machine learning studies approaches to that of the clinical experts. For this study, 23 studies were identified which used machine learning algorithms for the diagnosis, pre-surgical planning, and outcome prediction. In conclusion, this study identifies that machine learning models can augment decision-making capacity for the surgeons and clinicians in neurosurgical applications. Despite this, there still exist hurdles that involve creation, validation, and the deployment of the machine learning techniques in clinical settings.

Keywords: Machine Learning, Neurosurgery, artificial intelligence, telesurgery, robotics Clinical setups

Manuscript Received: 01 November 2020

- Revised: 15 December 2020

- Accepted: 20 December 2020

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INTRODUCTION

When conducting surgery, making the correct decision is the most critical and crucial step. The stakes are high when the surgeon is involved with a neurosurgical incision with high stakes on making a positive outcome tied to the risk of unfavorable consequences. Besides, a benefit from a single measure can sometimes come at the cost of another one. Thus extending the survival of an aggressive tumor can come at the cost of impairing the neurologic functioning and thus affect the normal function of the body. Surgical site infections are other risks which are associated with neurosurgical operations. Such complications have the potential to impact the morbidity, mortality, and life economics of individuals. Deo (2015) conducted a cost analysis of the craniotomy infections and identified that the cost per case for the infection in the UK alone stood at £9283. The financial costs such as this are often compounded further by direct costs incurred through prolonged hospitalization, costs of doing patient diagnostics, treatment, and reoperation (Ghahramani, 2015).

Machine learning has emerged in recent times, with the silver lining of cutting such cost by predicting outcomes in the neurosurgical field. Various machine learning algorithms have been developed through complex mathematical models learning from clinical data such as neuro-oncology, brain injury, epilepsy, and neurovascular surgery. In their study, Azimi et al. (2015) reported that multimodality of machine learning through linear discriminant analysis, naïve Bayes, and linear machines. Moreover, Rodrigues et al. (2016) in their study demonstrated that machine learning algorithms such as k-nearest neighbors (k-NN), logistics regression, and NB, which might be powerful in selecting surgical candidates with a high likelihood of remaining free from the seizures in the temporal lobe epilepsy. To date, however, there exist no adequate tools that have been developed which accurately predict surgical outcomes for the individual patients, which would help patients and physicians in making correct clinical and surgical decisions. Nucci et al. (2016)

note that prognostic indices are easy to apply in the clinical practice; however, this does go at the cost of predictive performance. In calculating prognosis, the numerical values can be simplified into categorical variables with the weight given to the predictive factors rounded up to integers (Mitchel et al. 2013).

Machine learning has been adopted recently in the field of clinical research at an increasing pace. Machine learning allows computer algorithms to learn from experience without computers being programmed (Zhang et al., 2017). Machine learning has been driven by data explosion combined with increased computational power and classical epidemiology, creating newer data sciences by incorporating newer data science techniques. By studying large data sets, such tools seek to approximate the existing relationship between input and output. With the learning aspects, machines can make up powerful predictions from unknown relationships in large and complex environments to adopt a dynamic environment.

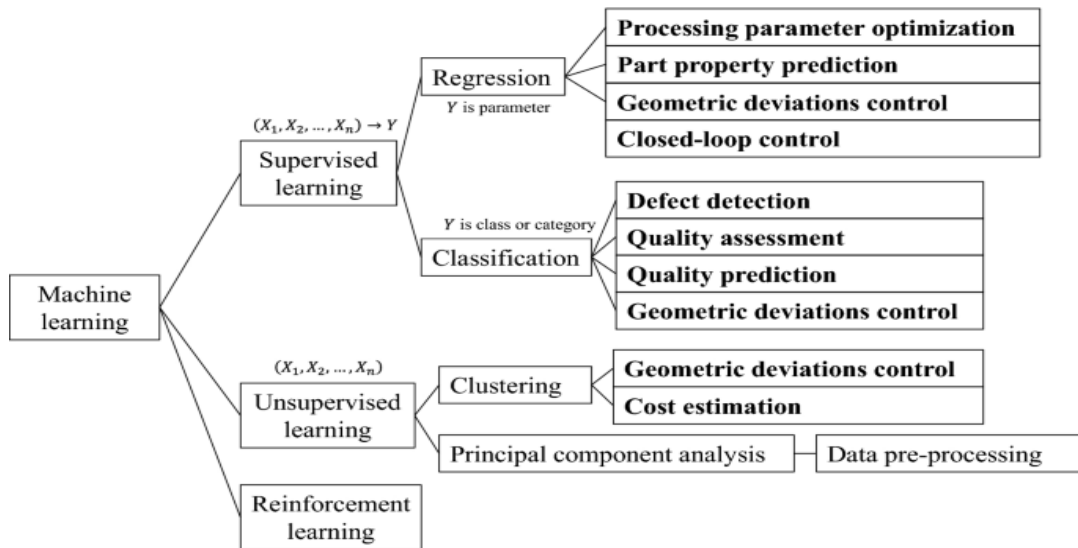


Figure 1: Showing ways data acquisition is done and used for supervised and unsupervised (Image Courtesy of SpringerLink)

The complex modalities and the multidimensional data involved in neurosurgeries are an incentive to build and create machine learning models to make precision surgery. Since precision lies at the core of making an eventful surgery with a negative outcome, this study seeks to do a systematic review of studies dealing with machine learning for neurosurgical outcome prediction (Rayfield et al. 2015). Thus, this study aims to evaluate the effectiveness of machine learning, its usefulness, and existing theoretical concepts of using machine learning. Further, this study would also evaluate machine learning performance compared to prognostic indices, statistical models, and views from clinical experts.

Research Gap Identification

Despite the advances made in technology, the application of machine learning in the clinical setup to help in diagnosis, pre-surgical planning, and the prediction of outcome is still not widely accepted and incorporated into practice. Health is a major concern for any nation, and increasing efficacy in health care systems and diagnosis has been a top priority for many governments. Robotics have, in recent years, made inroads into more specialized fields such as neurosurgery. Robots have many advantages, including increased accuracy, elimination of muscle fatigues, and psychological tremors during extended operations, which would improve outcomes and reduce potential complications. At present, machine learning has been adopted to guide surgeons into correctly localizing brain anatomy. Two main challenges, however, exist in the full automation of surgical practice; perception and tissue manipulation. This study reviews the efficacy and use of machine learning systematically through various peer-reviewed studies reviewed by PubMed and Embase databases.

Objectives

To review the neurosurgical application of machine learning and compare this with that of the clinical experts

LITERATURE REVIEW

Machine Learning

In machine learning, a broad distinction can be made between supervised and unsupervised learning. The supervised learning algorithms learn from the labeled training data and produce a model that makes predictions based on some

unseen data (Donepudi et al., 2020). Desired output during this training data is often known; thus, it is referred to as labeled. Learning is the main departure point from the programming as in traditional programming, an individual would manually write down a series of instructions termed as the programs and generate the desired output from a set of input variables. In machine learning, however, the input is provided with the desired output, and the computer algorithms are required to set and derive a set of rules from a given set of labeled trained data (Zhang et al., 2017). This process results not in the desired output but in a model that can predict what previously unseen data is. The automated learning process is an efficient and reliable way to analyze big data, model any hidden and complex relationships that exist within a given set of values, and provides much-needed versatility (Juntu et al. 2010). In a machine learning environment, the algorithms are better trained to find the optimal combination of various features.

The Past, the Present and the Future of Machine Learning in Neurosurgery

Machine learning and other artificial forms of intelligence, such as robotics, have the ability to enhance decision making by the surgeon and also extend his or her capabilities beyond human limitation. The ability of machine learning tools to act, perceive, act and increase precision during surgery has been a major factor that has contributed to their increasing presence and usage in surgery (Kitajima et al. 2009). Traditionally, surgeons relied on their experience and expertise in conducting operations in recent times; however, robots and artificial intelligence has been equipped with the software and algorithm, which helps them to learn without being programmed through machine teaching (Emblem et al., 2015). Donepudi et al. (2020) note that at the core of this transformation into machine learning is the robots and computerized machines' ability to exploit raw data and translate this into action, which would mimic otherwise typical surgical procedures that are performed by a trained surgeon. Algorithms are primarily used to postulate problem-solving models. Across the globe, the last few decades have witnessed an increased adoption, invention, invention, and the incorporation of machine usage into neurosurgery. Devices such as PUMA 200, NeuroMate, Pathfinder, Neuroarm, Spine assistant, SOCRATES, and ROSA have gained prominence in the neurosurgical practice. Clinically, each of these devices has been used to perform different surgical applications (Liu et al., 2011). For instance, PUMA, 200, one of the earliest robots to be used in surgery, was developed to aid in doing stereotactic surgery; the surgeons used a CT guided biopsy needle in accessing the brain. Another device, the Neuromate, is a stereotactic system that was developed to be used in doing deep brain surgical procedures, which includes stereo-encephalography and is often considered to be safer than the PUMA 200 for the biopsies in conducting surgeries (Liu et al., 2011). Renaissance, on the other the latest and relatively newer image-guided system applicable in keyhole neurosurgery and uses an automated system that relies largely on the MRI/CT scan images during needle insertion, catheters, and drilling of the brain skull.

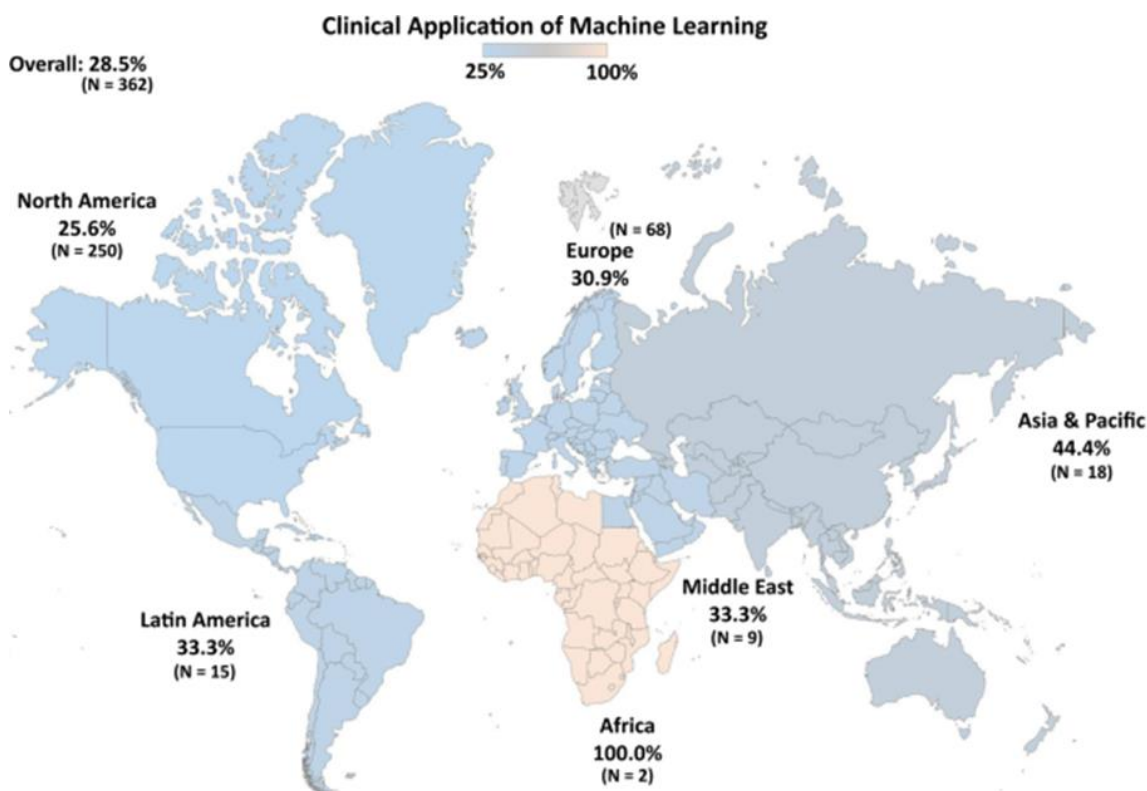


Figure 2: Global Survey on Machine Learning on Neurosurgery (Image Courtesy of SpringerLink)

To date, however, there exist no completely automated machines which have been deployed in the medical and neurosurgery field. On the contrary, there has been an increased optimization of the present technology with an increased master-slave relationship that exists between the human beings and the machines that have dominated the present integration of artificial intelligence in neurosurgery. It is important to note, however, that the adoption of modern technology has allowed for the use of various miniaturized systems, which allows for them to serve various purposes and specific elements of operations during surgeries. The outcome of this is self-evident with the use of robots in surgeries such as the neuroMate, Spine Assist, Renaissance, and steady hand system, which indicates that there is a bright future for the adoption of machine learning in neurosurgery. Despite this optimism and growth of the adoption of robots in surgery, there exist thoughts that the industry would not be able to reach full automation in the next two decades (Kassahun et al. 2014). It is argued that at the moment, there are two main challenges and issues which hinder complete automation into the use of such machines in hospitals without any patient-doctor interaction. This includes perception and manipulation abilities (Campillo-Gimenez et al., 2013). Unlike any other field, neurosurgery operates in a server spatial constraint, and the potential consequence of the slightest mistake or even minor surgical deviance would be catastrophic and fatal. To realize full potential, the machines would have to analyze digital data such as images on tissues and then act on it without the surgeon's presence. While artificial intelligence mirrors the use of machines alone, it is logical that machine learning would foresee inventions with a greater capacity and independence, the future of artificial intelligence would still include the active participation of surgeons in surgery, or just them being participants in any case that unforeseen events arise during the surgery. An example of this is the ability to tackle any unexpected injury to the blood vessel in the brain whose effect might be catastrophic. While the robot might cauterize the blood vessel and stop the bleeding, this might result in a massive stroke. When the safety margins are low, and the potential for serious consequences to occur is high, the focus should be based on prevention and safety (Donepudi, 2020).

Master-Slave Robot Relationship (Tele-surgery)

In the Master-Slave Robot relationship, the surgeon does control the robot. The introduction of the da Vinci surgical systems into surgery marked a new crop of robotics as it had seven degrees of freedom with four arms, which distinguished its predominantly from its predecessors. These machines revolutionized robotic surgery by providing a functional design improvement to the previous existing machines. Modern developments have also increased the relationships between the machines and the surgeons. Robotic systems can be categorized into three factions (handheld shared/controlled systems and the supervisory surgeon-controlled robot) depending on the level of relationship between the machines with the surgeons. Telesurgery robots, for instance, employ a master-slave relationship in which the surgeon does take control of the surgery by controlling the actions of the remote albeit remotely. The NeuroArm is one of the most applied telesurgical robots that was developed in 2001 as a refined master-slave system which was developed to aid in neurosurgery, allowing for the surgeon to perform microsurgical and stereotactic procedures through data collected from the real-time MRI data and structured in a way to withstand the strong magnetic field of the MRI without altering the quality of the procedure. This system can perform surgical operations, which includes making incisions, making needle insertion, making microsurgical cauterization, and irrigation.

Safety Issues with a Focus on use of Tele-surgery

The safety of tele-surgery and the use of robotics during surgery is largely dependent on the experience of the surgeon and the performance capacity of the machine that is being used. A study by Chan & Huang (2008) which investigated the efficacy of the use of telesurgery in removal of phantom pituitary tumor through a controlled robot, 800 kilometers away from the hospital. With a video latency of less than 100ms for the robot, the surgeons involved in the study gave it a perfect subjective safety score. Sinha et al. (2001) noted that during the research, the operation used a dedicated network to ensure that the telecommunications remained uninterrupted during the entire time. This is an important aspect as an intrinsic latency in the telecommunication network does determine the potential for risks to occur, slips during operation, and other safety issues even without the help of expert surgeons as a delay in relying on the real-time video could result in an incision either made too earlier or even later than it is expected. Various researchers such as Donepudi (2020) note that expert surgeons are better placed to adapt to such delays, and the safety of the telesurgery deteriorates slowly at 200ms and becomes fatal at above 1000ms. Thus in essence, the preventing damage to the central nervous systems during tele-surgery does require a dedicated high capacity network which would be able to ensure that the videos are displayed at latency of less than 100ms and the conditional on the fact that the surgeon is also skilled in doing the procedure.

Improved Safety through Machine Learning

The perception of the surgeon is the most important challenge when it comes to surgical safety. In most cases, the most experienced surgeons use the tactical sense between the instruments and the bones or the tissues which guide them in conducting the surgery. Yet however, the use of touch has been eliminated with the use of telesurgery in surgical

procedures (Sinha et al., 2001). For beginners and during complex operations and procedures, this can increase the risks of slips occurring of the misdirection of the robot, which might be catastrophic. How we can overcome this setback is the most important question.

At present times, the use of technology in surgery is in its testing and experimentation state. The hepatic feedback system should be integrated into the tele surgery to address issues of substituted contracts and assists in pure vision. In practice, the hepatic feedback system is only achievable through locus combination of the collision detection algorithms which aids in the calculation of the depth penetration and also through the coordinate transformation on the various systems in the machine which is translated to a virtual wall which a surgeon can visualize in a separate screen and monitor. Presently, technology in place allows for robots to have an instinct force or a deflection-based sensing machine and mechanism that mimics the haptic feedback system (Donepudi, 2020).

Neurosurgical Robots of the near Future

The role, functions, and ability of the robots of the near future are largely dependent on the advancement of main stakeholders in the industry, such as the engineers, healthcare workers and administrators, surgeons, and the public. While the pace of technological development could, in theory, replace surgeons in practice, however, this still seems to have a long way to go. Even if biomedical engineers develop fully automated robots in the future, the failure to change the public perception of the decision-making process of the surgeons as human beings could, by large, obstruct their adoption in hospitals. Further, with the recent development of fully autonomous systems, fewer surgeons have updated their practice and knowledge into the current machine operation; this trend could hinder the complete automation in the future and thus results in failed technological adoption. Furthermore, current regulatory bodies in the field focus on human behavior as compared to the success rates of the robots, largely due to the difficulty that is involved in defining and in the classification of robotics (Nadkarni et al., 2011). This trend shows that the surgeons would remain relevant during operations in the future.

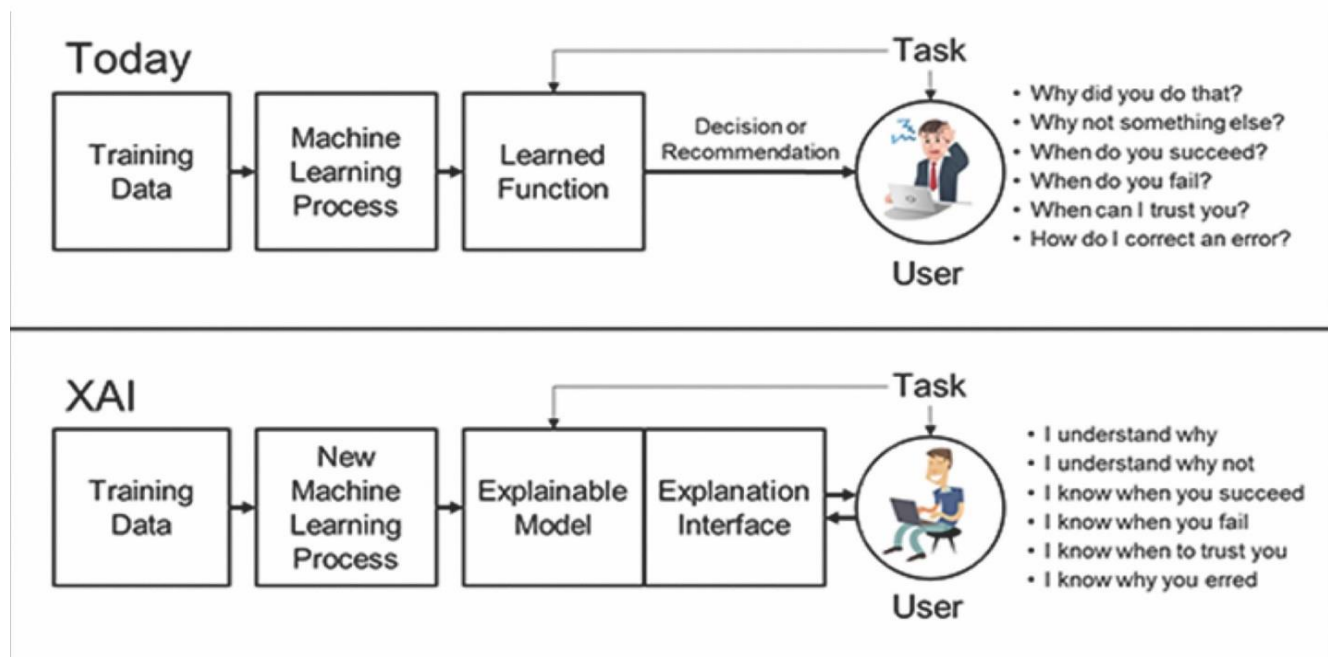


Figure 3: Describe the Future of Artificial Intelligence and Machine Learning in Healthcare

METHODOLOGY

For this study, we conducted a systematic search on websites such as Pubmed and Embase databases according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines to identify all the potentially relevant studies which we could use as of November 14, 2020. The search syntax for this study was done and built with guidance and help from a professional librarian using search terms related to machine learning, artificial intelligence, and neurosurgery. Studies that were included in this study compared the machine learning models against that of clinical experts applications that are relevant to the neurosurgical patient population, comparing them head-to-head and also to a third modality referred to as the growth truth. The neurosurgical patient population was defined as patients eligible for neurosurgical treatment for the disease. There was no specific limitation in regards to domain application (including the diagnosis, prognosis, treatment, and outcome prediction) to be as comprehensive as possible. Definition of the ground

truth does depend on various specific tasks that are evaluated on the study and also on the actual survival on that is presented on the survival prediction tasks, the historical diagnosis that is involved in the radiological diagnostic classification, the histological diagnosis, and the consensus between the various experts on the subject of the third objective modality that is available. For the exclusion criteria, this study excluded those study which lacked full text, those that used languages other than English, those studies that focused on animal studies and those studies which lacked the third modality and ground truth when comparing the machine learning and the expert's views. The data extracted were included a) the year of the study publication b) the disease condition c) specific machine application d) machine learning model used e) the input features f) the size of training set g) the validation method h) size of the test set involved i) the specialization of the clinical experts j) educational level of the experts k) ground truth l) model used for the statistical measure of performance m) the performance level of the machine learning systems and models n) the performance of the clinical experts and the lastly, o) the p-value obtained for the difference in the performance levels.

For this study, we considered the quantitative synthesis as being inappropriate; this is due to the heterogeneity of the neurosurgical applications. Thus, this study provided for a quality synthesis with the results and the assessments of the risks of bias of the outcome, study, and the review level being provided in a narrative approach. However, there is a need to summarize the results and the findings obtained in this study in the form of quantitative analysis for easy readability and comparison. Thus as a consequence, the median absolute improvement has been calculated for the most commonly used statistical measures, its accuracy, and the area under the receiver operating curve (AUC). Accuracy, in this sense, refers to the proportion of making correct predictions in a grand total number of predictions. The AUC corresponds to the probability in which a binary classifier can rank a randomly chosen positive instance through a higher chance as compared to a randomly chosen negative. This proportion of the superior/equal/inferior performance is then calculated in terms of percentages. Superior performance is defined as being a significantly better performance, which is P is less than .05 based on the statistical measure that is used for the evaluation. The equal performance is defined as being the non-significant difference that exists between the performances when P is greater than .05. The P -values were manually calculated if, by any chance, they were not reported in the actual papers. To gauge the outcome measure, this study used Fisher's exact tests with the binomial distribution (this included the accuracy, sensitivity, specificity, use of positive predictive value and also negative predictive values). Further, student's t -tests was used for comparison of the continuous outcome measurement. The bound continuous outcome scores, such as the F-measure of the AUC (both with range 0-1), were transformed further to the unbound scores (with range 0-infinity) through use of delta method to meet the assumption of the t -tests of the students. When using multiple machine learning models and or through the use of multiple clinicians when this is compared, the mean performance was used to calculate the p -value.

RESULTS

The first step involved in the study was to remove the duplicates. After the duplicates were removed, a total of 6052 citations found in the Pubmed and Embase were identified as being eligible to be used. From this, forty-four were selected as being potentially viable to be used through title/abstract screening. After the full screening was done, only 23 studies remained, which could be used for the study.

Study Characteristics

The median size for the training set for this study was set at 79 patients with an interquartile range between 36.5-123. The median ratio size set between the training set and the size of the tests set was set at 1:0.96. Twenty-one of the studies reviewed evaluated the supervised learning algorithms and two evaluated the two unsupervised learning algorithms. Of the various machine learning models used in the studies, artificial neural networks were 13, and the support-vector was 6, which represented the most commonly used algorithms. Further, other algorithms used include decision tree ($n=2$), two studies featuring the use of linear discriminant analysis, two studies using fuzzing C-means featuring unsupervised learning, one study using deep learning, one study based on naïve Bayess, and another one study on genetic algorithm. The clinical experts featured in this study include neurosurgeons, neurologists, neuro-radiologists, and hospital hygienist physicians with varying levels of education and technical subspecialty. The ground truth for this study was established through another diagnostic modality, clinical outcome, the database information, or even a combination of all of the above sources.

Descriptive Summary of the Results

The performance of the machine learning models evaluated as compared to that of the clinicians in the 23 studies, which evaluated the utility of the diagnosis, its preoperative planning, and the prediction based on a total of 61 outcome measures. The most common frequently used measure of performance between the two was accuracy, which signified 48% of the total studies and 22% of the total outcome, and AUC, which was featured in 43% of the total studies and 21% on the total outcome measures. Compared to the clinical experts, the median absolute improvement of the prediction accuracy and AUC of the machine learning models was 13% (with a range of 4% to 38%). A P -value

was also provided for 25 and calculated for 25 of the 61 of the outcome measures. In 58% of the studies, machine learning models did outperform that of the clinical experts. All the studies evaluated could be evaluated into three domains: diagnosis, preoperative planning, and outcome prediction. The results based on the performance of the machine learning models and the clinical experts were provided in each of these studies.

Diagnosis

Fourteen studies evaluated compared machine learning with the performance of diagnostic experts. Four of the studies did focus on the diagnostic classification of the pediatric posterior fossa tumors, the intra-axial tumors and sellar-suprasellar masses. All of these studies used to age and MRI techniques as input features with or without the use of clinical input (age, gender, medical history, and family history). The machine learning methods were also compared side to side to that of neuroradiologists with that of the general radiologists. Machine learning models performed significantly and also non-significantly better in the differential of the pediatric posterior fossa tumors. Two studies reviewed compared the performance of the surgeons assisted with the machine learning models against that of the clinicians alone. Machine learning models did increase significantly in the AUCs for the classification of the suprasellar masses in the general radiologists and that of the neuroradiologists. Further, machine learning has improved with the diagnostic classification of intracerebral tumors by radiologists. Further, five studies reviewed attempted to predict the World Health Organization (WHO) grade in the gliomas based on the MRI feature alone or with a combination with age for this. The machine learning models were then compared with the neuroradiologists, the general radiologists, and that of the neurosurgeons.

POLICY IMPLICATIONS FOR THE IMPLEMENTATION OF MACHINE LEARNING IN NEUROSURGICAL CARE

Although the output of these studies consisted of a wide range of neurosurgical applications, machine learning was the most frequently used in the analysis of the radiological data through means of artificial neural networks. Since every voxel can be used in assessing the individual input feature, the information which can be extracted through machine learning is too high, making it to be faster and more accurate than it is humanly possible. Automated analysis of surgical data for the analysis, segmentation, or prediction could be one of the first machine learning applications in actual clinical practice. Despite the challenges involved, there are potential challenges in regards to the machine learning models. One of the biggest challenges is that machine learning features a complex or sometimes different from evaluating algorithms, sometimes referred to as the black box. Another potential hurdle to this is that machine learning requires generating a large amount of complete but adequately categorized data. Due to the higher quality of data during research, the machine learning performance during research is higher, which could be overestimated during an actual clinical setting. For policymakers, there is a need to formulate a policy that would guide the application of machine learning in a clinical setting.

CONCLUSION

This systematic review shows that artificial intelligence can augment the decision-making capacity for clinicians when it comes to the realms of preoperative planning, diagnosis, and outcome prediction. However, it is also important to address existing challenges which is associated with creation, validation, and the deployment of machine learning techniques in clinical settings. The shift from the human-vs-machine relationship to that of the human-and-machine paradigm is essential and important to this analysis. Any future studies should be able to focus on not only the technical aspects in the construction of these models but also on the methods used to validate machine learning models before their deployment to increase their reproducibility and in the interpretation of the black-box algorithms, which improves the accessibility of the clinical data and investigating the combination of the machine.

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