# ARTIFICIAL INTELLIGENCE IN AMD IMAGING

Here is a look at what to expect as this tool becomes more ubiquitous in research and the clinic.

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AMD remains a major cause of severe and irreversible vision loss worldwide.[1] As life expectancy continues to increase, so does the prevalence of AMD, with an estimated 288 million people being diagnosed with AMD by 2040.[2,3]

The progress achieved in the treatment of AMD with the introduction of anti-VEGF therapies has greatly improved visual outcomes.[4-6] However, delayed intervention, the unpredictability of recurrent disease, and the need for chronic therapy are all factors that are associated with poor visual outcomes.[7,8]

In addition, no proven therapy is currently available for the prevention or treatment of geographic atrophy (GA).[9] The Age-Related Eye Disease Study demonstrated that micronutrient antioxidant supplements may play a role in reducing the progression of intermediate AMD to wet AMD, but the study also found no apparent benefit in preventing foveal atrophy.[10,11]

Advances in retinal imaging, such as OCT, have dramatically transformed ophthalmic clinical practice and research, allowing high-resolution visualization of the microarchitecture of the retina and choroid. More recently, the development of OCT angiography (OCTA) has allowed the study of the retinal microcirculation and the inner choroid in 3D.[12] Here, we discuss the advances in retinal imaging that have led to the identification of biomarkers for AMD progression that may one day shape how we diagnose, treat, and follow patients with AMD.

## THE CHALLENGE

With the increasing interest in earlier interventions to prevent or halt AMD progression, risk stratification is required to effectively design early intervention clinical trials with practical size and feasible duration. Retinal imaging now allows us to identify biomarkers that may predict the development of late-stage AMD. Studies have identified several high-risk biomarkers for AMD, including high central drusen volume, subretinal drusenoid deposits, hyporeflective drusen cores, intraretinal hyperreflective foci, and choriocapillaris flow deficits.[13-15]

The identification of these biomarkers has been facilitated by the availability of both OCT and OCTA, which allow for the detection of subclinical features that may not

## AT A GLANCE

- Advances in retinal imaging have led to the identification of biomarkers for AMD progression that may one day shape how we diagnose, treat, and follow patients with AMD.
- Artificial intelligence (AI) algorithms may be able to provide analyses to assist physicians in diagnosing conditions based on specific features extrapolated from large volumes of imaging data.
- Researchers have demonstrated AI's ability to objectively identify, localize, and quantify subretinal fluid and high-risk structural biomarkers on OCT using a fully automated tool.
- AI-based imaging may be particularly useful in the era of personalized medicine, where we may be able to accurately predict outcomes and choose the optimal therapeutic strategies.

AI CAN BE TRAINED TO DETECT SPECIFIC STRUCTURAL FEATURES THAT UNCOVER DISEASE-SPECIFIC PATTERNS, WHICH CAN BE USED BY CLINICIANS TO BETTER UNDERSTAND THE DISEASE AND MAKE APPROPRIATE TREATMENT DECISIONS.

be apparent during a standard ophthalmoscopic examination. Of note, the grading and annotation of these images requires extensive training and may be a challenging and time-consuming process, especially in the context of a busy clinical practice. Even with experienced centralized reading centers, there can be variability between graders due to the subjectivity of the assessments and subtlety of the features characterizing the disease process. Compounding this problem, OCT and OCTA volumes contain a large number of B-scans that must be carefully and qualitatively evaluated and interpreted; the quantitative assessment of biomarkers is even more challenging, frequently requiring analysis with a specialized manufacturer or third-party software.

## A PLACE FOR ARTIFICIAL INTELLIGENCE

These clinical challenges present an opportunity for the use of artificial intelligence (AI) algorithms and systems. They may be able to provide analyses to help physicians diagnose conditions based on specific features extrapolated from large volumes of imaging data—all in a short period of time. AI can be trained to detect specific structural features that uncover disease-specific patterns, which can be used by clinicians to better understand the disease and make appropriate treatment decisions.

In the retinal space, there are at least two disease states for which AI algorithms have already come into play: AMD and diabetic retinopathy. In this article, we focus on advances in the AMD space. Several investigators have created advanced AI algorithms designed to annotate color fundus photographs and have achieved performance similar to human graders with regard to the assessment of drusen, pseudodrusen, and GA.[16,17]

Biomarkers for the progression of GA are particularly important because slowing the progression or enlargement of atrophy is considered an FDA-approved clinical endpoint in many ongoing interventional clinical trials. Niu et al developed a model to predict future GA growth based on structural biomarkers on OCT as a potential tool for identifying patients at high risk for rapid progression.[18] Bogunovic et al focused on an earlier stage and studied a deep learning algorithm to predict the risk of progression in eyes with intermediate AMD based on drusen regression on OCT.[19] Other groups have developed AI algorithms to predict whether eyes with intermediate AMD would progress to macular neovascularization or GA.[20]

The activity of neovascular AMD is generally determined by the presence of fluid (subretinal, intraretinal, and subretinal pigment epithelium), which can be accurately identified on OCT. Resolution of retinal fluid is also the key indicator to assess responsiveness to anti-VEGF therapy. Schmidt-Erfurth et al demonstrated AI's ability to objectively identify, localize, and quantify fluid on OCT using a fully automated tool, which could potentially be used for personalized disease management.[21,22] In addition, machine learning approaches have shown the ability to predict BCVA at 1 year based on the initial therapeutic response in eyes with neovascular AMD, highlighting the importance of early treatment and control of disease activity.[23]

Our group has been focused on the development of AI models to automate the detection of structural OCT biomarkers associated with risk for progression of intermediate AMD, showing a performance superior to expert retinal imaging graders.[24]

## CLINICAL IMPLICATIONS

Although we may still be in the early days of AI in ophthalmology, imaging studies have already proven these tools to be valuable for detecting specific disease features, offering clinicians the opportunity to screen for disease, prognosticate the disease course, and uncover new insights into the pathophysiology of disease. The ability of AI-based tools to rapidly and accurately process large volumes of data makes it feasible to incorporate them into clinical practice.

AI-based imaging may be particularly useful in the era of personalized medicine, where we may be able to accurately predict outcomes and choose the optimal therapeutic strategies for our patients.

With continued development and training with larger datasets, the performance of AI algorithms will only improve over time. AI's ability to extrapolate useful clinical information from large volumes of imaging data will be of particular importance as our diagnostic technologies get more sophisticated. Thus, we can expect AI to play a significant role in the retina clinic of the future. ■

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