EDITORIAL

Glaucoma Screening: Is AI the Answer?

Shibal Bhartiya

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"If the only tool you have is a hammer, it is tempting to treat everything as if it were a nail"

Abraham Maslow

Glaucoma, a largely asymptomatic and progressive disease, remains a global healthcare crisis: its prevalence is almost 3.4% between the ages of 40–80 years, with as many as 112 million individuals projected to be affected by glaucoma by 2040.[1] As of date, it is estimated that more than nine out 10 of cases of glaucoma remain undiagnosed, with as many as 12 million people blind due to glaucoma.[2] Glaucoma blindness can be minimized by the timely recognition of a patient's risk of disease and ensuring that high-risk patients remain within the ambit of specialist care.[3] However, glaucoma screening is labor and time intensive, with the accuracy of diagnosis depending not only on the skill of the ophthalmologist but also on the availability and interpretation of long-term follow-up results.

The current recommendations for glaucoma screening, remain equivocal, as much because of lack of infrastructure, both personnel, and equipment, as because of the fact that there is no concrete evidence that the long-term outcomes for subjects who undergo glaucoma screening are better than those who have not been screened. It must be kept in mind that almost all in-person screening protocols have been reported to not be cost effective.[4] Interestingly, a Markov Model analysis by Tang et al. reported that when compared with no screening, combined screening of open and closed angle glaucoma in China, a representative low to a middle-income country, was found to be cost-effective. The cost remained below the WHO cost-effectiveness threshold of one to three times rural gross domestic product, for rural settings, and was considerably less in urban areas.[5] The researchers, however, recommended further evaluation of the cost of acceptance of definitive care among positive screens and also measures to improve the same.

Similarly, an analysis by John et al.[6] evaluated the cost of glaucoma screening in rural India, using the ratio of willingness-to-pay thresholds as per WHO-CHOICE guidelines. They also found community screening to be cost-effective, using a decision analytical model using treatment pathways for both, open and angle closure glaucoma.

The AI Solution: Cheaper, Faster, Better

The world is stepping into the fourth industrial revolution powered by Artificial Intelligence (AI) and Deep Learning (DL) algorithms that use representation-learning methods that automatically process and recognize intricate structures in high dimensional images, without any manual engineering. Its efficacy and accuracy have been proven in many domains, including natural language and image processing, as well as face and voice recognition. These techniques have demonstrated robust classification performance in various eye diseases, especially those dependent on ancillary imaging tests,[7] and have the potential to surpass the performances of trained personnel, especially for tasks related to image classification and pattern recognition.[8]

Salazar et al. have reported that newly developed machine learning classifiers and DL algorithms are capable of autonomously detecting early morphological as well as vision and function changes of[9] glaucoma, using fundus photographs, optical coherence tomography (OCT), and perimetry.[10]

Hood and De Moraes[11] and Ting et al.[12] have reported that computer algorithms may be trained to detect the disks which may be glaucomatous, using a vertical cup disk ratio of 0.7 and 0.8, respectively. Kim et al. used four machine learning algorithms and found that the random forest model has the highest accuracy in classifying glaucoma and healthy eyes,[13] a finding corroborated by An et al.[14]

The esoteric paradigms of predictive health care, especially the problems of glaucoma screening, seem to be the ideal use case scenario for AI and DL algorithms. AI, thus, could very well be instrumental in drafting cost-effective glaucoma screening protocols, assisting in disease detection, assessing of risk of blindness, as well as documenting and predicting progressive structural and functional damage.[15]

Beyond Store-and-forward

The synchronous maturation of multiple digital and telecommunications technologies, and their widespread adoption worldwide, especially during the COVID-19 pandemic, has enabled AI-based tools to enter ophthalmologists' clinics. Removing the need for specialists trained in optic nerve head (ONH) grading on site, along with optimized techniques and instrumentation for imaging of the optic nerve remotely, can dramatically decrease the cost of screening, making it possible even for underserved populations with limited healthcare access and resources.

Tan et al. have postulated that in the Asia Pacific, especially India and China, with high rates of glaucoma remaining undiagnosed,

Department of Ophthalmology, Glaucoma Services, Fortis Memorial Research Institute, Gurugram, Haryana, India

Corresponding Author: Shibal Bhartiya, Department of Ophthalmology, Glaucoma Services, Fortis Memorial Research Institute, Gurugram, Haryana, India, e-mail: shibalbhartiya@gmail.com

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AI-based glaucoma screening can potentially increase accuracy, at a significantly lower cost, and reach hitherto unserved populations for glaucoma screening and diagnosis.[16] This can potentially make glaucoma screening more cost-effective, accessible, and less time-consuming. Better sensitivity and specificity would mean better clinical outcomes and a lesser economic burden of disease management from a public health perspective.

The Actual Cost of Glaucoma Screening

For evaluating the actual cost-effectiveness of any population-based screening protocol, it is important to keep in mind the impact of the screening in terms of health outcomes, and in this case, specifically, the reduced prevalence of glaucoma blindness. Also, the real-world cost of glaucoma screening is not just the unit cost per case detected. It includes the cost of bringing the individual within the care network, first for screening, and then its validation by an in-person consultation with a specialist, loss of man-days at work due to wait times, and duration of tests. It also includes costs related to ensuring adherence: that the individual would remain within the purview of care over time, counseling for ensuring compliance to recommendations of the screening, customized to the unique sociocultural and economic context of the individual, not to mention the cost of care itself. While most of these interventions may be amenable to technological intervention, their efficacy in terms of acceptability, and their synchronicity with AI-enabled screening protocols are yet to be evaluated.

A proof-of-concept evaluation of the Markov model by Xiao et al., in fact, evaluated the budgetary concerns of glaucoma screening to project health outcomes and costs. The authors concluded that screening costs could never be offset by a reduction in disease progression. In fact, they also recommended further evaluation of the cost-effectiveness and cost-utility of AI-assisted glaucoma screening, before the techniques were adopted by public health decision-makers.[17]

Experts agree that glaucoma screening may not be cost-effective,[9] and may only be considered so in conjunction with screening for the other big four: refractive error, cataract, diabetic retinopathy, and age-related macular degeneration (ARMD). A comprehensive screening program, if aided by AI, can mean significantly reduced costs and time, with significant improvements in yield and clinical outcomes. Further evaluation of these multidisease screening programs may provide useful insights for future public health policies.

Challenges for Validation and Clinical Implementation

The potential challenges with DL application in glaucoma screening are several:[18] technical, ethical, methodological, regulatory, social, and infrastructural.[19] These include reliability and explanation of algorithm results, medicolegal and ethical concerns,[20] acceptability of the AI "black-box" algorithms, standardization and quality assurance,[21] as well marketing of AI Systems as Medical Devices.[22]

Furthermore, even though AI has demonstrated capabilities in delineating the structure-function correlation in glaucoma, there has been limited success in using complex statistical modeling, in detecting glaucoma progression, as also predicting it.[23] To date, no AI models have been approved for clinical use for diagnosis or screening, even though experts are hopeful of a breakthrough in their use for both, diagnosis and the subsequent management of glaucoma.

There will also be a continuing need for postmarketing surveillance as these self-modifiable, and trainable systems can develop beyond the existing approval and licensing criteria. Concerns around data privacy and protection, data de-identification and re-identification, as well as the patient's rights[24] of explanation, and to be forgotten- are real and need to be addressed.[25]

AI is a Tool– Not a Panacea

That said, there is no doubt that AI-enabled identification the individuals who may be at risk of glaucoma can decrease the burden of screening tests by healthcare professionals, saving both cost and time. This can increase the feasibility and viability of any glaucoma screening program manifold, decreasing its costs and logistical complications.

However, it may be a little too early to celebrate just yet, and there may be considerable flaws and consequences to its blind adaptation. The universal standardization for both, sensitivity and specificity, as well as the ethical and regulatory compliances for the optimal implementation of AI in glaucoma screening, are yet to be established. Moreover, it is important to remember the cognitive biases of AI- data sets curated by humans depend on the values and judgments of those developing the AI models, those implementing it, as well as the end users.

Artificial intelligence is a powerful tool, one as powerful as the hands that wield it. In the context of glaucoma screening, AI may not be the solution unto itself just yet; but it has shown great promise. It has proven itself to be a promising efficiency tool for several aspects of glaucoma screening, and it is for the best among us use it to its fullest current capabilities and provide feedback to the AI experts so that they can rewrite and retrain the models.

What use is a New Baby?

Doctor Benjamin Franklin excitedly watched the magical ascension of the first balloon from the Champ de Mars, in Paris, when an unknown cynic asked the one question that plagues all that is new to mankind—what good is it? Dr Franklin replied: "What good is a newborn baby?"[26] an apothegm that has continued to resonate through time.

We are beyond the new baby stage for AI as a tool in glaucoma, and so it is best to commit it to the care of the best glaucoma practitioners who can help it grow and achieve its fullest potential. Without a doubt, there must be continued research into its responsible application in clinical practice, along with a simultaneous exploration of alternate solutions, for the best possible clinical outcomes.

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