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).

AI 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, hemorrhage, 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 was aimed at evaluating the performance of the Medios AI - an offline artificial intelligence algorithm that can be used on a smart phone without the need for internet infrastructure to connect to the cloud, to detect RDR on images taken on Remidio's Fundus on Phone (NMFOP10). This study analysed a total of 231 patients with Diabetes Mellitus visiting various dispensaries under the municipality of Greater Mumbai(13).

The results showed impeccable 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).

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, hemorrhage, 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 iteration 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, Cataracts and other anterior segment diseases

Cataract and glaucoma are very common diseases in ophthalmology. Cataracts lead to clouding of the lens and whereas Glaucoma damages the optic nerve, which can cause irreversible blindness(10). Conditions like these, although irreversible, their progress can be significantly lowered by early diagnosis and reasonable 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 capture clear and coherent images to be fed as input images
- High computational costs and in-depth training experiences are needed for developing AI algorithms; hence, one might only bear such investments when it comes to conditions with higher morbidity and mortality rates, but not so much for rare diseases
- 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

- A wide range of complex algorithms are necessary to execute AI operations and designing these algorithms is itself, complicated; a slight error in programming could lead to higher levels of damage
- 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

Bangalore-based startup, Remidio Innovative Solutions Pvt. Ltd., have truly revolutionised automated eye-testing for millions of patients in India and abroad. Simplifying healthcare using disruptive technologies being their motto, they have pioneered an automated eye-testing employing the benefits of AI by using economical smart phone-based imaging devices (17).

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 an FDA 510k registered fundus camera consisting of an annular illumination design that eliminated corneal reflection, 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: a truly revolutionary feat that has been brought to the Indian scenario by Remidio.

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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REFERENCES

1. Copel M. The Difference Between AI, Machine Learning, and Deep Learning? | NVIDIA Blog [Internet]. The Official NVIDIA Blog. 2016 [cited 2019 Jan 22]. Available from: https://blogs.nvidia.com/blog/2016/07/29/whats-difference-artificial-intelligence-machine-learning-deep-learning-ai/

2. Lu W, Tong Y, Yu Y, Xing Y, Chen C, Shen Y. Applications of Artificial Intelligence in Ophthalmology: General Overview [Internet]. Journal of Ophthalmology. 2018 [cited 2019 Jan 22]. Available from: https://www.hindawi.com/journals/joph/2018/5278196/

3. (PDF) Deep learning in ophthalmology: a review [Internet]. ResearchGate. [cited 2019 Jan 22]. Available from: https://www.researchgate.net/publication/325471007_Deep_learning_in_ophthalmology_a_review

4. Machine Learning Has Arrived! - Ophthalmology [Internet]. [cited 2019 Jan 23]. Available from: https://www.aaojournal.org/article/S0161-6420(17)31563-4/fulltext

5. Ting DSW, Pasquale LR, Peng L, Campbell JP, Lee AY, Raman R, et al. Artificial intelligence and deep learning in ophthalmology. Br J Ophthalmol. 2018 Oct 25;bjophthalmol-2018-313173.

6. Marr B. What Is The Difference Between Deep Learning, Machine Learning and AI? [Internet]. Forbes. [cited 2019 Jan 23]. Available from: https://www.forbes.com/sites/bernardmarr/2016/12/08/what-is-the-difference-between-deep-learning-machine-learning-and-ai/

7. AI & Ophthalmology: The Pros and Cons [Internet]. [cited 2019 Jan 24]. Available from: https://www.reviewofophthalmology.com/article/ai-and-ophthalmology-the-pros-and-cons

8. Where is Deep Learning in Retina Headed? [Internet]. [cited 2019 Jan 24]. Available from: http://www.retina-specialist.com/article/where-is-deep-learning-in-retina-headed-1-1

9. Artificial Intelligence [Internet]. American Academy of Ophthalmology. 2017 [cited 2019 Jan 23]. Available from: https://www.aao.org/eyenet/article/artificial-intelligence

10. Application of artificial intelligence in ophthalmology [Internet]. [cited 2019 Jan 24]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6133903/

11. Ph.D KS. Massive-Training Artificial Neural Networks (MTANN) in Computer-Aided Detection of Colorectal Polyps and Lung Nodules in CT. Mach Learn [Internet]. 2010 Feb 1 [cited 2019 Jan 25]; Available from: https://www.intechopen.com/books/machine-learning/massive-training-artificial-neural-networks-mtann-in-computer-aided-detection-of-colorectal-polyps-a

12. How AI benefits patients and physicians: Page 2 of 3 [Internet]. Ophthalmology Times. [cited 2019 Jan 26]. Available from: http://www.ophthalmologytimes.com/article/how-ai-benefits-patients-and-physicians

13. NatarajanMD S, Optom A. OfflineArtificialIntelligenceDeployedonaSmartphonetoenableCommunity BasedDiabeticRetinopathyScreening. :15.

14. AI algorithm detects retinopathy of prematurity - EPR [Internet]. European Pharmaceutical Review. [cited 2019 Jan 26]. Available from: https://www.europeanpharmaceuticalreview.com/news/75494/ai-retinopathy-prematurity/

15. Gelman R, Jiang L, Du YE, Martinez-Perez ME, Flynn JT, Chiang MF. Plus Disease in Retinopathy of Prematurity: Pilot Study of Computer-Based and Expert Diagnosis. J AAPOS Off Publ Am Assoc Pediatr Ophthalmol Strabismus Am Assoc Pediatr Ophthalmol Strabismus. 2007 Dec;11(6):532–40.

16. Bathaee Y. The Artificial Intelligence Black Box and the Failure of Intent and Causation. 31:50.

17. Rajalakshmi R, Subashini R, Anjana RM, Mohan V. Automated diabetic retinopathy detection in smartphone-based fundus photography using artificial intelligence. Eye. 2018 Jun;32(6):1138.

18. Sandeep Bhat. Eyenuk Inc.'s AI-based diabetic retinopathy screening software EyeArt™ tested with portable smartphone-based imaging device in new study indicating potential for highly sensitive yet cost-effective mass retinal screening | Eyenuk, Inc. [Internet]. [cited 2019 Jan 30]. Available from: http://eyenuk.com/blog/company-news/eyenuk-inc-s-ai-based-diabetic-retinopathy-screening-software-eyeart-tested-with-smartphone-based-imaging-device/