LEVERAGING AI TO ALLEVIATE DIABETIC VISION LOSS

New tools may help clinicians screen, diagnose, and monitor patients with diabetic eye disease.

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In less than a decade, the number of individuals diagnosed with diabetic retinopathy (DR) is projected to surpass 24 million.[1] While 90% of vision loss due to DR can be prevented by early detection, 40% to 60% of Americans are unable to obtain regular eye examinations.[2,3]

Although high-resolution fundus imaging is available across the nation, interpretation of images by skilled eye care providers continues to be a rate-limiting and costly step. Even when employing expert graders, effective end-to-end screening that leads to the preservation of a patient's vision is difficult to implement and scale. Machine learning-based solutions have the potential to bridge this gap and have garnered significant interest in academia and industry. In this article, we highlight some of the DR screening initiatives.

RECENT ADVANCES

In 2016, Gulshan et al presented a deep-learning algorithm capable of detecting referable DR using color fundus photographs (CFP) with remarkable speed and accuracy. The model predicted the disease severity in each CFP based on pixel intensities and made binary predictions on whether the disease was referable or not. This network was trained on more than 128,000 images and validated on 12,000 images. The reference standard was the majority vote of a panel of seven to eight expert ophthalmologists. The model's performance was noted to be on par with that of the expert panel, with F-scores of 0.95 and 0.91 (a measure of the model's accuracy calculated as a geometric mean of the precision and recall) for the model and expert physician panel, respectively, as demonstrated by the area under the curves.[4]

In 2018, Krause et al published a more robust network for automated grading of DR. The model made more granular predictions of the five-point severity grading scale as opposed to the two-point output in the prior version. In addition, the reference standard included an adjudication process in which a panel of expert retina specialists discussed each case until reaching a consensus on the final grade. Even using a small set of adjudicated DR grades led to enhanced identification of subtle findings, such as microaneurysms, and significantly improved the model's performance. Using a subset of 0.22% of images as a tuning set, the model's hyper-parameters yielded a kappa score (measurement of agreement that ranges from 0 [random] to 1 [perfect agreement]) of 0.84, which was similar to that of ophthalmologists (range: 0.80–0.84) and retina specialists (range: 0.82–0.91).[5]

In another study, a deep-learning system was trained to predict diabetic macular edema (DME) from 2D CFPs with the help of retinal thickness and fluid labels identified in the paired OCT images.[6] The network performed better when predicting DME with OCT-derived parameters as reference standards as opposed to expert CFP labels alone. The model generalized data from multiple international populations (ie, Australia, India, and Thailand) and exceeded the performance accuracy of experts with higher specificity—80% for the network versus 59% for human experts ($P = .008$)—and noninferior sensitivity—81% for the network versus 70% for human experts ($P < .001$).

AT A GLANCE

- Artificial intelligence-based solutions for diabetic retinopathy (DR) screening promise to improve access to and delivery of care for patients.
- Although high-resolution fundus imaging is available for remote screening, interpretation by skilled providers is a rate-limiting and costly step.
- In addition to DR grade, deep-learning systems can be trained to predict diabetic macular edema from fundus images with the help of OCT images that can provide retinal thickness and fluid measures.

IMPLEMENTATION HURDLES

A long-standing limitation of deep-learning models has been the *black box effect*: the model takes inputs and provides prediction scores with no insight into the inner workings of the process. This lack of understanding has led to mistrust among the scientific community, thereby limiting the widespread adoption and use of deep-learning models, especially in clinical care.

To overcome this, Sayers et al showed the final disease predictions as well as the model's decision process; along with the DR severity scores, physicians could view heatmaps that highlighted the regions of the CFPs that most strongly drove the predictions. Having overcome some of the black box effect, more clinicians began to use these deep-learning models to help improve their diagnostic accuracy and confidence in CFP interpretations.[7]

Although OCT has become ubiquitous in retina clinics, it still presents a challenge to the successful implementation of artificial intelligence (AI)-based solutions due to a dearth of annotated training images, hundreds of thousands of which are needed to train neural networks. In 2018, De Fauw et al published a novel deep-learning architecture to address this issue. This model used autosegmented OCT scans to create device-independent tissue-segmentation maps.[8] These features were then combined with clinical labels to detect retinal diseases and determine the need for *urgent*, *semi-urgent*, or *routine and observation-only* referrals to ophthalmologists. The creation of device-independent segmentation of OCT scans eliminated interdevice heterogeneity and standardized the images for more accurate analysis.[8]

In addition, this model created a report that was readily viewable by clinical experts, thereby alleviating part of the black box effect. This technique allowed for the detection of a range of retinal diseases, including rare diseases, and was not limited to DR. With this robust architecture and after training on more than 14,000 scans, the model's performance was on par with expert physicians. The expert performance of the network was achieved without missing clinically important, sight-threatening diseases.[8]

NOVEL APPROACHES

Despite the advanced tools, patient adherence to screening appointments remains challenging because people often trivialize the importance of routine diabetic examinations when their vision is still adequate. To address this, Google partnered with Verily to create the Verily Retinal Service, which combines a fundus camera (Verily Retinal Camera) with end-to-end workflow software (Verily Retinal Platform) to provide seamless integration into clinical workflows with minimal operator training.[9]

Telemedicine, which has been successfully used in other medical specialties for routine visits, especially during the COVID-19 pandemic, also has the potential to address this issue. The need for specialized eye equipment has made it difficult to translate well to an ophthalmic telemedicine platform. Babenko et al showed that one can detect diabetic eye disease by looking at external eye photos alone.[10] Thus, the use of AI and deep-learning algorithms on photos taken by a patient at their home using their smartphone, particularly when paired with telemedicine, may enable and scale real-time screening and prevent vision loss.

When assessing the utility of AI to minimize the burden of vision-threatening disease, detecting referable DR is only the tip of the iceberg. This technology may one day help physicians determine the best treatment approach (eg, steroids vs anti-VEGF therapy) for a particular patient, as well as determine appropriate treatment intervals to maintain good vision.[11] Such personalized care may not be limited to DR, as researchers work to expand the indications to other conditions such as AMD and glaucoma.[11]

In short, AI-based solutions for DR screening promise to improve access to and delivery of care to patients with diabetes. As clinicians, we are eager to see the diagnostic and therapeutic implications of any given intervention. Still, we must also focus on how we can leverage this technology to provide safe and equitable care, especially to those who have the most limited access to timely, accurate, and quality health care. ■

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