Artificial Intelligence in Ophthalmology: Opportunities & Challenges

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Introduction

Ever since a handful of scientists coined the term in Dartmouth in 1956 (1), Artificial Intelligence (AI) has been the locus of innovation in the scientific world for decades. With its capabilities and potential gradually being unearthed by scientists, it can be safely said that AI is a game-changer in the contemporary scenario. Medicine and healthcare are the latest advocates of AI's revolutionary potential and image recognition & analysis seem to be one of its strongest fortes (2).

Artificial Intelligence: An Efficient Tool to Augment Human Intelligence

AI is best described as an efficient implication of an amalgamation of ideas fed into a system, in order to augment human intelligence(3). These ideas are meant to mimic a human brain and are fed into the system in terms of algorithms and neural networks. These form the basis of two pivotal aspects of AI: Machine Learning (ML) and Deep Learning (DL) respectively (1) (4).

ML uses datasets / algorithms which may comprise of past experiences or different levels of information needed to assess a condition / situation, aimed at optimizing a performance criteria(4). These datasets are used to 'train the computer', build a model of complex relationships, analyse a given situation and find the best possible solution for that particular situation through repeated learning and assessment of the same sets of data.

DL, on the other hand, is an advanced subset of ML that uses neural networks comprising of multiple layers of representation-learning & abstraction between the input and final output with higher precision(5). Since DL involves huge sets of data and takes into account every possible permutation and combination between these, constantly learning from the repetitions and self-corrections before arriving on a reasoned conclusion on any given case, the accuracy quotient of such analyses becomes higher (6).

Artificial Intelligence in Ophthalmology: Opportunities & Potential in Different Ophthalmological Conditions

AI finds obvious applications in ophthalmology where the amount of data to be analysed are complex and the number of patients to be analysed is huge, but the outcomes are simple and well-defined.

DL has always shown significantly robust skills in medical imaging analysis as it involves constant refining, weighting and comparing of details in the images as a part of the constant learning process, in order to accommodate every piece of information possible (7) (8). The most common DL models are convolutional neural network (CNN) and massive-training artificial neural network (MTANN), both of which analyze pixels and groups of pixels in fundus photographs, or 3-dimensional "voxels" in Optical Coherent Tomography (OCT) images to get an appropriate output(3) (9) (10) (11).

The most common conditions which are being managed with the help of AI include,

- Diabetic retinopathy (DR)
- Age-related Macular Degeneration(AMD)
- Retinopathy of Prematurity (ROP)
- Glaucoma, cataracts and other anterior segment diseases

DR & AI

DR has evolved to be a hotspot for AI. With more than 400 million diabetics worldwide, DR is touted to be one of the leading causes of blindness among working-age people (10). The overall prevalence of DR is 34.6%, with 7% vision-threatening diabetic retinopathy (5). DR being a global health burden, teleretinal screening programs employing DL based imaging scans either using wide-angle fundus photography or OCT or executing multimodal image screening have garnered praise among ophthalmologists. A host of studies have been reported by various ophthalmologists who have implemented DL algorithms for diagnosis of microaneurysm, haemorrhage, exudation, cotton-wool spot and neovascularization among DR patients. Some of the algorithms used in this respect included morphological component analysis (MCA), Lattice Neural Network with Dendritic Processing (LNNDP) & k-nearest neighbour (kNN) (2) (10).

A potential benefit with AI-enhanced diagnosis is the sheer increase number of patients who get screened and receive an instant report on their diagnosis. This not only gives them an edge in terms of early initiation of treatment but also imparts educational insights to the patient immediately after scanning, which motivates them to adhere to their treatment regimen and subsequently increases compliance(7).

DL algorithms for DR detection have been reported to have higher sensitivity (~97%) as compared to manual efforts by ophthalmologists (~83%). Adding credibility to AI's potential in screening DR, tech-giant Google (Health) has reported to have created a dataset of 128,000 images fed by scientists to train a DL network for DR (4).

Google Brain's AI system was evaluated with the help of two test runs using fundus photos from pre-diagnosed DR patients by expert physicians (The EyePACS-1 data set and Messidor-2 data set). These tests resulted in high sensitivity values of 97.5% and 96.1% in each practice set, and specificity values of 98.1% and 98.5%. This has also prompted Google Brain to partner with Aravind Eye Care System in India to integrate their AI system as part of their global DR care initiative (12).

A recent study evaluated the performance of Medios- an offline artificial intelligence algorithm to detect RDR (defined as more than mild NPDR, with or without CSME) on images taken on Remidio's Fundus on Phone NMFOP10 (Remidio Innovative Solutions, India). This study analysed three segment fundus images from a total of 231 patients with Diabetes Mellitus visiting various dispensaries under the municipality of Greater Mumbai (13). The Medios AI was trained on images from the Remidio Fundus on Phone and is able to instantly provide a binary classification of NO DR or RDR, by running the neural network right on the smartphone, without any need for internet access.

The results showed high sensitivity and specificity of an offline AI algorithm in grading RDR with values of 100% and 88.4% respectively and of any grade of DR as 85.2% and 92% respectively, when compared to manual reports generated by trained ophthalmologists(13). These are higher than the FDA mandated minimum superiority end points of 82.5% Specificity and 85% Sensitivity for detection of RDR.

AMD & AI

Age-related Macular Degeneration (AMD) is a chronic, irreversible condition, being one of the leading causes of loss of central vision in patients over the age of fifty. AMD is characterised by characterized by drusen, retinal pigment changes, choroidal neovascularization, haemorrhage, exudation and even geographic atrophy(10).

DL systems can be effectively used to identify anatomic OCT-based features aiding in early diagnosis, by predicting the timing and extent of disease progression(12). The sensitivity using such methods varies between 87-100% with very high accuracy. Multimodal interventions, combining spectral domains of OCT images with deep learning about different aspects of AMD, like the macular fluid quantity of neovascular AMD (nAMD), the retinal layers segmentation of dry AMD and the quality of intra-retinal fluid in patients with wet AMD, have also yielded accuracies of 100% post iterative training and validation.

ROP & AI

ROP is a leading cause of childhood blindness all over the world, but it can be treated effectively with timely diagnosis and proper treatment. Blindness can be prevented if ROP with plus disease or retinopathy in zone one stage 3 even without plus disease is treated on time. Infants with pre-plus disease require close and repeated observation. However, repeated observations and testing requires huge manpower and energy and this is where AI could make a huge impact in improving the efficacy of ROP treatment (10).

Researchers at The Massachusetts General Hospital & OHSU have been working on combining two existing AI models to create an algorithm, and making reference standards to train the same, respectively. On comparing this algorithm with the analysis by trained ophthalmologists, its accuracy was detected to be better (91%) than that by the experts (82%)(14).

Other studies have reported the automatic identification of ROP through algorithms that focussed on two-level classification (plus or not plus disease) some of which were based on tortuosity and dilation features from arteries and veins, with an accuracy of 95% accuracy, which is comparable to diagnosis made by experts(10)(15).

AI in Glaucoma, Cataract and other anterior segment diseases

Cataracts lead to clouding of the lens and Glaucoma damages the optic nerve, which can cause irreversible blindness(10). A chronic condition like Glaucoma, although irreversible, their progress can be significantly lowered by early diagnosis and effective treatment.

Slit-lamp images have been fed into CNN algorithms to evaluate the severity of nuclear cataracts. On further iteration and validation, their accuracy was found to be 70% against clinical grading. Significant progress has also been made in terms of identification of paediatric cataracts in terms of achieving exceptional accuracy and sensitivity in lens classification and density(10). ML algorithms like Radial Basis functions or support-vector machines have improved lens implant power selection prior to cataract surgeries. They have been useful in conducting anterior segment area analysis like that in corneal topography scans and intra-ocular lens power predictions, to name a few(4).

Glaucoma detection primarily depends on the intraocular pressure, thickness of retinal nerve fiber, optic nerve and visual field examination. Researchers have devised an algorithm to classify the optic disc of open-angle glaucoma from OCT images. This algorithm has reported an accuracy of 87.8%(10). ML algorithms to identify glaucoma in its early stages assessing the cup disc ratio in fundus images or the thickness of the retinal nerve-fiber in OCT images have reported accuracies ranging between 63.7% and 93.1% depending on the input images.

Potential Pitfalls

Despite all that is right with AI, there are a few potential pitfalls that one needs to weigh out before being prompted to blindly trust its decisions and diagnoses(7).

- AI algorithms would need equally skilled manpower (annotators) to provide accurate ground truth for training images
- The basis of identification and diagnoses made by AI algorithms is mechanical, and some amount of human intervention is always necessary for detecting each and every feature or variation of a disease; AI will always miss

things it is not instructed to look for, something which a human reader will not

- The 'Black Box' mode of learning where what goes on inside a neural network or ML algorithm remains unclear, despite familiar inputs and outputs, remains a dubious area; complete clarity is needed for taking accountability for treatment decisions for patients(16)
- An ML algorithm would only be reliable on a population which is exactly similar to the one it learnt from, and whenever there is a slight change in the input data, a whole new set of learning algorithms need to be programmed to maintain the same accuracy

Remidio's Tryst with AI in India

One study reported the use of Remidio's Fundus on Phone (FOP) a low-cost, smart phone-based device was used to screen approximately three hundred DR patients at a tertiary care diabetes centre in Chennai. This device principally contained a portable FDA 510k registered fundus camera, the Remidio NM FOP, consisting of an annular illumination design that eliminated corneal reflections, and it easily combined with any commercially available smart phone to acquire retinal photographs (18). LA-based Eyenuk's EyeArt™ screening software was used to analyse a total of 2408 Remidio FOP retinal images of 301 patients. Grading of these retinal images was done as per the standard International Clinical DR (ICDR) scale. Alongside, the DR-detection algorithm also evaluated the presence of Clinically Significant Macular Edema (CSME) depending on the presence of hard exudates within one disc diameter of the centre of the macula.

The results thus obtained were compared with those prepared manually by ophthalmologists and specialists. The automated AI-assisted software correctly identified 95.8% of patients with retinopathy and 80.2% of patients without retinopathy. The sensitivity for detection of DR, Sight Threatening DR and Referable DR (above 95% for DR, 99% for STDR and RDR) using the EyeArt software when used on retinal images taken with FOP was extremely high and comparable to the Google AI algorithm which showed a high sensitivity and specificity for RDR when used on conventional retinal photography as well(17).

The aforementioned studies only highlight the huge potential and reliability of using AI algorithms on smart phone-based devices, for community-based screening programs

Conclusion

All said and done, the many boons of AI far outweigh its limitations. When used wisely and cautiously, with proper amount of tracking and reporting, AI could most definitely provide the desired output that would help patients to improvise on their treatment regimens and increase adherence and compliance. One should always remember that AI provides the best results only when augmented by skilled human workforce, and not replaced by it.

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