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Commentary

Artificial intelligence in ophthalmology: A multidisciplinary approach

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1. Introduction

Artificial Intelligence (AI) is playing an increasingly prominent role in medicine because of advances in computing power, learning algorithms, and the availability of large datasets (big data) sourced from medical records and wearable health monitors. Disruptions in healthcare resulting from the COVID-19 pandemic have only further encouraged the integration of AI into a variety of medical subfields. While AI is being used in other medical specializations such as radiology, pathology, and cardiology, the use of AI-based approaches has expanded in ophthalmology due to widespread availability of ophthalmic imaging. In particular, the AI subfields of machine learning (ML) and deep learning (DL) are currently being used in ophthalmology practices to revolutionize vision care. This paper aims to investigate the role of AI-based systems in performing medical work in each subfield of ophthalmology and evaluate the progress made in this area along with challenges.

2. Machine learning and deep learning

AI is a subfield of computer science that aims to create intelligent machines.[1] ML is a subset of AI which focuses on the learning feature of intelligence and imitates the neural structure of the nervous system through the creation of artificial neural networks (ANNs), responsible for signal processing. ANNs are limited in that they require large amounts of image data for pattern detection and a descriptive label for each image during the training phase. DL is an improvement over ANN, consisting of more layers that permit higher levels of abstraction and improved predictions from data. The basic idea is that a neural network, instead of just acting as a classifier, can also serve as the feature extractor as well.[1] Therefore, a single deep neural network performs both tasks and can learn to both extract features that are suitable for a given classification problem and to classify them.[1]

3. Advances in the use of AI in ophthalmology

The application of AI in ophthalmology has focused on diseases such as diabetic retinopathy (DR), age related macular degeneration (AMD), cataract, and glaucoma. DR is the primary cause of blindness and visual loss amongst working-age men and women in the United States, with cataract and glaucoma as leading causes of blindness worldwide. The wide prevalence of these diseases as well as the availability of imaging make these areas attractive for the application of AI-based approaches. This extensive imaging has provided the large data sets (big data) for such applications. Big data when combined with AI allows for the detection of subtle associations that would be missed with smaller scale datasets.[2]

3.1. Retinal disorders

The immediate impact has been observed in the field of retinal diseases where colour fundus photography and optical coherence tomography (OCT) are widely used.[3] Since interpreting such large sets of imaging data is very time intensive for the ophthalmologist and can lead to delays in care for patients facing treatable eye

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conditions, AI tools that could be trained to interpret OCT scans as accurately as humans provide a path forward. This has the potential to reduce the burden of the ophthalmologist, giving them a better chance to treat sight-threatening diseases. Point-of-care DR screening using autonomous AI is now available and provides immediate results in a primary care setting. As a significant number of patients with diabetes do not get annual diabetic eye exams, autonomous systems such as IDx-DR (Digital Diagnostics, formerly IDx) have the ability to create a large impact in primary care settings.[4,5] IDx-DR, developed by Dr. Michael D. Abràmoff, is an autonomous, FDA-approved AI system designed to detect DR and diabetic macular oedema (DME) .[5] IDx-DR was validated against clinical outcomes, including OCT, and demonstrated promising results, with an observed 87% sensitivity and 90% specificity for detecting more-than-mild DR.[5,6] Similarly, Shah et al. in[7] validated a DL algorithm based on deep convolutional neural networks as a tool for screening to detect referable DR with an overall sensitivity and specificity of 99.7% and 98.5% for any DR detection.

Various DL-based systems have been designed with the intent to diagnose and track the progression of AMD and other associated retinal conditions. In particular, Faes et al. developed DL algorithms to detect drusen, neovascular AMD, and DME after training with 101,418 OCT images of the retina from 5761 patients with a sensitivity of 97.3%, a specificity of 100%, and a positive predictive value (PPV) of 97.7%.[2,8] Schlegl et al. in[9] developed a DL-based system to automatically detect and quantify intraretinal cystoid fluid (IRC) and subretinal fluid (SRF). This system accurately characterized the pattern of intraretinal fluid in patients with wet AMD or retinal vein occlusion (RVO) and distinguished between intraretinal cysts and SRF.[9] The authors conclude that DL in retinal image analysis provides an accurate means “for the differential detection of retinal fluid types across the most prevalent exudative macular diseases and OCT devices” .[9]

3.2. Cataract

The use of AI systems is now extending beyond retinal diseases and has numerous applications in the field of cataract management, including diagnosis, referral, and the prediction of refractive outcomes. Wu et al. utilized DL using residual neural network (ResNet) to establish a 3-step sequential AI algorithm for the diagnosis and referral of cataracts.[10] Per the authors the performance in three-step tasks was robust as follows: (1) capture mode recognition [area under the curve (AUC) 99.28%–99.71%], (2) cataract diagnosis (normal lens, cataract, or postoperative eye with AUCs of 99.82%, 99.96% and 99.93% for mydriatic-slit lamp mode and AUCs >99% for other capture modes) and (3) detection of referable cataracts (AUCs >91% in all tests) .[10]

AI has additionally shown great promise in the prediction of refractive outcomes and is currently utilized by several intraocular lens (IOL) formulae.[11] In particular, Sramka et al. found the prediction accuracy of two ML-based algorithms [the Support Vector Machine Regression model (SVM-RM) and Multilayer Neural Network Ensemble model (MLNN-EM)] to compare favourably to that of traditional clinical methods.[11,12] Prediction accuracy of the Hill-radial basis function (RBF) calculator, a system of ANNs which implements pattern recognition and sophisticated interpolation to analyse big data, has compared favourably to traditional methods but unfavourably to newer IOL formulae (Kane, EVO 2.0, and VRF-G IOL formulae) .[11,13,14]

3.3. Glaucoma

AI systems may be used to diagnose or monitor the progression of glaucoma. AI systems are being developed to diagnose glaucoma based on measurement of the retinal nerve fibre layer (RNFL) thickness and assessment of the visual field (VF) .[15] Systems are also employing AI strategies to detect glaucomatous damage (*i.e.*, optic nerve head abnormalities) from a dataset of fundus photographs.[16] Two ML-based systems – which utilized neural network classifiers and multiclass support vector machines (SVMs) to detect glaucoma from 61 to 100 fundus images – achieved 100% sensitivity, with specificity values of 80% and 87%, respectively.[17,18] In regard to disease progression, Yousefi et al. have introduced a ML-based index for glaucoma progression detection and concluded that ML analysis detects progressing eyes earlier than other methods consistently.[19]

3.4. Corneal diseases

While the integration of AI in ophthalmology has primarily focused on the subfields of retinal disorders, cataract, and glaucoma, AI systems are also being used to diagnose corneal diseases. Previous studies have shown AI-based systems can diagnose keratoconus and Fuchs’ dystrophy based on Scheimpflug tonometry[20,21] and high definition OCT images,[22] respectively.

4. Challenges in using AI in ophthalmology

One of the challenges with the use of AI based systems in medicine, including ophthalmology, has to do with the well-known ‘black-box’ problem. This has to do with physicians being unable to fully trust the decisions of such systems because the AI decision-making process is often-times opaque.[23,24] The algorithms used to arrive at a decision can be proprietary or difficult to understand. Hence the physician is unable to figure out how the AI system arrived at its conclusion.[23,24] For physicians to trust AI, systems must not lock their secrets inside a black box.

The limited screening scope of AI-based systems can be of concern to some physicians. An ophthalmologist will screen a patient for a range of eye diseases such as glaucoma, cataracts, diabetes, tumors etc. .[5] However, AI systems can only screen for what they are trained. While this may be a concern, one can appreciate that not being screened at all is far worse for patient outcome.[5]

As mentioned by Krause et al. in[25] in their study of grader variability in ML models, most common discrepancies in grading DR were due to missing microaneurysm, artifacts, and misclassified hemorrhages. False positives are also possible if the fundus image has artefacts due to poor image capturing, though this cannot be attributed to the AI- algorithm itself.

Lee et al. point out some data-specific limitations that must be kept in mind before interpreting study results associated with big data in AI.[2] For example, statistical significance becomes less meaningful when handling millions of data points because even minor differences will show statistical significance.[2] Hence, the clinical significance is important when results are analysed. Secondly, physicians need an understanding of the data used to train AI algorithms because the resulting algorithm may not be generalizable to the targeted population.[2] Results of these studies need to independently validated.[2]

5. Complementary and alternative medicine

Worldwide use of complementary and alternative medicine (CAM) has expanded as a result of greater resources, poor health, and unmet medical needs.[26,27] AI has been integrated into various CAM modalities and has shown great promise in the classification of herbal medicine prescriptions.[28,29] In the field of ophthalmology, AI models may be used to predict compounds to treat various ocular pathologies (DR, AMD, anterior uveitis, cataract, and glaucoma). Curcumin is a herbal remedy with widespread antioxidant and antifibrinolytic properties which may reinstate homoeostasis and slow the progression of glaucoma and/or other eye diseases.[30] Similarly, resveratrol exhibits anti-inflammatory properties which can minimize the apoptosis and neuroinflammation commonly observed in glaucomatous eyes.[31] Additional herbal medicines associated with glaucoma treatment include marijuana,[32] bilberry,[33] and gingko.[34],[35] Future applications of AI in integrative medicine include the potential to explicitly screen for integrative techniques which can mediate the inflammatory response and vascularization resulting from several ophthalmological conditions.

6. Conclusions

Advances in computing power combined with disruptions in healthcare resulting from unprecedented circumstances of the COVID-19 pandemic have prompted the worldwide exploration of AI-based systems in several medical subfields, including ophthalmology. Ophthalmic AI systems are advantageous in that they decrease time required to interpret image data, enable ophthalmologists to gain a greater understanding of disease progression, and assist with early-stage diagnosis, staging, and prognosis. Future directions include addressing the limited screening scope, false positives, and 'black box' problem associated with AI-based systems. Although more studies on patient outcomes are needed, based on the results seen thus far there is now the expectation that the use of AI in ophthalmology will improve patient outcomes across an increasing range of ophthalmic diseases.

Conflict of interests

The authors have no conflict of interests to declare.

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