Current and Future Implications of Using Artificial Intelligence in Glaucoma Care

INTRODUCTION

The use of artificial intelligence (AI) has recently shown tremendous promise in the field of glaucoma. Several studies have already shown success in the use of AI for glaucoma diagnosis as well as monitoring of disease progression.

Applications of AI in ophthalmology began with machine learning (ML) techniques which required expert ophthalmologists to label individual clinical features and severity to develop the AI solutions, which were then used to train those same AI algorithms. Deep learning (DL) is a newer model of AI which has the option of external labeling depending on if the program is trained through supervised or unsupervised learning. Supervised learning includes using a completely labeled dataset to train the algorithm while unsupervised learning involves unlabeled data with the hopes that the DL will discover a structure or pattern to the data.[1,2]

CURRENT USES

Automated evaluation of electronic health records

The adoption of electronic health records (EHR) has positively transformed ophthalmic research by providing vast amounts of accessible, longitudinal data regarding patient care and disease progression.[3] However, the heterogeneity of EHR patient data can make interpretation difficult and requires a variety of extraction and predictive modeling techniques.[3] In recent years AI-based techniques have shown great efficiency in predicting risks of cataract surgery complications,[4] the diagnosis of age-related macular degeneration (AMD),[5] and suggesting the use of predictive models to interpret EHR data. As glaucoma has become increasingly prevalent worldwide, the need for AI to perform risk stratification and monitor disease progression has become attractive.

Glaucoma diagnosis

Glaucoma is one of the leading causes of visual impairment, along with diabetic retinopathy and AMD, all of which are driven by the increasing aging population. Although AI is being used in diabetic retinopathy, refractive errors, retinal detachment, ocular cancers, retinal vascular occlusions, retinopathy of prematurity, and AMD, its use in glaucoma is currently limited.

In clinical practice, the corresponding visual field defects of glaucoma can be detected in various ways (static vs. kinetic; automated versus manual, etc.), but the interpretation of these reports is rather challenging. Patients with early-stage glaucoma may be missed due to misinterpretation of the reports by nonspecialists.[6] Utilizing AI techniques to either detect glaucomatous eyes, especially early-stage eyes, would be vital and could reduce the number of missed patients.

DL algorithms have been shown to demonstrate accuracy in either identifying glaucomatous eyes or predicting the presence of glaucoma. Maetschke *et al*. used a DL approach that classifies eyes as either healthy or glaucomatous from raw, unsegmented optical coherence tomography values and found that this method achieved favorable accuracy to traditional, manually designed feature-based approaches.[7] Similarly, Asaoka *et al*. constructed and evaluated a DL model which achieved a comparable area under curve (AUC) value to the aforementioned model.[8] The pretraining data included 4316 optical coherence tomography images from 1371 eyes with open-angle glaucoma and 193 normal eyes. The training data included images from 94 eyes of 94 patients with early open-angle glaucoma and 84 eyes of 84 normal individuals.[8] Li *et al*. also developed a DL algorithm which achieved comparably higher accuracy (AUC of 0.986) with a sensitivity of 95.6% and specificity of 92.0% for detecting referable glaucomatous optic neuropathy.[9] All of these DL models are evidence that AI is able to detect glaucomatous eyes, even early-stage ones, to a high degree of accuracy. The implementation of AI models such as those above could greatly increase the efficacy in diagnosing patients.

iGlaucoma was a smartphone, cloud-based glaucoma detection tool that used a multimodal visual field-based DL algorithm, with a performance accuracy exceeding that of six general attending ophthalmologists.[6] Alongside its accuracy, its accessibility as an iOS and Android-compatible application opens a gateway to potential home detection systems for glaucoma. iGlaucoma was also faster than the general ophthalmologists, which can prove beneficial in faster and more widespread detection of glaucoma.[9] However, the misdiagnosed cases by iGlaucoma should be addressed. False negatives were primarily due to glaucoma with preperimetric changes or peripheral defects, and false-positive results were mostly caused by cataract.[6] Even with the misdiagnosed cases, the DL algorithm outperformed general ophthalmologists overall and is a multimodal approach compared to many DL algorithms which tend to be trained using only one glaucoma parameter. Models able to incorporate multiple glaucoma parameters may fare better in both diagnostic accuracies.

Monitoring glaucoma progression

AI is also well suited to identify glaucoma progression, especially due to the program's ability to not only incorporate changes over time but to also have the potential to monitor those changes and alert physicians about them. Medeiros *et al*. demonstrated a DL approach that can continuously predict estimated retinal nerve fiber layer (RNFL) thickness, which can be used to track and predict the progression of glaucoma.[10] Similarly, Kim *et al*. used four ML algorithms to evaluate RNFL thickness and visual field changes, both of which may predict disease progression.[11] Both models achieved comparable accuracy and model performance.

FUTURE APPLICATIONS AND BENEFITS

As AI is avidly being used for other ophthalmologic conditions, adapting AI programs to detecting and monitoring glaucoma is a logical next step.

In order to improve the early detection of glaucoma, AI that can diagnose the disease in patients with myopia or brain tumors would be highly beneficial. The current diagnosis of glaucoma in these patients is difficult due to their eye shapes and visual field defects. However, if an AI program was able to detect the disease, treatment could then be initiated immediately and progression slowed.[10] Along with detection, if an AI algorithm was able to measure the RNFL thickness accurately, the diagnosis would be made more effective, as that is the most common parameter used for glaucoma diagnosis.[12,13]

AI should also be used to predict glaucoma progression for patients as mentioned earlier. Kalman filtering is a forecasting method that has been used for the past 50 years in fields such as spacecraft, planes, or satellites to help automatically control their systems.[14] Recently, Kalman filtering has been used in a clinical setting to help predict disease progression. Three studies all used Kalman filtering to predict glaucoma progression for patients.[15-17] One was able to detect the progression of glaucoma 57% earlier than if they had used a yearly monitoring system.[15] The next was able to accurately predict the progression of glaucoma in normal-tension glaucoma patients, and the last study used Kalman filtering to target intraocular pressures for their patients.[16,17] This personalization of care would be highly beneficial for patients and increase the bond between physician and patient.[18]

If AI is developed with higher specificity and sensitivity, there will be fewer clinic visits by individuals who do not have glaucoma and this itself can allow for a more efficient use of healthcare resources as an added benefit.[12] Alongside this, the centers for Medicare and Medicaid Services have finalized plans to reimburse healthcare providers for telehealth and remote patient monitoring services. If AI is implemented for patients with glaucoma, there may be an added incentive for healthcare providers to utilize these methods.[19]

There is also an added benefit of using AI in more rural areas. In these resource-limited areas, specialists tend to practice in tertiary hospitals with patient referrals from a wide geographical basis. If an asynchronous teleophthalmology platform is introduced, this may reduce false positives as well as patient travel time from rural settlements to the nearest specialist.[1]

Limitations

Although AI's application for glaucoma is being heavily researched, there are still limitations with both the algorithms being used and the implications of using AI that need to be addressed.

A set standard for diagnosis has not been set between algorithms and this poses a problem in differentiating between eyes that truly have a disease or not. It is also difficult to compare the accuracy of the algorithms as they all have differing training criteria and methodologies to them. Large-scale population-based algorithm validation is needed to implement these algorithms in the clinical setting.[12]

The way a deep ML approach is trained can be a limitation as well. Studies have used methods where human graders were asked to label photos for glaucomatous damage, and that labeling was then used as the reference standard. If this is the case, the mistakes that the human graders may have made would then be continuously replicated by the approach itself. [10]

Similarly, neural network performance is affected by the sets used to train it. The sets need to be well balanced with both normal and glaucoma-affected eyes as well as severity and location. The sets should also be large and varied by the criteria above.[12]

The quality of the images used to train the algorithms is also a limiting factor. DL algorithms require high image quality to accurately predict outcomes.[18]

Another area of concern is false negatives of glaucoma in patients with adjunct ophthalmologic conditions. Li *et al*. reported that the most common reasons for false negatives of glaucoma optic neuropathy were when patients had high myopia, diabetic retinopathy, or AMD. The main reason for false positives was having eye cupping present at 55.6%. However, misclassifications with a normal fundus were low at 4.6%.[9]

The relationship between AI and physicians is a burgeoning one and physicians may be reluctant to adopt AI into their practice, whether that is from a lack of trust or a cost perspective. Physicians' bias against AI programs may come from what is known as the "black box" problem where if physicians do not understand the way an AI system makes its decisions, they may not trust it. An example of this was IBM's supercomputer program designed for cancer diagnoses in Watson. Physicians used the Watson program for confirmation of their diagnoses, but if the program disagreed with the physician's diagnosis, the physicians thought the program was incorrect.[20] A way to navigate this distrust could be to use AI systems that are simple enough to be explained to clinicians that use them while still maintaining their accuracy.[20] Another way to bridge the distrust could be to have physicians attend training sessions on AI, if their field would benefit from AI use, so that the complexity of the AI programs could be maintained. Convincing physicians to adopt AI methods may take repeated encouragement and patience.

Diagnostic scalability is a potential limitation for AI as well. The implementation of high-volume screening for glaucoma may result in hundreds of thousands of false-negative or false-positive results.[21] Furthermore, these false results may be skewed toward certain population groups due to scarcity of representative data which then may lead to health inequity. Whether or not this will happen when AI is implemented is unknown, but racial bias in ophthalmologic clinical trials has been demonstrated and in turn, may continue into AI as well.[21]

Finally, to utilize AI for full-scale glaucoma diagnosis, permission for the US Food and Drug Administration and the European Medicines Agency would need to be obtained.[10]

CONCLUSION

Limitations to AI and its use in glaucoma do exist and should be acknowledged. Physician's distrust of AI and cost are two major areas of concern. Physicians should be encouraged to adopt AI methods into their practice; however, AI should not replace the physician's expertise but should be used as a tool adjunct to their experience. Although cost is also a concern, if the implementation of AI is focused on higher-risk groups, it may end up being cost-effective.[12] Finally, there is much promise in using AI in detecting and monitoring glaucoma which makes it a valuable tool in a physician's office and for patient care.

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REFERENCES

1. Gunasekeran DV, Wong TY. Artificial intelligence in ophthalmology in 2020: A technology on the cusp for translation and implementation. Asia Pac J Ophthalmol (Phila) 2020;9:61-6.
2. Thompson AC, Jammal AA, Medeiros FA. A review of deep learning for screening, diagnosis, and detection of glaucoma progression. Transl Vis Sci Technol 2020;9:42.
3. Lin WC, Chen JS, Chiang MF, Hribar MR. Applications of artificial intelligence to electronic health record data in ophthalmology. Transl Vis Sci Technol 2020;9:13.
4. Gaskin GL, Pershing S, Cole TS, Shah NH. Predictive modeling of risk factors and complications of cataract surgery. Eur J Ophthalmol 2016;26:328-37.
5. Fraccaro P, Nicolo M, Bonetto M, Giacomini M, Weller P, Traverso CE, *et al.* Combining macula clinical signs and patient characteristics for age-related macular degeneration diagnosis: A machine learning approach. BMC Ophthalmol 2015;15:10.
6. Li F, Song D, Chen H, Xiong J, Li X, Zhong H, *et al.* Development and clinical deployment of a smartphone-based visual field deep learning system for glaucoma detection. NPJ Digit Med 2020;3:123.
7. Maetschke S, Antony B, Ishikawa H, Wollstein G, Schuman J, Garnavi R. A feature agnostic approach for glaucoma detection in OCT volumes. PLoS One 2019;14:e0219126.
8. Asaoka R, Murata H, Hirasawa K, Fujino Y, Matsuura M, Miki A, *et al.* Using deep learning and transfer learning to accurately diagnose early-onset glaucoma from macular optical coherence tomography images. Am J Ophthalmol 2019;198:136-45.
9. Li Z, He Y, Keel S, Meng W, Chang RT, He M. Efficacy of a deep learning system for detecting glaucomatous optic neuropathy based on color fundus photographs. Ophthalmology 2018;125:1199-206.
10. Medeiros FA, Jammal AA, Thompson AC. From machine to machine: An OCT-trained deep learning algorithm for objective quantification of glaucomatous damage in fundus photographs. Ophthalmology 2019;126:513-21.
11. Kim SJ, Cho KJ, Oh S. Development of machine learning models for diagnosis of glaucoma. PLoS One 2017;12:e0177726.
12. Mursch-Edlmayr AS, Ng WS, Diniz-Filho A, Sousa DC, Arnold L, Schlenker MB, *et al.* Artificial intelligence algorithms to diagnose glaucoma and detect glaucoma progression: Translation to clinical practice. Transl Vis Sci Technol 2020;9:55.
13. Huang X, Sun J, Majoor J, Vermeer KA, Lemij H, Elze T, *et al.* Estimating the severity of visual field damage from retinal nerve fiber layer thickness measurements with artificial intelligence. Transl Vis Sci Technol 2021;10:16.
14. Valade A, Acco P, Grabolosa P, Fourniols JY. A study about Kalman filters applied to embedded sensors. Sensors (Basel) 2017;17:2810.
15. Schell GJ, Lavieri MS, Helm JE, Liu X, Musch DC, Van Oyen MP, *et al.* Using filtered forecasting techniques to determine personalized monitoring schedules for patients with open-angle glaucoma. Ophthalmology 2014;121:1539-46.
16. Garcia GP, Nitta K, Lavieri MS, Andrews C, Liu X, Lobaza E, *et al.* Using Kalman filtering to forecast disease trajectory for patients with normal tension glaucoma. Am J Ophthalmol 2019;199:111-9.
17. Kazemian P, Lavieri MS, Van Oyen MP, Andrews C, Stein JD. Personalized prediction of glaucoma progression under different

target intraocular pressure levels using filtered forecasting methods. Ophthalmology 2018;125:569-77.
18. Mayro EL, Wang M, Elze T, Pasquale LR. The impact of artificial intelligence in the diagnosis and management of glaucoma. Eye (Lond) 2020;34:1-11.
19. Wicklund E. CMS to Reimburse Providers for Remote Patient Monitoring Services; 2021. Available from: https://mhealthintelligence.com/news/cms-to-reimburse-providers-for-remote-patient-monitoring-services. [Last accessed on 2021 Dec 06].
20. Bloomberg J. Don't Trust Artificial Intelligence? Time to Open the AI "Black Box." Forbes. Published September 16, 2018. Available from: https://www.forbes.com/sites/jasonbloomberg/2018/09/16/dont-trust-artificial-intelligence-time-to-open-the-ai-black-box/?sh=4dc121133b4a. [Last accessed on 2022 Jan 11].
21. Evans NG, Wenner DM, Cohen IG, Purves D, Chiang MF, Ting DS, *et al*. Emerging ethical considerations for the use of artificial intelligence in ophthalmology. Ophthalmol Sci 2022;2. [Doi: 10.1016/j.xops.2022.100141].

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