ULTRA-WIDEFIELD IMAGING FOR AGE-RELATED MACULAR DEGENERATION

This technology holds promise for the study of peripheral abnormalities.

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Age-related macular degeneration (AMD) is the leading cause of blindness in the elderly in the developed world. AMD is a multifactorial disorder with dysregulation of complement, lipid, inflammation, and extracellular matrix pathways all implicated in its pathogenesis. The diagnosis and classification of AMD has always been focused on the macula, given the historical understanding of the disease. Thorough investigation of the periphery with photography has been limited by an inability to reliably and efficiently capture high-quality photographs of the peripheral retina as well as the absence of a standardized, systematic method of interpreting peripheral retinal changes. Although it is well established that drusen and changes in the retinal pigment epithelium occur in the peripheral fundus of patients with AMD, the clinical significance and impact of these developments on disease progression has yet to be elucidated.[1-3]

Advances in ultra-widefield (UWF) fundus photography have made it possible to obtain high-resolution images of both the peripheral and central retina in a rapid manner. UWF imaging has already been used for the diagnosis and grading of diabetic retinopathy, and its use for AMD research is currently being explored.[4]

PERIPHERAL CHANGES MAY HAVE A ROLE TO PLAY NOT ONLY IN THE DIAGNOSIS OF AMD BUT ALSO IN DETERMINING PROGNOSIS OF DISEASE.

Investigators have demonstrated that peripheral abnormalities seen on pseudocolor and autofluorescence UWF imaging are more prevalent in patients with AMD than in healthy patients.[2] Systematic study and correlation of these findings with genotypic polymorphisms, disease states, or functional markers could facilitate diagnosis, prognosis, and treatment. Of note, peripheral drusen have proven associations with complement factor H genotypic variations.[5]

A NOVEL GRID SYSTEM

UWF imaging for AMD opens up an entirely new field of research. UWF cameras can produce high-quality images with minimal distortion, allowing clinicians to assess perimacular and peripheral lesions such as drusen, peripheral reticular changes, atrophy, fibrosis, choroidal neovascularization, and subretinal drusenoid deposits in eyes with AMD. The Early Treatment of Diabetic Retinopathy (ETDRS) grid has enabled the standardization and classification of macular disease. With that in mind, we have developed a novel grid that can be used to study the macular area and the peripheral retina simultaneously in AMD patients.

The novel grid system has 12 zones—three concentric circles centered on the fovea, with horizontal lines dividing nasal and temporal retina and vertical lines dividing superior and inferior retina. The concentric circles create four zones that extend radially.[6] The first and smallest is the macular

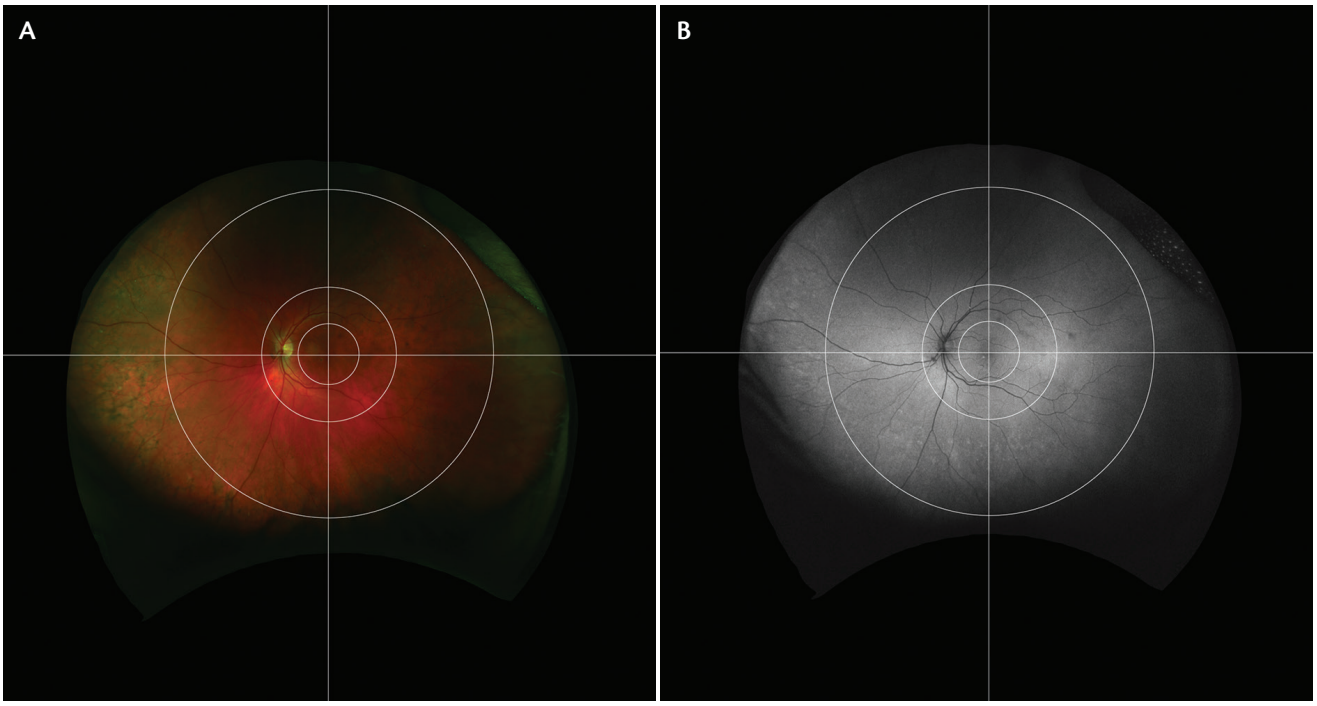

Figure. This novel UWF grid enables synchronous study of peripheral and posterior AMD lesions. Pseudocolor UWF image (A) demonstrates peripheral reticular pigmentary changes, and autofluorescence UWF image (B) shows granular increased FAF changes in a patient with AMD.

zone, which is based on the ETDRS grid as used in the landmark Age-Related Eye Disease Study. The perimacular zone extends beyond the macula and involves the optic disc. It permits a precise description of pathology that is not quite in the macula but is not far enough out to be considered peripheral. The midperiphery and far periphery are divided by a circle marked by vortex veins. This division allows a more precise description of peripheral findings.

The specific way in which images are captured using UWF technology (Optos) requires an ellipsoid mirror that can distort the peripheral retina. This distortion can make measurements of anatomic irregularities imprecise and increase the number of artifacts. Geometric distortion correction software, available in recently manufactured cameras, addresses these problems to create a reproducible, color-corrected view of the retina that can be reliably applied from patient to patient. Combining our grid with distortion-corrected UWF images offers a reproducible way to study anterior and posterior regional abnormalities in AMD.

DARK ADAPTION LINKED TO ULTRA-WIDEFIELD PERIPHERAL CHANGES IN AMD

UWF imaging in AMD research has already yielded fresh insights into the clinical significance of peripheral AMD lesions. For example, in a prospective, cross-sectional study by Laíns and colleagues, the technology helped to demonstrate an association between dark adaption time and peripheral reticular pigmentary changes in patients with AMD.[7]

Patients with AMD and a control group (N = 128 eyes) were included in the study. Images on UWF and fundus autofluorescence (FAF) modalities were assessed by two graders who were tasked with detecting perimacular, midperipheral, and far peripheral abnormalities. Patients were evaluated with a standard dark adaptation protocol. The study authors observed that the presence of reticular pigmentary changes on UWF fundus photography in the midperipheral and far peripheral zones were associated with more prolonged time to dark adaptation. Similarly, decreased and mottled FAF patterns in the midperipheral zone were also associated with longer dark adaptation times (Figure). Of note, reticular pigmentary changes were found exclusively in patients with AMD in this study.

Although visual acuity is widely used as a measure of retinal function, it is most useful for the detection of late-stage AMD. Time to dark adaption can identify individuals with AMD and successfully stratify them by disease severity. As detailed above, our group reported a statistically significant correlation between patients with prolonged dark adaptation and peripheral reticular pigmentary changes. The significance of this association suggests that peripheral changes may have a role to play not only in the diagnosis of AMD but also in determining prognosis of disease.

(Continued on page 46)

(Continued from page 16)

CONCLUSION

UWF imaging is ushering in an exciting new era in AMD research. Future studies could provide important information on the clinical significance of peripheral abnormalities in AMD. ■

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