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REVIEW ARTICLE

Introduction to artificial intelligence in medicine

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ABSTRACT

The term Artificial Intelligence (AI) was coined by John McCarthy in 1956 during a conference held on this subject. However, the possibility of machines being able to simulate human behavior and actually think was raised earlier by Alan Turing who developed the Turing test in order to differentiate humans from machines. Since then, computational power has grown to the point of instant calculations and the ability evaluate new data, according to previously assessed data, in real time.

Today, AI is integrated into our daily lives in many forms, such as personal assistants (Siri, Alexa, Google assistant etc.), automated mass transportation, aviation and computer gaming. More recently, AI has also begun to be incorporated into medicine to improve patient care by speeding up processes and achieving greater accuracy, opening the path to providing better healthcare overall. Radiological images, pathology slides, and patients' electronic medical records (EMR) are being evaluated by machine learning, aiding in the process of diagnosis and treatment of patients and augmenting physicians' capabilities. Herein we describe the current status of AI in medicine, the way it is used in the different disciplines and future trends.

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Introduction

When you ask physicians what the most important factors are for successful patient care, two words come to mind: knowledge and experience. The more you know and the more patients you treat the better patient care you can provide. Usually, this happens with time, meaning physicians acquire knowledge and experience during their career, while taking care of patients and increasing their knowledge in their specific interests through continued education.

This concept of experience and knowledge is central to understanding artificial intelligence and its implications in medicine. The more experience and data (analysis of information) we have, the more we are enabled to make better knowledge-based decisions. Data can be derived from evidence-based medicine like textbooks, and published peer-reviewed manuscripts, while experience is gained by the actual results and outcomes from the treatment of patients including patient files, patient lab results and radiological findings.

The main limitation of the human mind in the acquisition of large amounts of data is primarily time constraints. The process of learning requires the integration of knowledge and experience which is acquired along the years. In the era of silicone chips vast amounts of patient data can be accessed, acquired and stored for processing. Harnessing these enormous data banks and transforming them to gain experience is the mainstay of AI [1]. Computer software through the application of algorithms, thus can gain far more experience in a significantly shorter amount of time than human subjects can acquire in their lifetime. Over 40 productive career years, a radiologist will look at approximately 225,000 MRI/CT exams [2], while AI can start off with this number and within a short period of time reach into the millions of scans, thus further improving its accuracy. The resultant speed with which CTs are read and diagnosed via AI should therefore be more accurate and much faster than the average human.

Artificial intelligence (AI), in general while not well defined, is the capability of a machine to imitate intelligent human behavior [3]. While this comprehensive term encompasses many forms of computer science, in medicine one can focus mainly on the following terms:

- ***Image processing*** - a mathematical process that enhances an image for the purpose of clarity,

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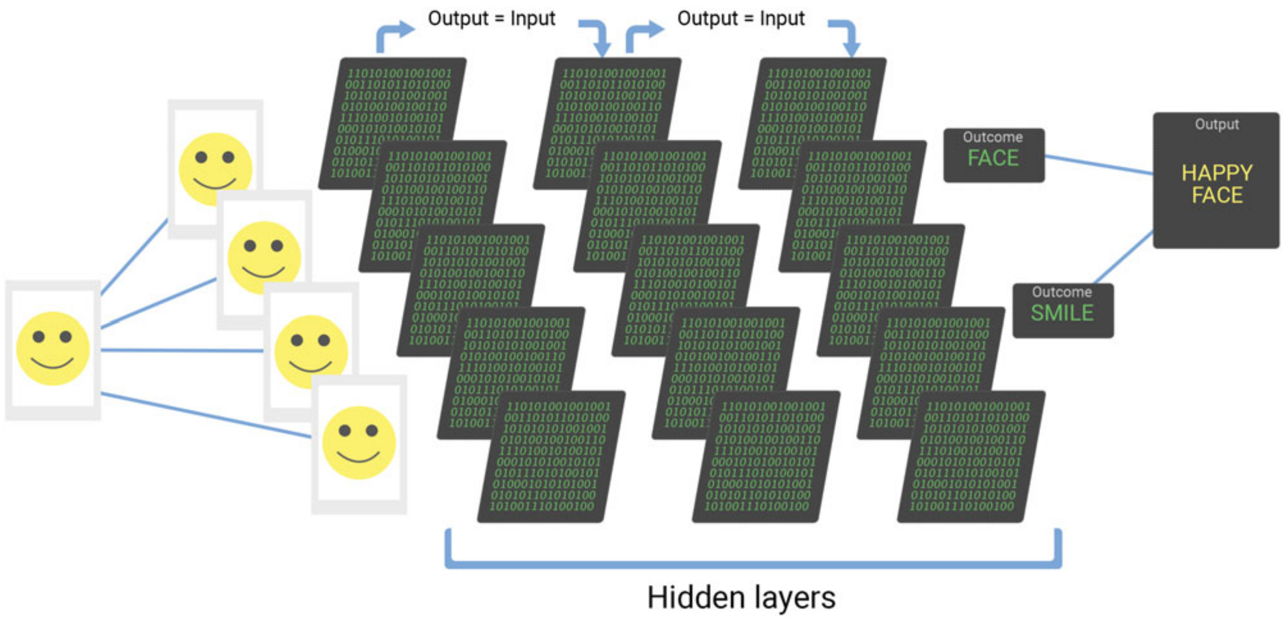

Figure 1. An image as an input to a CNN. The image is pushed through several algorithms in hidden layers, where the output of one layer is the input of the next one. Once all layers are processed the outcome can be reached, in this case a definition of the image.

retrieval of specific information, or pattern measurements. Basically the input is a picture and the output is a better defined picture for a specific applied purpose.

- ***Computer vision*** - the processing of an image to enable identification of the image input and to provide an appropriate output, i.e. interpretation of the image.
- ***Artificial neural network (ANN)*** - a mathematical model based on nonlinear statistical data modelling tools where complex relationships occur between inputs and the output. This process imitates the human brain in processing several types of data and creating patterns for use in a decision-making process through neural networks. Basically in ANN the input is entered into a set of algorithms and their output is re-entered to a different set of algorithms in order to reach the final output.
- ***Machine learning*** - the ability of a computer to learn from experience, i.e. to modify its processing on the basis of newly acquired information. This process can be based on a simple decision-making tree such as: if-then, which leads to a conclusion, or using deep learning algorithms which imitate the human brain in processing several types of data and creating patterns for use in decision making through neural networks [4]. For simplicity one can say that deep learning is a process in which an algorithm receives data (i.e. excel charts, images etc.) and then examines the data according to a predetermined pathway (artificial neural network) that was developed specifically to solve the desired task. The ANN is developed according to a training set of data provided to train the algorithm to answer a specific question. The training data set must represent the problem it is being asked to solve, to ensure accurate results.
- ***Convolutional neural network (CNN)*** - a specific type of ANN, typically based on deep learning algorithms with several hidden layers to analyse data. The relationships between layers are complex (hence the term convolutional) and multiple hidden layers exist in each CNN.
- ***Deep learning*** - deep learning is a subset of machine learning which is structured similar to human brain processing, taking in account multiple data sets at the same time, which are evaluated and reprocessed for second and third different evaluations and so on, until reaching an output. Every evaluation is carried out in a different layer, meaning that it is based on the output of the previous layer. These layers of computation are called hidden layers because their inputs and outputs are not visible. For example, if the data entered is a colonoscopy image looking for polyps, the image will first be multiplied. Each image will then be scanned using different filters. Each filter will receive a score which will then be transferred to another layer of filters (e.g. - colour filters, edges markings filters etc.). This workflow continues with multiple layers as needed (hence the term

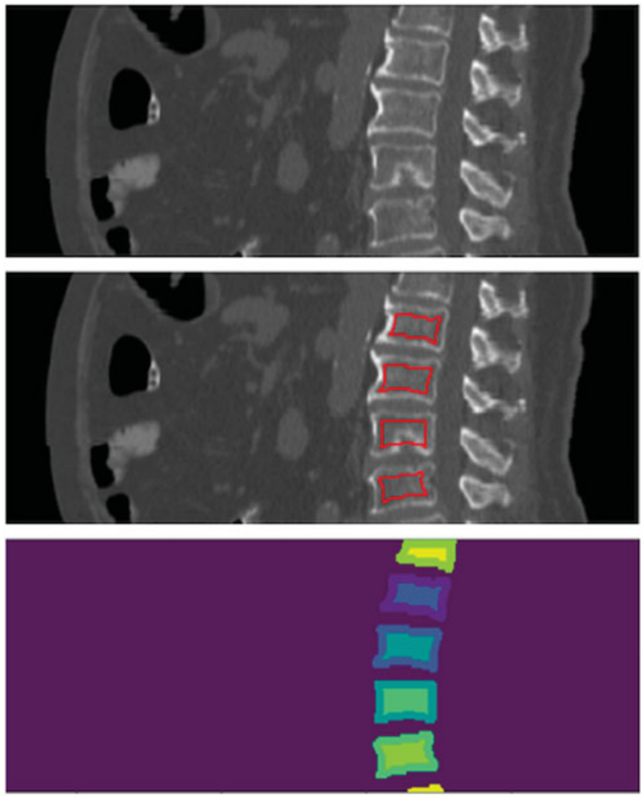

Figure 2. Automatic sagittal reconstruction of CT scan for identification of vertebral bodies and further delineation of cortex and medullary bone compartments (*Zebra Medical vision Ltd.*). This segmentation is used for detection of fractures and for automatic calculation of the trabecular bone density.

deep learning) while each filter creates an output score which is the input score of the next layer until a final result is achieved. The result can be a diagnosis, outlining of a polyp in an image, etc. (Figure 1).

AI in radiology

AI is gaining popularity in medicine, with the widest application being in the field of radiology. This is due in part to the remarkable progress in image-recognition tasks, which in recent years has seen growth in the amount of sufficient digital data accumulation and availability as well as significant computational power. Combined with the increase in access to radiological exams, the resultant increased workload for radiologists and a shortage of trained experienced radiologists, AI and its capabilities has been driven to the frontlines in medicine. Multiple groups have developed image processing and computer vision algorithms to enable faster diagnosis [5–7], enhance visualization of pathologies [8–12], alert emergency situations [13–15] and assist in the critical manpower deficiency problem [16,17]. The development, however, should not be with the intent to replace the human radiologist, rather to augment and provide applications which highlight information that would otherwise not be obtained by human vision, or provide knowledge not widely available in a shorter amount of time [18]. A platform that highlights intracranial bleeding for radiologists is already CE approved and was developed by MaxQ-AI Ltd. (Tel Aviv, Israel). This start-up company from Israel is focusing on real-time decision support tools to improve clinical outcomes in acute medical scenarios [19]. They process three-dimensional CT data, detect intracranial bleeding and highlight the bleeding area for the reader. Taking this concept one step further, Viz.ai Inc, a spinoff company from Stanford University, San Francisco, is aiming to decrease the time to treatment once a CT scan was performed. This FDA approved platform can detect large vessel occlusion (LVO) in the brain causing stokes. The system can analyse the images and when there is a suspected LVO, a text message alert is sent to the radiologist/neurologist bypassing the usual workflow of manual image post processing, manual read and ED patient care [14].

Integration of such algorithms into the PACS (picture archiving and communication system) is therefore warranted. Algorithms by a start-up company Zebra Medical Vision Ltd. (Shefayim, Israel) is already running in PACS systems of more than 50 hospitals globally and has analysed more than one million patient scans [20]. Current capabilities include automatic detection of liver, lung, cardiovascular and bone disease. For example, automatic detection of vertebral fractures is performed using a set of algorithms which run on chest and abdomen CT scans (Figure 2). The spinal column is segmented and sagittal patches are extracted using CNN, followed by a prediction of the presence of vertebral fracture [7]. Similar algorithms exist for detection of calcium in the coronary arteries from non-contrast chest CT scans which predicts cardiovascular events and mortality [21,22], as well as algorithms detecting osteoporosis which calculate bone mineral density similar to the DEXA score (Dual Energy X-ray Absorptiometry) [23].

Using deep learning for diagnosis has been proven to be as good as if not better than human performance in some areas such as lymph node metastasis detection and mammography malignancy detection [6,10]. Detection of meningiomas in MRIs e.g. shows great potential and value for the application of AI. Laukamp et al. used a multi-parametric deep learning model applied to MRIs for the detection and segmentation of meningiomas as compared with manual segmentation. Using a training set of 249 preoperative MRI glioma cases and segmented different tumour classes as defined by the brain tumour image segmentation benchmark (BRATS benchmark), the program was able to detect 55 of 56 gliomas accurately as compared with results from manual readings by two radiologists [9].

IBM research

In 2011, IBMs computer system Watson beat the two highest ranked players on the classic television game show “Jeopardy!”, in which answers are given first and the contestants must determine the questions. Following this success, IBM research took the challenge to modify the Deep QA technology towards medicine [24]. The driving force for this adaptation was the high medical and medication error rates [25–27], as well as the high cost, and low productivity in this area. The concept was to collect information, organize it and provide insights to improve clinical decision making. The first task of gathering evidence proved to be a huge challenge having different vocabularies and coding systems used by different sources which must be harmonized and transformed into usable evidence in the clinical setting. Once this was achieved, data of patients could be gathered and stored according to their symptoms, lab tests, findings, patient history, family history, demographics, current medications, and many others. One option then is to use this clinical content management database, together with specialized advanced analytics and compare it to the patient in question. When this patient is classified with similar databased patients, a diagnosis could be suggested as well as treatment protocols, outcomes and prognosis, all based on evidence-based medicine such as RCTs (randomized controlled studies), best practice guidelines, electronic medical records (EMRs), public health records etc. [11,28–31]. In such a method, Bakkar et al. were able to identify five additional RNA- binding proteins that are altered in ALS (Amyotrophic Lateral Sclerosis) and eventually improve diagnosis of this disease [32].

Similarly, other machine learning based studies demonstrate the benefits of incorporating AI into EMRs, improving diagnosis rates of patients. As the case with hyperparathyroidism, a significantly underdiagnosed condition due to under recognition, with only 50% of patients referred for the necessary surgery [33]. Somnay et al. in a multi-center retrospective study, using a labelled training set and 10-fold cross validation found that AI correctly identified 97% of cases. The diagnosis was based on access to patient medical records which included age, gender, calcium, phosphate, PTH, vitamin D, and creatinine levels. This study suggests that implementation of ML into EMRs may in fact improve patient diagnosis and thereby improve patient care and outcomes.

Despite showing great promise in the field of AI in medicine, IBMs Watson decision support system was recently called into question. As with any medical device, it is not uncommon during the clinical trial period to make changes and adjustments in order to further develop the product. Clinical decision making support systems like Watson are still in a relatively early stage of clinical trials and with experience, alterations will need to be made. Such alterations should include transparency so that the user can understand the basis of the recommendation. The system should also be user-friendly and intuitive with no major training required to use or analyse the results [34] Additionally, it is of importance to remember that these systems are support systems and not meant to replace physicians or their knowledge, but rather to augment it.

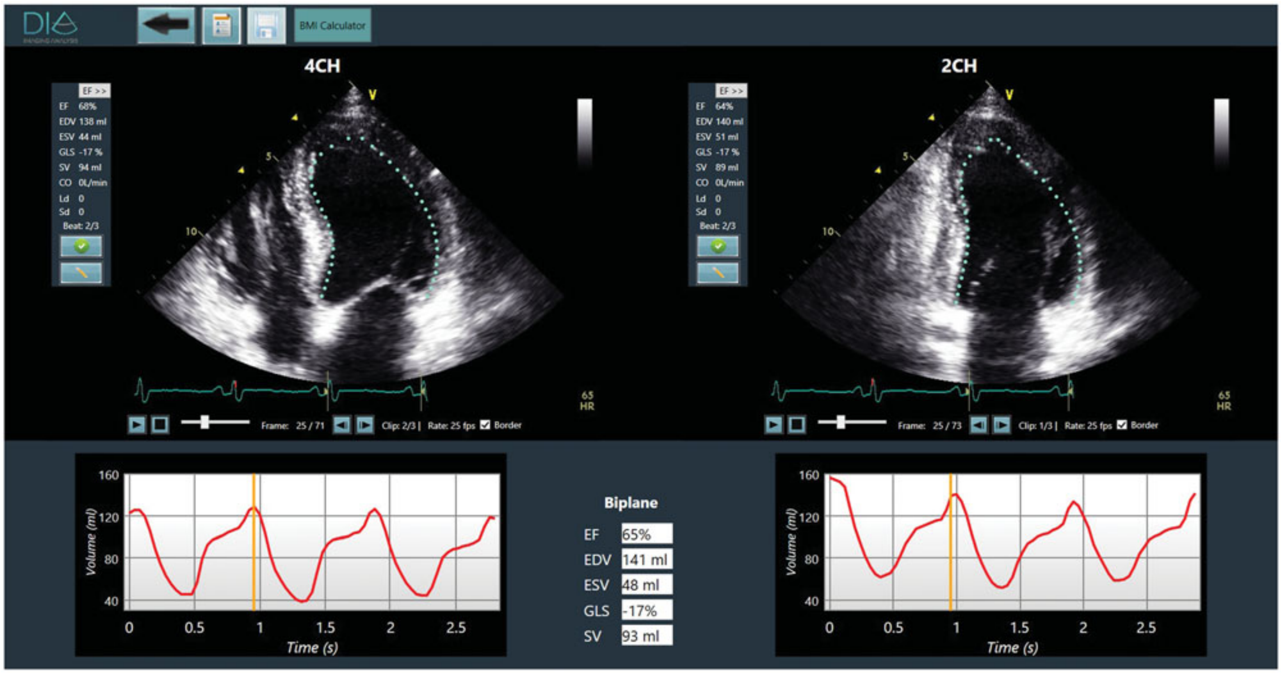

Figure 3. A representation of an echocardiography software to analyze and automatically evaluate ejection fraction (*DiA imaging Analysis Ltd.*).

AI in oncology

Breast cancer diagnosis and staging are areas in which AI application may actually prove to provide better results than human readings. Somashekhar et al. demonstrated that machine learning is reliable for the diagnosis of cancer [28]. In their double-blinded validation study, Watson was found to have a 93% concordance rate with an expert multidisciplinary tumour board on recommendations regarding breast cancer treatments. In a study by Bejnordi et al. [10], using a training set of 129 slides (49 with metastases to lymph nodes and 80 without), when compared with 11 pathologies, the algorithm actually achieved better diagnostic performance. Additionally, the pathologists required 30 h for assessment of all 129 slides, while the running time of the algorithm was presumed to be negligible.

In the detection of lung cancer, AI algorithms have been shown to be more effective than a human. In a study using 2186 stained histopathology whole-slide images of lung adenocarcinoma and squamous cell carcinoma, Yu et al. demonstrated the accuracy of AI for pathological diagnosis [35]. Their results suggest that AI can accurately predict the prognosis of lung cancer patients and thereby improve patient care via determination of oncological treatment.

In dermatology the diagnosis and classification of skin lesions is primarily based on visual images, therefore AI has shown promise. In their study Esteva et al. used a single CNN, trained form images alone using pixels and disease labels as inputs to classify various skin lesions. Using a data set of 129,450 clinical images, they tested its performance against 21 board certified dermatologists on biopsy proven clinical images. They used two groups of images representing the most common cancers as well as those with highest mortality (keratinocyte carcinomas versus benign seborrheic keratosis and malignant melanomas versus benign nevi). In this study, AI was concordant with the experts in all cases across both tasks, thus demonstrating that AI is as competent as human dermatologists [5].

AI in cardiology

The application of ML and AI results in faster interpretation and diagnosis in many areas of cardiology. Electrocardiogram readings are automatically interpreted, echocardiography with 3D mode cardiac imaging automatically provides measurements of cardiac function (Figure 3), SPECT imaging can automatically determine cardiac perfusion, and cardiac CT angiography can determine calcification of the coronary vessels. Cardiac MRI can perform automatic segmentation as well as measure perfusion and blood flow [36]. The integration of AI into EMR has been shown to be effective in the reduction of mortality via early detection of heart failure. This is due to the ability of AI to perform a longitudinal evaluation of data to find patterns and thereby determine predictors for heart failure [37].

When including AI in the decision making process as to which interventional procedure patients with angina should undergo - either a coronary artery bypass grafting (CABG) or percutaneous cardiac intervention – AI, utilizing access to patients' EMRs, had a better predictive value resulting in reduced mortality [38].

AI in gastroenterology

Diagnosis and treatment in gastroenterology are based on flexible endoscopic images of the stomach duodenum and colon. Early detection of cancers is a key factor for patient care and screening regimens are implemented worldwide. In order to improve detection in a clinical exam that lasts a few minutes only, and is performed numerous times a day an AI based system was developed [39]. The CADe system (computer aided diagnosis system) alerts the endoscopist to abnormal findings on the screen by highlighting the area of abnormality. After focusing on the abnormality and switching to NBI (narrow band imaging) view, the CADx system can define the endoscopic images further to a real time suggested diagnosis.

The CADe was shown to have a 94% detection rate of colonic polyps [40]. This study provides good evidence for the ability of AI based platforms to fill in the gaps between experienced endoscopists and those less experienced providing accurate and faster diagnosis.

The CADx system was shown to detect early gastric and colonic cancers in endoscopy. It was demonstrated to have a 96.3% precision in the detection of early gastric cancers with a sensitivity of 96% and specificity of 95% [41].

AI in ophthalmology

Diabetic retinopathy (DR), affects 38% of the 400 million people worldwide who suffer from diabetes. This condition affects the tiny blood vessels which supply the retina and may cause haemorrhage or retinal detachment, leading to reduced vision and blindness [42,43]. The American Academy of Ophthalmology recommends screening of this huge patient population to diagnose DR in its early stage [44].

The application of AI and deep learning for the detection of diabetic retinopathy has been proven to be effective for earlier diagnosis. In their study Gulshan et al. used two validation sets of 9963 and 1748 images and found a high sensitivity and specificity rate when compared with seven board-certified ophthalmology experts. One may conclude from this study that deep learning has significant potential in the field of ophthalmology in the detection of diabetic retinopathy and macular edema from retinal images; however, further study is needed [8].

Cloud-based AI

The concept of cloud-based AI is an idea of providing artificial intelligence as a fee-for-service allowing the customer access to continuously updated algorithms. Another advantage is availability of service regardless of hardware used allowing for interoperability.

Several companies have developed cloud-based AI platforms to assist in a variety of medical applications. Companies such as Zebra Medical Vision Ltd, Arterys Inc. (San Francisco, CA, USA), and VIDA Diagnostics Inc. (Coralville, IA, USA) provide cloud-based AI services to assist in the analysis of lung diseases, cardiac imaging processing, liver imaging and bone health [20,45].

AI in surgery

While computer science has already entered the operating room in the form of robotic assisted surgery, it is not associated with artificial intelligence. Indeed, the technology available today augments the surgeon's vision (3D cameras, near infra-red imaging) and mechanical capabilities (intuitive instrument articulation, tremor elimination and movement scaling), but it fails to translate into improved patient outcome. Consensus documents from the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) and the European Association for Endoscopic Surgery (EAES) regarding robotic assisted surgery [46,47] show no improvement in patient outcome when comparing standard laparoscopic surgery to robotic assisted surgery. Expectations are high therefore for improved patient care when AI is incorporated into the operating rooms. Artificial intelligence can be applied in the OR in many forms: anesthesia support [48], improving operating room workflow for more efficient time management and improved patient safety [49], as well as monitoring of surgical instrumentation. OR.NET [50] is a new initiative aiming to integrate the operating room devices into one common interface enabling communication between devices to improve workflow and increase patient safety.

The ambitious vision of having AI assistance in an actual surgery is still in its infancy. The concept, however, of learning from experience is more than true in surgery. The more surgeries one performs and the more anatomical variability one encounters, the better anatomical understanding the surgeon has, as such they can perform safer and faster surgery. The value of incorporating AI in surgery is anticipated to improve precision, increase safety, reduce man power, allow for reproducibility and may even allow for some autonomous functions. Misconceptions that push the brakes for this direction, however, are based on the illogical fact that a machine will be in charge of a human life and that mechanical failures in the operating room may result in death. The reality is that AI is already incorporated in our daily lives and in charge of large numbers of human lives every day in the form of mass transportation by automatic train operation in major cities, as well as commercial aviation, and most recently self-driving cars. Commercial aviation is heavily automated and planes are flown by automatic pilots with human control just for three to seven minutes per flight in the new Airbus and Boeing planes [51]. AI software, therefore, is already in charge of millions of travellers each year 30,000 feet up in the air and having similar technology assisting surgeons operating a single patient is inevitable. For this to happen, there must be an evolution of thought that AI can assist a surgeon not only by enhancing motor skills, but also augment the surgeon's thought process and knowledge, which will improve patient outcome.

Summary

Artificial intelligence is a technology that is rapidly being adopted in many industries primarily to improve performance, precision, time efficiency as well as to reduce cost. In medicine this technology translates into improved patient care via earlier detection and diagnosis, improved workflow, thus reducing medical errors, reducing medical costs, as well as reducing morbidity and mortality.

Machine learning is not meant to replace human physicians, but rather assists or augments the medical care. The number of radiology scans is continuously increasing while the number of radiologist is not. AI assistance in this area can reduce the time frame from exam to results due to faster readings as well as 24/7 working capability. In addition, AI software is not encumbered by human issues such as fatigue or other environmental interruptions that may slow it down or reduce its accuracy. The increased workload in pathology combined with the insufficient manpower in this area may also gain from incorporating AI into the workflow. AI can perform the tedious work of evaluating morphology and assessing quantitative tasks such as the number of mitoses per high power field. Following this preliminary AI evaluation, the pathologists could utilize the data to determine diagnosis rather than dealing with time-consuming tasks. This in turn will provide subjective, more quantitative, reproducible results, thereby reducing variability.

Video-based AI software in gastroenterology will assist in the identification of pathologies that might otherwise be missed by humans, preventing misdiagnosis and promoting earlier diagnoses. The concept of AI alerting the human physician to a specific field of an image which might otherwise be overlooked can improve patient outcome, thereby shortening the learning curve of the less experienced gastroenterologist. In surgery, the next trend of AI application may be via the introduction of laparoscopic surgical assistants that can identify anatomical variances similar to AI applications in GI. It is important to note, however, that contrary to popular belief the human physician role will not be eliminated by the incorporation of AI into medicine or surgery. Quite the contrary, AI augmented medical systems will serve to improve workflow, provide safer more consistent more quantitative results grounded on knowledge – based decisions.

The road to implementing AI is still long, fraught with various issues to be addressed along the way, including FDA approvals, ethical issues relating to data sharing, as well as addressing misconceptions in the public relating to AI. The concept of using AI in medicine should be as a decision support system with the final action being from humans.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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