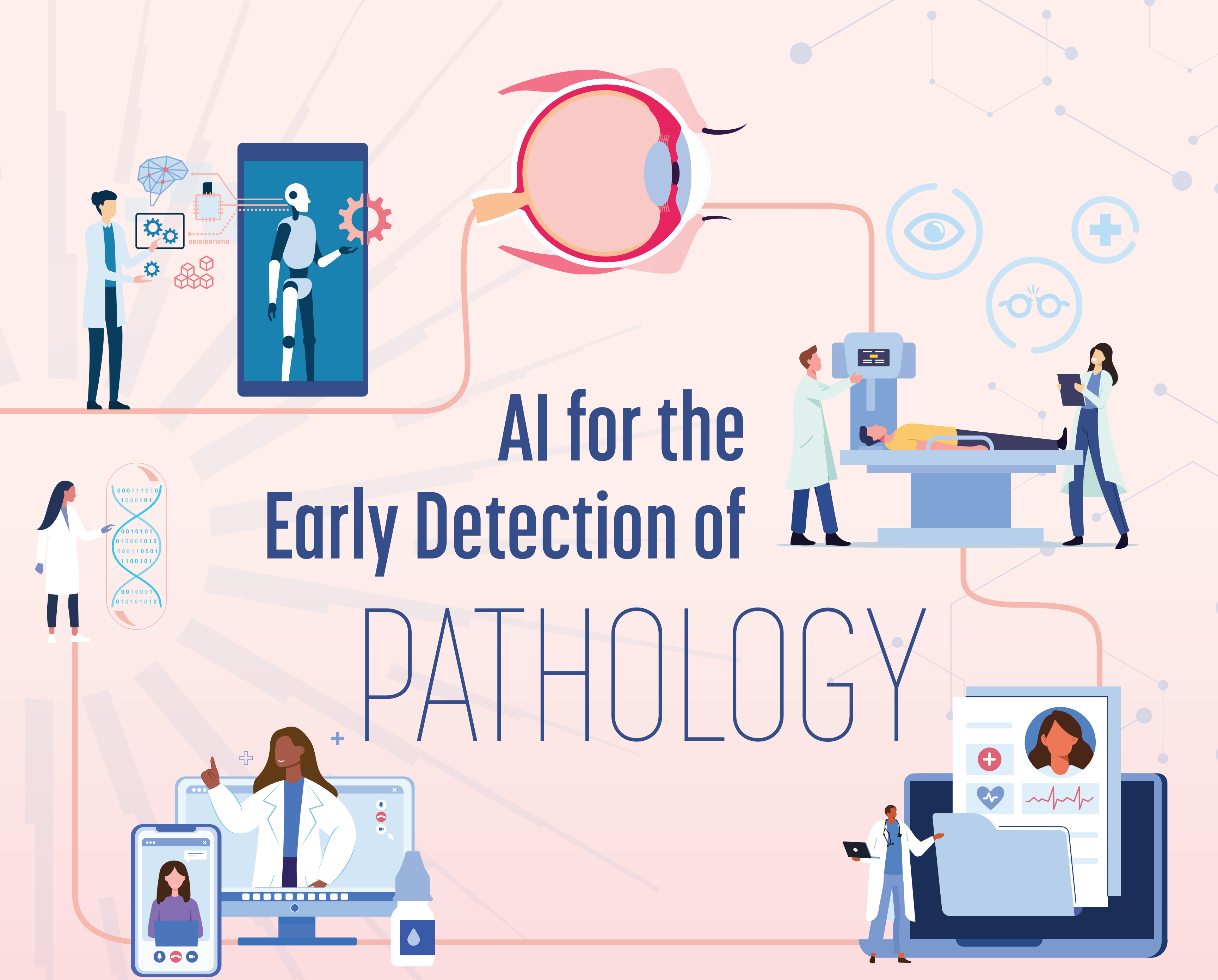
AI for the Early Detection of PATHOLOGY



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> The need for accurate and efficient diagnosis is growing.

 

Ophthalmology is at the forefront of AI research and clinical integration in part because of the large volumes of clinical and imaging data physicians collect. Deep learning (DL) algorithms are a subset of AI that allow machines to learn from data and improve their accuracy over time without manual programming.[1] The biggest potential clinical impact of AI-based technology in ophthalmology is for the detection of diseases that are highly prevalent and visually significant and for which, when the conditions are identified early, treatments are available to improve patient outcomes. This article provides an overview of how AI is being used and studied for the detection of ocular diseases in the posterior and anterior segments.

POSTERIOR SEGMENT

Diabetic retinopathy detection. Damage to the neurosensory retina from diabetic microvascular changes is referred to as *diabetic retinopathy* (DR). The first US FDA-approved AI platform for disease detection is for DR.[2] It has therefore been the case study for all of medicine for the evaluation and implementation of a clinically meaningful autonomous, AI-based diagnostic system.

By the year 2040, an estimated 600 million people will have diabetes, one-third of whom are expected to have DR,[3] the leading cause of blindness among working-aged adults.[4] Early detection through screening coupled with appropriate referral and treatment is critical to prevent blindness. Only 50% of all individuals with diabetes follow proper screening guidelines, and less than 40% of those at high risk of vision loss receive appropriate treatment.[5,6] Barriers include proximity to screening facilities and a lack of infrastructure and specialists. The use of AI to diagnose DR may reduce the cost of screening, bias, and specialist labor and increase efficiency and accessibility.[7]

Clinical screening involves methods such as a dilated posterior segment examination, mydriatic or nonmydriatic fundus photography, and teleretinal screening. In 2016, a DL system was used and successfully achieved an area under the receiver operating characteristic curve (AUC) of 0.98 with sensitivity and specificity of 96.8% and 87%, respectively, to detect referable DR defined as moderate or worse nonproliferative DR or diabetic macular edema.[8] Since then, similar results have been achieved with other DL systems using publicly available imaging datasets.[9,10] None of the results, however, has been validated in a real-world setting.

A DL system has been developed and validated to detect referable DR and other ocular diseases such as age-related macular degeneration (AMD) and glaucoma from a community-based national DR screening program in Singapore. External validation in 10 diverse datasets from six countries around the globe was achieved.[11] An autonomous AI platform approved by the US FDA in 2019, LumineticsCore (formerly IDx-DR, Digital Diagnostics), is being integrated into clinical use. Real-world patient outcomes are critical to determine the platform's true impact and increase utilization.

AMD detection. Acquired degeneration of the central retina can lead to significant visual impairment via geographic atrophy and/or choroidal neovascularization. The individual and societal impact is great: AMD is the leading cause of vision loss in people 50 years of age or older in the United States. Early intervention for neovascular AMD can restore and maintain good vision. With the recent US FDA approval of a treatment for geographic atrophy, moreover, continued monitoring and early detection of intervenable disease are necessary.

Based on the Age-Related Eye Disease Study (AREDS) stages of AMD,[12] the AAO recommends routine ophthalmologic follow-up visits every 2 years for individuals with intermediate AMD. By 2040, an estimated 288 million people will have some form of AMD, and 10% will have intermediate or worse disease.[13] Screening the entire at-risk population in the United States would include more than 110 million people.[14] The global burden continues to grow as the population ages. The potential impact of an AI-based diagnostic program is great.

AMD is diagnosed through an examination of the macula and OCT imaging. An early DL system trained on a DR screening population of 72,610 macular fundus images demonstrated an acceptable ability to detect referable AMD.[11] Subsequent systems have been developed using the AREDS dataset.[15,16] One study using six convolutional neural networks (CNNs) to train its models demonstrated 84.2% sensitivity in detecting AMD with fundus photographs.[16] A further proof of concept for a DL-based, automated assessment of referable AMD from fundus images found an accuracy of 88.4% to 91.6% for detecting intermediate or worse AMD with their deep CNN, which was comparable to the performance of human experts.[15] A major limitation of both studies was the lack of external validation on separate datasets, which will be necessary to make the technology clinically useful. The integration of both fundus and OCT imaging is also likely necessary.

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Glaucoma detection. A potentially blinding, progressive disease of the optic nerve, glaucoma clinically manifests as a loss of the neuroretinal rim and increased optic nerve head cupping. An estimated 112 million individuals globally will have glaucoma by 2040.[17] Patient outcomes tend to be better when the disease is diagnosed early. The diagnosis of glaucoma can be challenging, however, with no specific disease defining cup-to-disc ratio. Algorithms have nevertheless been developed to detect glaucomatous-appearing optic nerve heads on fundus photographs, defined as discs with a vertical cup-to-disc ratio of 0.7 or 0.8.[11,18] Using OCT images, machine learning AI has been able to distinguish between eyes with glaucomatous damage to the nerve fiber layer and unaffected eyes.[19]

The clinical examination for glaucoma is considered in the context of function, as determined with visual field (VF) testing. An AI algorithm that can integrate imaging and functional testing would likely be of greatest benefit. Systems that analyze VFs and recognize patterns associated with glaucomatous loss have demonstrated utility for the detection of early VF loss from glaucoma.[20,21] Advances continue; a machine-learning algorithm was able to detect VF progression even earlier,[22] and a DL algorithm was able to forecast future VF deficits from a single baseline photograph.[23]

One challenge in applying AI to the detection and diagnosis of glaucoma is the correlation between structure and function in the clinical diagnosis of the disease. Variability in so-called normal optic nerve head cupping makes diagnosing the disease with a single imaging modality unlikely. As machine learning algorithms evolve, however, there is the potential for systems that can diagnose glaucoma before VF changes become manifest, detect subtle signs of disease progression, and forecast an expected clinical course while integrating multiple ophthalmic data points.

ANTERIOR SEGMENT

AI-related research in ophthalmology has focused primarily on the detection and diagnosis of posterior segment diseases, but applications are emerging for anterior segment pathology, particularly in the detection of corneal ectatic disease and cataracts. The impact of the research could be significant because cataracts are the leading cause of reversible blindness worldwide, affecting nearly 12.6 million people. Annually, 20 million cataract procedures are performed.[24] The prevalence of visually significant cataracts, moreover, is expected to increase.

Cataracts are detected with slit-lamp microscopy. Several research groups are examining the use of AI for the diagnosis and grading of cataracts with slit-lamp photography. ResNet, a validated DL algorithm, can differentiate between a cataract, an IOL, and a healthy crystalline lens (AUC > 0.99); detect referable disease defined as grade 3 and 4 cataracts based on the Lens Opacities Classification System (AUC > 0.91)[25]; and identify anterior or posterior subcapsular cataracts and posterior capsular opacification. Fundus photographs are being used for the same purpose.[26-30] AlexNet and VisualDN, CNN-based ensemble algorithms, have demonstrated an accuracy of 86.2% in the grading and diagnosis of cataracts on fundus images.[26] The benefits of this approach are technical and practical. Slit-lamp photography requires multiple imaging techniques—slit beam, retroillumination, and diffuse—making it more challenging and less efficient. Additionally, fundus imaging permits the simultaneous detection of posterior segment diseases. Small pupils and other opacities in the visual axis, however, present challenges. Beyond cataracts, AI technology has been applied to the prediction of the progression of posterior capsular opacification and the development of corneal ectasia after refractive surgery, the detection of corneal ectatic disease, and the optimization of biometry for IOL power calculations.[31]

THE FUTURE OF AI IN EYE PATHOLOGY DETECTION

As the prevalence of eye diseases increases, the need for accurate and efficient diagnosis grows. AI algorithms have the demonstrated ability to detect conditions with high accuracy. The technology's performance is expected to improve with the development of more sophisticated machine learning techniques and greater availability of medical data. It is reasonable to think AI will become a valuable tool in everyday clinical practice to facilitate earlier disease diagnosis and intervention and, ultimately, improve patient outcomes. ■

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