In recent years, powerful imaging and diagnostic technology has revolutionized and redefined clinical retina practice. Fundus autofluorescence (FAF) is becoming an increasingly important diagnostic tool in a spectrum of retinal diseases, particularly age-related macular degeneration (AMD). This is a fast-emerging, noninvasive technique that permits the topographic mapping of lipofuscin distribution in the retinal pigment epithelial (RPE) cell monolayer and provides information additional to conventional mapping techniques. Excessive accumulation of lipofuscin commonly represents a negative pathogenetic pathway in AMD, as well as other hereditary retinal diseases.

FAF imaging has been shown to be useful with regard to understanding of pathophysiologic mechanisms, diagnostics, phenotype-genotype correlation, identification of predictive markers for disease progression, and monitoring of novel therapies. FAF imaging gives information above and beyond that obtained by conventional imaging methods, such as fundus photography, fluorescein angiography, and optical coherence tomography. Its clinical value, coupled with its simple, efficient, and noninvasive nature, is increasingly appreciated.

Clinically, the Spectralis (Heidelberg Engineering, Vista, CA) models are combined confocal scanning laser ophthalmoscopy (cSLO) fundus imaging and spectral-domain (OSD) OCT BluePeak imaging, four of which are enabled with blue laser autofluorescence capabilities.

**APPLICATIONS OF FUNDUS AUTOFLUORESCENCE**

FAF has a variety of useful applications in the clinic. First, it is helpful with making a differential diagnosis of macular degeneration. There are a number of “mimicker” diseases, such as adult-onset foveal macular dystrophy or pseudovitelliform degeneration, in which optical coherence tomography (OCT) images and fluorescein angiography (FA) can appear similar to wet AMD. Because the material that has been deposited under the retina is very hyperfluorescent, however, using FAF on these eyes shows a tremendous amount of autofluorescence, which is not present with standard AMD. Anything that eliminates misdiagnosis has, without question, utility.

A second application for FAF in the clinic is in following patients with geographic atrophy (GA). The literature supports the notion that increased rim autofluorescence is associated with an increased rate of expansion of GA. Brar et al correlated high-resolution OCT images to FAF imaging to study the changes in appearance of the margins of GA and found that spectral-domain SD-OCT provided in vivo insight into the pathogenesis of GA and its progression (Figure 1). Visualization of reactive changes in the retinal pigment epithelial cells at the junctional zone...
tern of autofluorescence seen in a patient with early AMD (Figure 2). A study by Dandeker et al\(^4\) showed that pre-
choroidal neovascularization (CNV) in patients with AMD than with fundus photography.

Identifying that the area of GA can be better quantified with FAF than with fundus photography.

A third utility for FAF is to increase our understanding of choroidal neovascularization (CNV) in patients with AMD (Figure 2). A study by Dandeker et al\(^4\) showed that preserved autofluorescence in subjects with recent-onset CNV indicates viable retinal pigment epithelium initially, which has implications for visual prognosis. Decreased autofluorescence in subjects 1 to 6 months after diagnosis or with late-stage CNV indicates loss of RPE and photoreceptors.

Although these data are more speculative, identifying patterns of autofluorescence within the fovea of patients receiving anti-vascular endothelial growth factor (VEGF) therapy may be helpful in assigning a treatment regimen. If there is complete lack of autofluorescence, suggesting that the RPE is extremely sick or absent, there is the suggestion that the likelihood of vision improvement in those patients is diminished. If a normal autofluorescence pattern is maintained, there are some data to suggest that that patient has the capacity to improve vision. Again, this is speculative, but because we do not know whose vision improves and whose does not, and how to titrate our anti-VEGF therapies, this might prove to be a useful modality for following patients undergoing Anti-VEGF therapy for CNV.

The most cutting-edge investigations of FAF involve defining recurring patterns of autofluorescence in early AMD patients. An important advancement in studying the particular patterns of autofluorescence within AMD patients is possible now that an automated eye-tracker allows repeated OCT scans to be made of the exact same spot on the eye. The Spectralis HRA+OCT (Heidelberg Engineering, Vista, CA) contains an eye-tracking system that compensates for eye movement during the scan and results in multiple benefits. First, it allows multiple scans of the same area, producing a mean image that has much greater detail than a single image. Second, it allows precise correlation in changes of lipofuscin patterns on the retina. Whereas previously we studied greater or lesser quantities of autofluorescence, now specific names are being assigned to autofluorescence patterns—speckled, deflect, and butterfly.\(^5\) The particular pattern of autofluorescence seen in a patient with early AMD might predict if they end up with GA or CNV. Although at this point, these types of studies require much more research, FAF could be a powerful adjunct to the way that patients with high-risk dry AMD are managed.

**SUMMARY**

Data from the trials currently under way should add to the existing data correlating GA and CNV with quantities of autofluorescence, supporting FAF as an indispensable diagnostic tool in the clinic. This will make experience with FAF images essential. The variability in generating FAF images is operator-dependent, and there is a learning curve. An experienced operator will be more successful in generating good images, analyzing the images, and following patients. Having the ability to create FAF images and the experience to analyze them will allow the practitioner to determine which patients should be followed and which patients should be treated. \(\square\)

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