

Multimodal Imaging: Implications for Clinical Practice



Multimodal imaging with the Mirante platform represents the next step forward in diagnosing and following routine and rare pathologic findings.

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Improvements in imaging technology over the past several years have provided retina specialists with increasingly finite structural and functional detail about the tissue of the posterior segment. Collectively, the variety of imaging modalities used in daily clinical practice improve the ability to diagnose pathology, follow it over time, stage disease, and ultimately assist in making decisions about treatment and determining prognosis. The field is now on the precipice of a new era in imaging capabilities with the market availability of devices that combine multimodal imaging on a single platform.

The new Mirante (NIDEK) marks a step forward in this regard, providing an unprecedented number of imaging modalities in one single device. The Mirante offers high-definition OCT and confocal scanning laser ophthalmoscopy (cSLO), both with widefield capabilities. With this device, clinicians have access to a wide range of imaging modalities: OCT, OCT angiography (OCTA), fundus color, contrast angiography (ie, fluorescein [FA] and indocyanine green [ICG] angiography), and green and blue fundus autofluorescence (FAF). Although certain pathologic markers, such as subretinal drusenoid deposits, are best identified using blue light, there are situations where using green autofluorescence is advantageous (ie, for identifying the

foveal edge of geographic atrophy and tracking it over time). Green FAF is absorbed to a lesser extent compared to blue FAF by the macular pigment, and therefore does not produce the classic dark halo associated with the latter, thereby improving visualization. In addition, comparing images from both modes may give insight on changes in the luteal pigment in the macula, such as in an eye with suspected macular telangiectasia.

One additional mode bears mentioning: Retro mode imaging is analogous to retroillumination that is used in anterior segment imaging to see subtle features of the cornea and lens. Retro mode imaging is a unique mechanism for discerning pathologic features that might be missed with other types of imaging. Beyond the obvious convenience factor of having all of these modalities on the same device, the fact they are all integrated and registered to one another assures there is strong correlation in findings between different modalities.

WIDEFIELD AND COLOR SCANNING: IMPORTANCE FOR CLINICAL PRACTICE

Having access to multiple imaging modalities provides the clinician a means to understand how pathology is affecting the structures of the eye at a near histologic level. If OCT can loosely be thought

of as an optical biopsy, then multimodal imaging expands this capability to better understand morphologic features *in situ*. The versatility of the Mirante for diagnosing and following routine and rare pathology is further enhanced by the integration of color scanning functionality and widefield capabilities into its variety of imaging modes. The Mirante has four separate lasers, each of which penetrates to different depths: blue (480 nm; reflected by the nerve fiber layer), green (532 nm; reflected by the ganglion cell layer), red (670 nm; penetrates through the retina), and infrared (790 nm; through the choroidal layer). Each of these lasers can scan the retina through a confocal optical setup with a small coaxially-placed pinhole that lets only the light coming from the focal planes in while discarding back-scattered and out-of-focus light. This may be useful, for example, in improving detection of atrophy in an eye with age-related macular degeneration.

Mirante also has a wider field on OCT imaging compared to other devices at 16.5 mm, which is helpful in tracking progression and response to treatment in pathology that spans long distances—such as in inflammatory disorders. There is also an optional Widefield lens attachment (163°; measured from the center of the eye) for the Mirante that is compatible with color, FA, ICG, and Retro mode imaging.

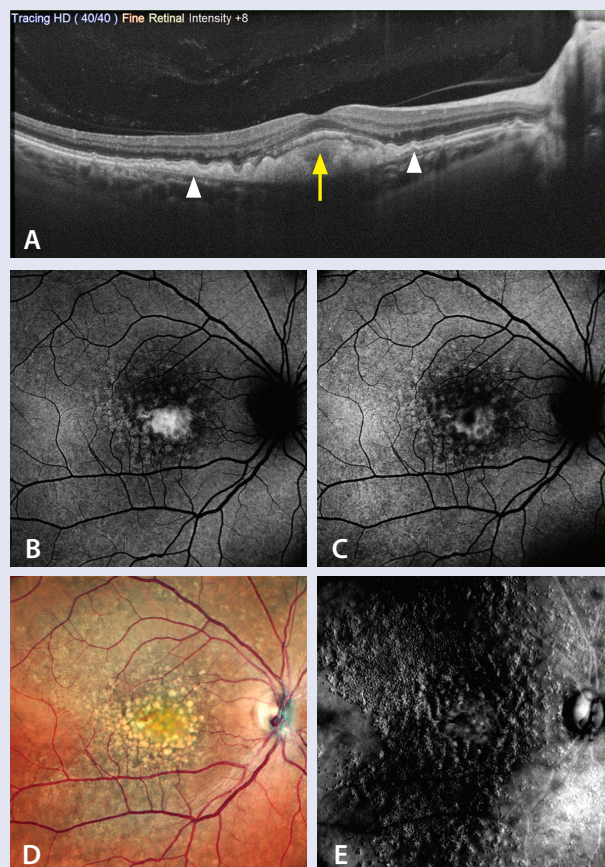
CASES

The utility of multimodal imaging in clinical practice is best understood in the context of how it helps delineate pathologic findings, thereby assisting the clinician in arriving at or confirming a diagnosis. Following are case examples from the authors that highlight how the various imaging modalities on the Mirante (NIDEK) were used to diagnose and make treatment decisions.

Case No. 1

**Mariano Cozzi, MSc,
and Giovanni Staurenghi, MD**

- Multimodal imaging is shown in a case of acquired vitelliform lesions involving the center of the macula associated with cuticular drusen phenotype of a 65-year-old female. Each imaging modality highlights different aspects of the disease.
- A high-definition, cross-sectional OCT image reveals hyper-reflective material above the retinal pigment epithelium (arrow) and multiple cuticular drusen (arrowhead) (A).
- Green autofluorescence shows a hyperautofluorescence signal, which indicates lipofuscin-like material accumulating between the retinal pigment epithelium and neuroretina (B).
- Blue autofluorescence barely displays the macula hyperautofluorescence signal because the blue wavelength is partially absorbed by the macular pigment (C).
- A color confocal image allows the ability to visualize a yellowish foveal material with presence of multiple drusen nearly filling the macular area (D).
- Retro mode infrared illumination image dramatically highlights the topographic distribution of cuticular drusen, which are known to be strongly associated with acquired vitelliform lesions (E).



RETRO MODE IMAGING

Many of the capabilities of the Mirante will already be familiar to retina physicians, even if they are performed in a slightly different manner. However, the Mirante also introduces a new imaging mode, Retro mode imaging, which is poised to enhance the ability to detect abnormalities.

In a typical imaging set-up with cSLO using a confocal aperture, direct back-scattered light returning from the fundus is gathered, while other sources of light scatter are blocked, thereby yielding a representative image of the confocal plane of interest. In Retro mode, an

aperture with a central stop is used to do the opposite: a laterally-oriented (either right- or left-deviated), oval-shaped opening prevents direct light reflection from entering the image processor, while scattered light from a single direction passes through the aperture. As this mode uses an infrared light source, the detector acquires images from the surface to the deep retinal layers, thereby producing an image with a shadow adjacent to any abnormal features. The result is a pseudo-3D image that delineates abnormalities in the deeper retinal and choroidal tissue planes. Of interest, both right- and left-deviated

apertures can be used in imaging to assure more complete data collection.

Retro mode is a modification of indirect (or dark-field) imaging, in which an aperture with a central stop is used to block direct light and gather other sources of scattered light, but it is more so analogous to retroillumination principles used in anterior segment imaging. The simplest way to understand Retro mode is that the resulting image is as though the retina were being lit from behind.

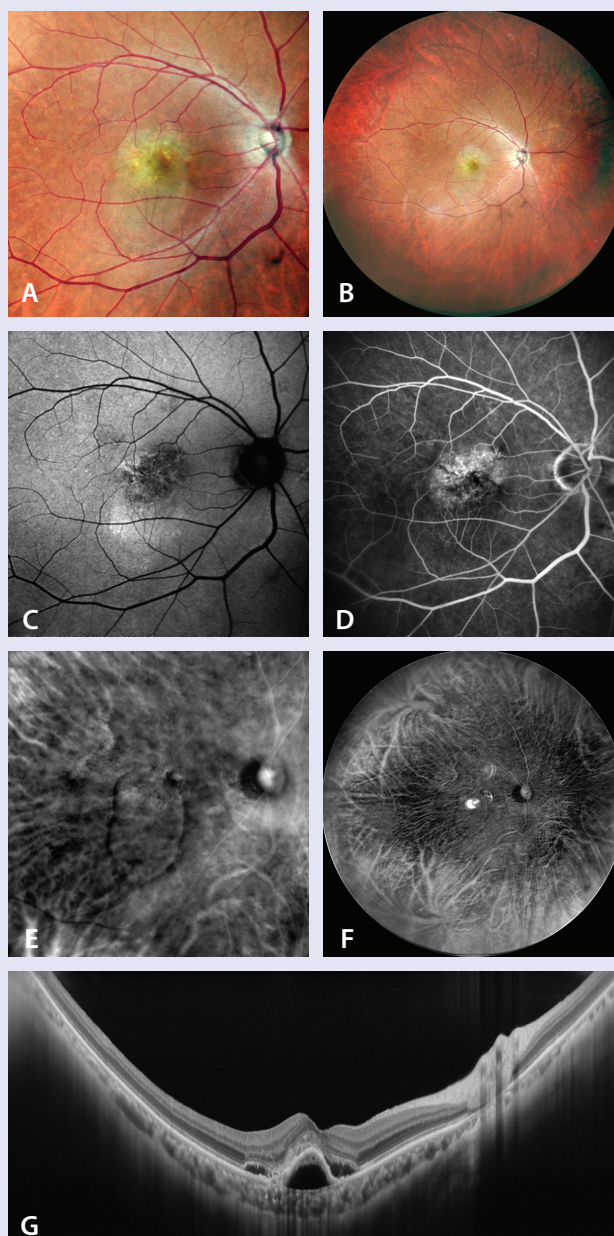
In previous research, Retro mode has been used to characterize morphologic features in a variety of clinical entities, including, but not limited to, cystoid

CASES

Case No. 2

Giulia Corradetti, MD,
and Srinivas R. Sadda, MD

- Multimodal imaging is shown in a case of choroidal neovascularization associated with age-related macular degeneration with some central serous chorioretinopathy (CSCR)-like features in an 85-year-old male.
- Widefield and Ultra-Widefield color fundus photographs captured with the Mirante (NIDEK) confocal scanning laser ophthalmoscopy are shown using three different channels (blue, green, and red) with central angles of 89° and 163°, respectively (A, B). Both images show a smooth and well-circumscribed yellowish fibrovascular pigment epithelial detachment (PED) involving the central macula.
- Green autofluorescence shows a central area of mottled hypo-autofluorescence highlighting the presence of retinal pigment epithelium alterations in the region of the PED, with adjacent hyperautofluorescence inferiorly corresponding to the subretinal fluid (C). Early phase fluorescein angiography shows irregular, stippled hyperfluorescence corresponding to the fibrovascular PED (D).
- Retro mode left-deviated, Widefield, and Ultra-Widefield images, respectively, show a vertical oval-shaped slightly hyper-reflective region with a rim of hyporeflectivity, which corresponds to the neurosensory detachment (E, F). The vertically-oblong shape suggests the gravitational nature of the fluid distribution. The Retro mode technology, using an eccentric confocal aperture, provides the additional contrast to display the fluid and its extent.
- An ultrafine cross-sectional spectral-domain OCT image through the foveal center (120x averaged) demonstrates a fibrovascular PED with secondary elevation of the overlying retina and subretinal fluid (G). Note, the internal characteristics of the PED are visible, with fibrovascular tissue at the apex of the PED and subretinal pigment epithelium fluid at the base. The full extent of the choroid is visualized and appears to be thick given the patient's age.



macular edema secondary to polypoidal choroidal vasculopathy, retinitis pigmentosa, and retinal vascular disorders; macular retinoschisis in eyes with high myopia and foveal schisis in eyes with X-linked retinoschisis; drusen and other subretinal deposits (indeed, Retro mode imaging depicts significantly more drusen

than conventional fundus photography); retinal pigment epithelium alterations in central serous chorioretinopathy; leaking microaneurysms in diabetic retinopathy; sites of subthreshold laser scars; and abnormalities in a variety of retinal dystrophies.¹ Ongoing research will help to elucidate how such findings may be

used in the clinical setting, and there are still many unanswered questions regarding how to interpret findings identified using Retro mode imaging. Nevertheless, there is strong potential to use this novel modality to highlight features that are currently undetectable using standard imaging.

DETECTION AND CHARACTERIZATION OF DRUSEN USING MULTIMODAL IMAGING

By Mariano Cozzi, MSc, and Giovanni Staurenghi, MD

We recently conducted a prospective observational study to assess the contribution of Retro mode imaging in the detection and characterization of drusen and subretinal drusenoid deposits.¹

For the study, 38 eyes of 31 consecutive patients with different types of drusen or subretinal drusenoid deposits (mean age, 78.8 years) were imaged using various modalities on the Mirante (NIDEK), including infrared reflectance, fundus autofluorescence, real confocal color fundus imaging, OCT, and Retro mode imaging using both a right- (DR) and left-deviated (DL) annular aperture.

Overall, retinal color fundus imaging was superior to other imaging for detecting soft drusen and ribbon subretinal drusenoid deposits. Our clinical impression was that Retro mode imaging readily depicted the 3D shape of the various types of drusen and deposits while also helping to appreciate the geographic distribution of the drusen at the back of the eye. However, there were some important differences in the appearance of different types of drusen using DR and DL

apertures, with DR mode depicting cuticular and soft drusen as tiny and wide depressions, respectively, whereas in DL mode, they appear as mounds of different sizes. Moreover, ribbon subretinoid deposits were identified with both modalities, showing a classic reticular pattern. Although DR mode appeared to barely differentiate dot subretinoid deposits from cuticular drusen, the DL modality showed a more precise identification of both entities.

It is hoped that this data will help to build on previous studies that suggest that different kinds of drusen are associated with different clinical outcomes. It may be the case that using multimodal imaging will help to identify different types of drusen and subretinal deposits, which at the current time is useful for understanding prognosis and potential for progression. In the future, and as new forms of treatment become available, such findings may be useful for directing appropriate intervention strategies.

1. Monteduro D, Cozzi M, Parrulli S, Staurenghi G. Topographic detection and characterization of drusen and subretinal drusenoid deposits: contribution of Retro mode modality in a multimodal imaging approach. Abstract 3471. Presented at: ARVO 2019; April 28-May 2, 2019; Vancouver, British Columbia, Canada.

CONCLUSION

There is a growing sentiment in retina practice that OCT, and perhaps OCTA, are sufficient for understanding and making decisions about pathology. We would contend that they are necessary, but not entirely sufficient. Rather, the growing variety of imaging modalities available for clinical use provides unique insights about different areas of the retina in the X-, Y-, and Z-planes; each different modality has a role in understanding how different disease states are affecting different parts of the globe. Collectively, they improve the ability to understand important details that can help us become better diagnosticians. When they are all available on the same platform, it

makes it more efficient to use them; it also provides greater correlation between separate modalities due to registration and tracking software.

The former does not suggest that clinicians should work through each modality while building a differential diagnosis; instead, it underscores that relying on one imaging modality may provide incomplete information regarding the status of the retina. Admittedly, having access to so many different imaging techniques does create practical challenges, and there may be a learning curve associated with adopting multimodal imaging into practice. On the other hand, this can be shortened by understanding how each mode captures images and at what planar level.

Understanding what each modality provides, including its limitations, will allow the clinician to home in on the specific modality that will be useful in a given clinical situation.

In some ways the capabilities and clinical utility of the Mirante are ahead of the science. The availability of Retro mode imaging is somewhat reflective of this, as it is more so an exciting research tool at this point and time. And yet, the potential to discover and detect pathology using Retro mode imaging that would be missed with other imaging techniques also exemplifies what is truly revolutionary about multimodal imaging. The more data clinicians have at their disposal, the better equipped they will be to diagnose pathology early and initiate intervention strategies that will help patients save vision. ■

1. Lee WJ, Lee BR, Shin YU. Retromode imaging: review and perspectives. *Saudi J Ophthalmol*. 2014;28(2):88-94.

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