Saudi Journal of Ophthalmology (2014) 28, 88–94

Retinal and Choroidal Imaging Update

Retromode imaging: Review and perspectives

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Abstract

Retromode imaging with infrared lasers is a novel imaging method which has been made possible by the newly introduced confocal scanning laser ophthalmoscope. Retromode imaging uses a laterally deviated confocal aperture with a central stop, which creates a shadow and allows deep retinal and retinal pigment epithelium changes to be visualized as pseudo-3-dimensional images. Its clinical value coupled with its simple, rapid, and noninvasive nature is increasingly appreciated. The combination of retromode imaging with conventional imaging methods such as fundus photography, fluorescein angiography, and optical coherence tomography can help to precisely and comprehensively evaluate pathophysiologic features of retinal disorders. This review summarizes basic principles of imaging and retromode findings in various retinal disorders and is expected to guide future investigations of retromode imaging.

Keywords: Retromode, Confocal, Scanning laser ophthalmoscope

http://dx.doi.org/10.1016/j.sjopt.2014.02.003

Introduction and principles of retromode imaging

Recently, based on the principles of retro-illumination, retromode imaging has been used to investigate several retinal pathologies. The newly introduced F-10 confocal scanning laser ophthalmoscope (cSLO; Nidek, Gamagori, Japan) implements retromode imaging to view the retina with an infrared laser. Retromode imaging can be useful to study deep retinal pathologies and retinal pigment epithelium (RPE) changes.

The F-10 is a newly developed cSLO apparatus that has 4 different wavelengths (blue, 490 nm; green, 532 nm; red, 660 nm; infrared, 790 nm) and 8 apertures (5 confocal apertures and 3 apertures with a central stop). In the cSLO, the light returning from the fundus consists of direct backscattered light as well as more multiply scattered light. A confocal aperture collects the directly backscattered light from the confocal plane. In the indirect (dark-field) mode, an aperture with a central stop (ring aperture) is used and direct backscattered light is blocked with a central stop. The detector collects more multiply scattered light than direct backscattered light. Retromode imaging, which is a modified version of indirect (dark field) imaging, uses infrared laser light because of its ability to penetrate deeper layers. Instead of the ring aperture used in indirect (dark-field) mode, retromode uses only part of the annular aperture. The annular aperture deviates laterally from the light pathway supplied by the confocal aperture, which collects backscattered light from one direction and blocks it from other directions. This creates a shadow to one side of the abnormal feature, creating pseudo-3-dimensional (3D) images (Fig. 1). The scattered light passing through the deviated aperture gives a shadow to abnormal features, thus enhancing their contrast and delineation. The shadows of lesions appear differently according to the laterality of the annular aperture. Both right-deviated and left-deviated annular apertures (''DR'' and ''DL'') are used.

Received 30 December 2013; accepted 12 February 2014; available online 20 February 2014

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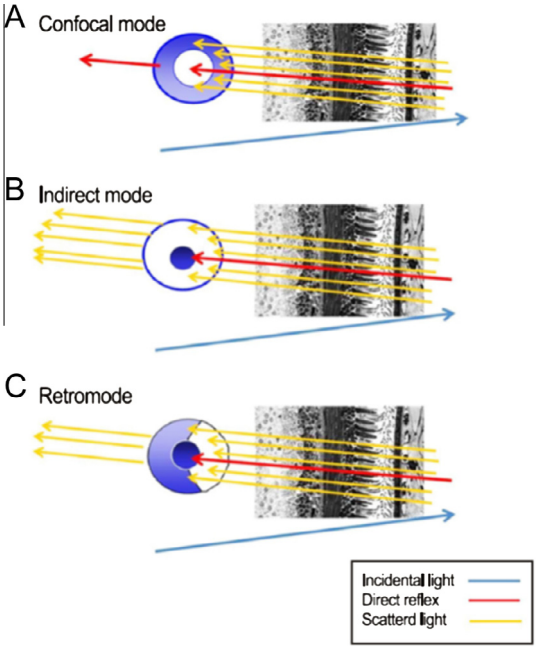

Figure 1. Schematic mechanism underlying retromode imaging with a confocal scanning laser ophthalmoscope. (A) Confocal mode: images consist primarily of direct backscattered light from the fundus. (B) Indirect (dark-field) mode using an aperture with a central stop (ring aperture): direct backscattered light is blocked with a central stop. More multiply scattered light from intraretinal structures is collected by the detector. (C) Retro-mode: The opening of the ring aperture is restricted and deviates laterally from the confocal light path. Multiply scattered light from only one direction is collected by the detector.

Clinical applications

Retromode imaging is used to investigate several retinal pathologies. Multiple clinical applications of retromode imaging are introduced below.

Cystoid macular edema (CME)

Retromode imaging is able to characterize CME secondary to polypoidal choroidal vasculopathy (PCV), retinitis pigmentosa, and retinal vascular disorders such as diabetic retinopathy (DR) and retinal vein occlusion.[1–3] In retromode imaging, scattered light that has passed through the aperture deviates laterally, shadowing the silhouetted cystoid spaces and enabling CME visualization. Retromode imaging shows numerous oval or polygonal cystoid spaces located in any layer of the retina (Fig. 2). Using retromode imaging, most eyes with CME show a large cystoid space beneath the fovea with surrounding small cystoid spaces. The area of the foveal cystoid space correlates with its height, as measured by optical coherence tomography (OCT).[2]

Retinoschisis

Retromode imaging shows characteristic alterations of the retina that correspond to the site of macular retinoschisis in highly myopic eyes. Retromode imaging shows two characteristic fingerprint patterns that contain either radiating retinal striae centered on the fovea and many light dots and lines in parallel to the striae, or a whorled pattern surrounding the radiating striae (Fig. 3). The central radiating retinal striae ob-

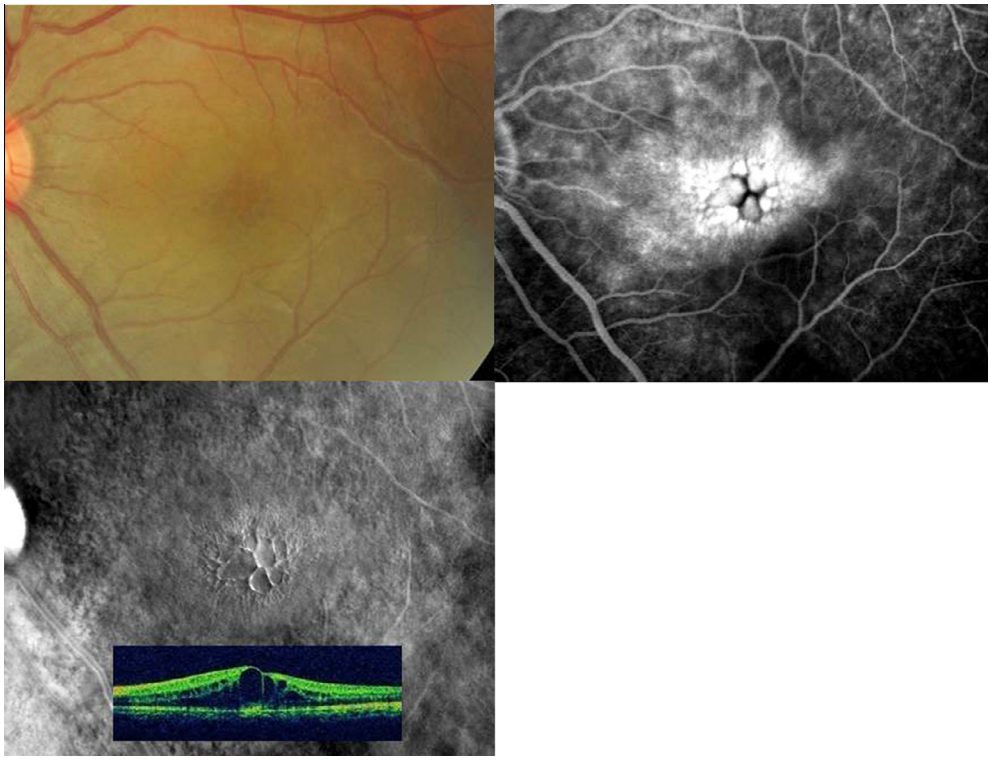

Figure 2. Representative retromode images of an eye with cystoid macular edema. (Top left) No cystoid spaces are detected on fundus photography. (Top right) Late-phase fluorescein angiography shows many cystoid spaces. (Bottom) Retromode imaging shows numerous polygonal cystoid spaces.

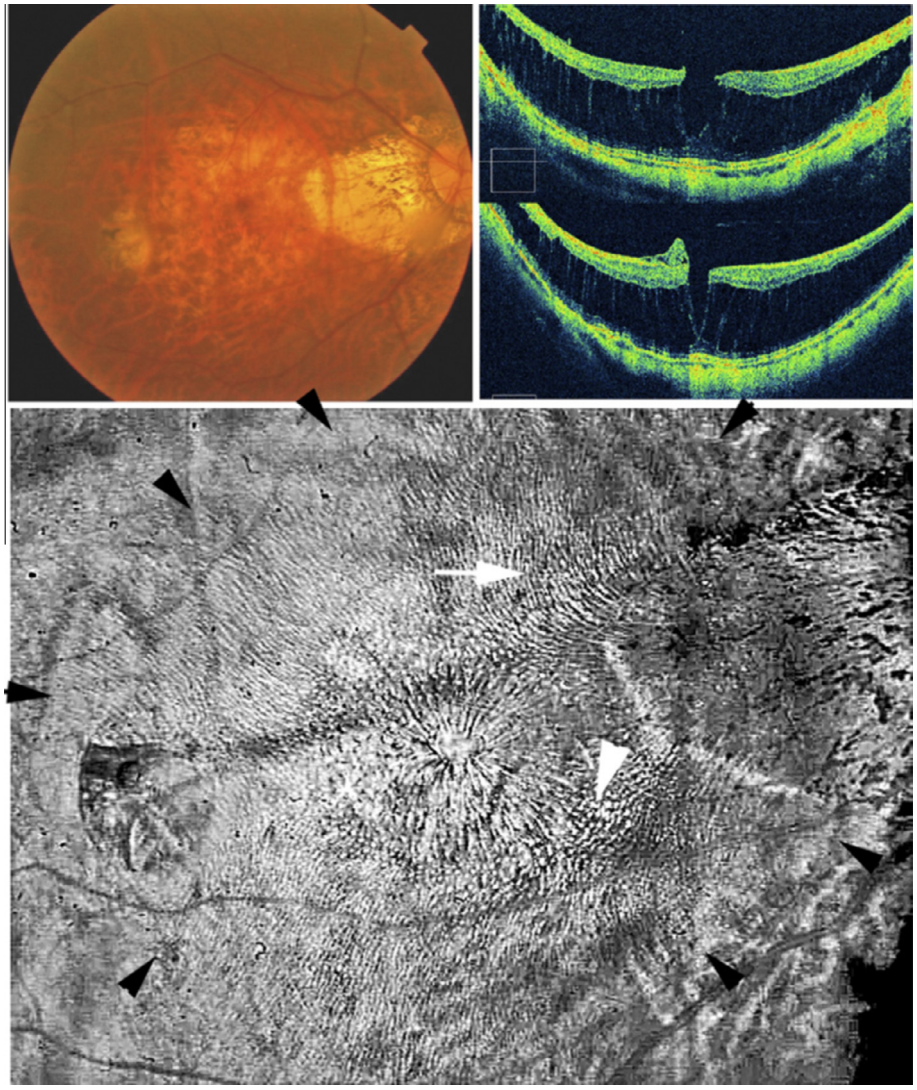

Figure 3. Representative retromode images of an eye with outer macular retinoschisis. (Top left) Fundus photograph of the right eye of a 77-year-old woman showing diffuse chorioretinal atrophy in the posterior fundus. (Top and middle right) Horizontal and vertical scans across the central fovea by optical coherence tomography (OCT) show macular retinoschisis with an inner lamellar hole in the central fovea. (Bottom) Retromode image by F10 shows a fingerprint pattern (black arrowheads) consisting of central radiating retinal striae and surrounding multiple dots (arrowhead) and lines (arrow). Many lines appear in parallel or in a whorled pattern. The inner lamellar hole is observed as a circular defect at the central fovea. Data are from *Am J Ophthalmol* (Tanaka et al.[4]).

served in retromode imaging may represent the splitting of the horizontally oriented internal cone fibers.[4]

In eyes with X-linked retinoschisis, it is occasionally difficult to detect a foveal schisis ophthalmoscopically. However, the foveal schisis is clearly delineated by retromode imaging, which also clearly delineates the stellate spoke-like foveal schisis.[5]

Drusen

Retromode imaging shows a pseudo-3D appearance to drusen, which is consistent with the appearance of drusen on OCT imaging (Fig. 4). Retromode imaging detects significantly more subretinal deposits than conventional color fundus photography.[6] In addition, retromode imaging detects higher numbers of drusen than cSLO using another infrared confocal aperture. In fact, the mean number of drusen detected with the ''DR'' retromode is almost two times greater than the number detected by color fundus photography. Small drusen are more easily visualized with retromode imaging. This suggests that retromode imaging may be a sensitive modality for the detection of drusen, especially when a patient is early in the disease course and/or when the drusen are small or subtle.[7]

Comparing the second and first set of retromode images revealed appreciable changes, such as enlargement and confluence of the deposits; however, no changes over time were evident on fundus photography. Therefore, retromode imaging may be useful in monitoring the response of drusen to future therapeutic interventions[6] as well as subtle changes and progression of age-related macular degeneration (AMD).

Central serous chorioretinopathy (CSCR)

Retromode imaging can provide topographic information regarding RPE alterations in CSCR; this topographic map is similar to a surface RPE map of the posterior pole.[8]

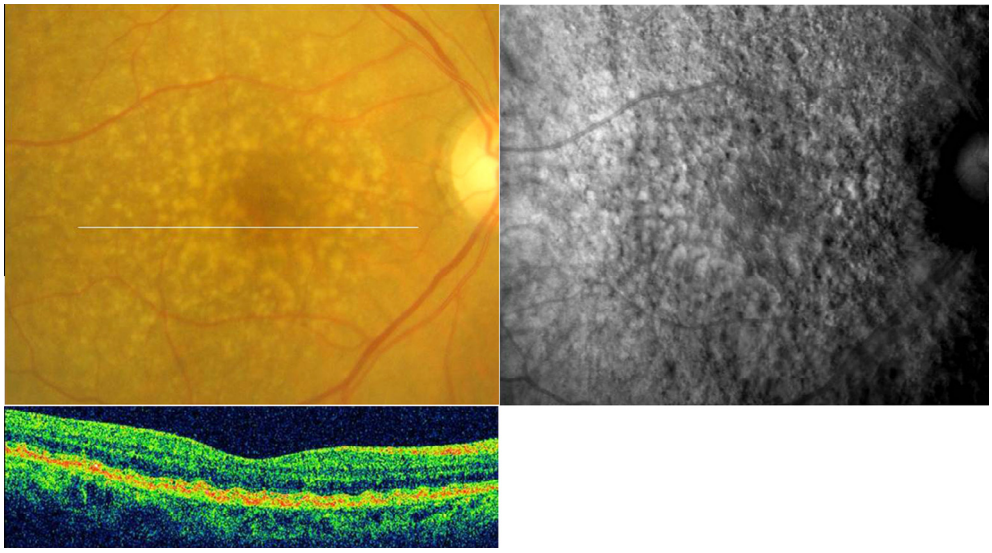

Figure 4. Representative retromode images of an eye with drusen in the fellow eyes of unilateral exudative age-related macular degeneration patients. Soft drusen and hard drusen are mixed. (Top left) Fundus photography. (Topright) Retromode imaging (Bottom) Optical coherence tomography (OCT). The drusen in retromode imaging appear pseudo-3-dimensional and are clearer than in fundus photography. The OCT finding is retinal pigment epithelium elevation, which is consistent with the appearance of drusen.

Retromode imaging identifies subretinal fluid (SRF) as a well-defined, circular to ovoid, translucent prominence with low to moderate convexity and a dark shadow. Semicircular pigment epithelial detachment (PED) is identified as a well-defined, circular to slightly irregular, translucent prominence with low to moderate convexity and a dark shadow. Low to flat PED and RPE protrusion are identified as a well- to ill-defined, flat to slightly convex, slightly irregular, and translucent to opaque prominences with a dark shadow. Subretinal precipitations appear as multiple small, relatively hyperreflective dots. In cases of resolved CSCR, disrupted outer photoreceptors appear as a well-defined, ragged, plate-like surface (Fig. 5).[8]

Diabetic retinopathy (DR)

In the evaluation of diabetic macular edema (DME), retromode imaging and OCT show high agreement. Although OCT is the new gold standard in evaluating DME, retromode imaging also allows for early DME detection. Moreover, retromode imaging provides immediate visualization of macular edema location and the extension of thickened area.

Retromode imaging can visualize leaking microaneurysms as localized elevations. These elevations correspond to microaneurysms that show significant dye diffusion in late-phase fluorescein angiography (FA).[3] Retromode imaging may be useful in evaluating neovascular vessels and fibrovascular membranes and determining precise retinal changes in proliferative DR.[9]

Subthreshold laser scar

Retromode imaging is useful in detecting sites of subthreshold micropulse laser application that cannot be detected by color fundus photography (Fig. 6). The dark spots detected by retromode imaging are probably related to swelling of the RPE after laser application. Since subthreshold diode laser micropulse photocoagulation is selective for the RPE, the dark spots are assumed to be related to structural RPE changes. Retromode imaging provides useful confirmation of the invisible spots created by subthreshold diode laser micropulse photocoagulation.[10]

Retinal dystrophies

Retromode imaging is able to detect abnormalities in retinal dystrophies, including Best vitelliform macular dystrophy, autosomal recessive Stargardt disease (fundus flavimaculatus), pattern dystrophy of the RPE, choroideremia, benign concentric annular macular dystrophy, and Bietti crystalline dystrophy. The main finding is a pseudo-3D pattern of all the lesions at the posterior pole. Any accumulation of material within the retina appears as an elevated area with varied shapes and sizes, showing irregular and darker borders. On the other hand, atrophic regions are accurately outlined by the precise visualization of the choroidal vasculature, both in the macula and, in cases where the fovea is spared, outside the macular region as well.[11,12]

Other uses

Retromode imaging is able to clearly visualize the morphological features of PCV, including polypoidal lesions and branching vascular networks.[13] Retromode imaging is also useful in detecting retinal changes secondary to exudative AMD associated with CNV, particularly CME.[14]

Perspectives

Directionality of retromode imaging

The interpretation of lesion morphologies seen with retromode imaging requires attention to the dark shadows surrounding specific lesions, because they appear as dark

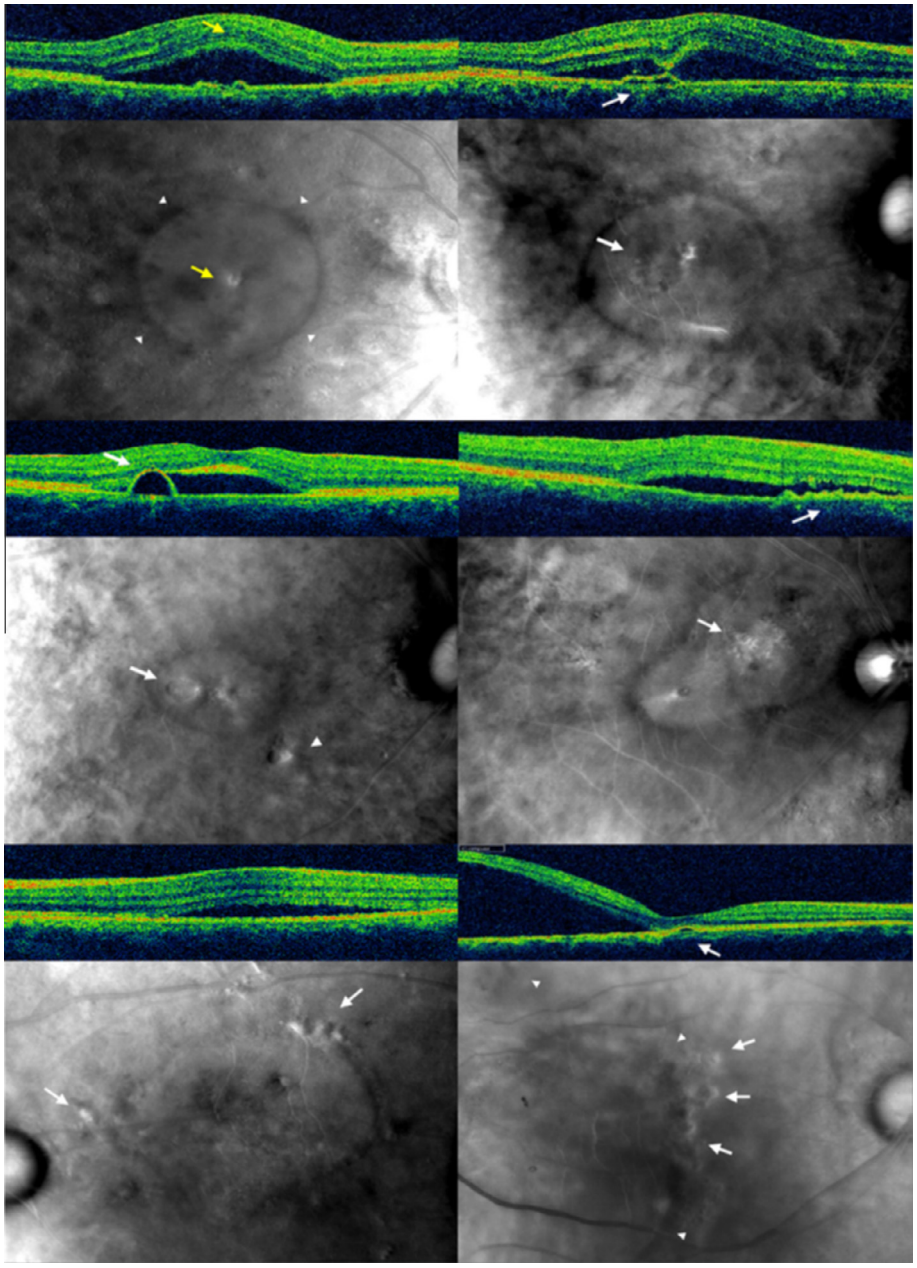

Figure 5. Representative retromode images of eyes with central serous chorioretinopathy (CSCR): a case series of acute CSCR. Various alterations in the retinal pigment epithelium (RPE) are observed using retro-mode imaging and spectral-domain optical coherence tomography (OCT). (Top left) Subretinal fluid (SRF) in OCT appears as a well-defined, convex, circular, and translucent prominence with a dark shadow in retromode images (white arrowheads). The vertex of the SRF is the highly reflective focal spot (yellow arrow) in retromode images. Small pigment epithelial detachments (PED) seen on OCT are not observed in this retromode image because of the SRF's blocking effect. (Top right) Low to flat PED in OCT (white arrow) appears as a relatively well-defined, flat-convex, slightly irregular, translucent prominence with a dark shadow (white arrow) in retromode images. Even if the PED is located within the SRF, it can be seen clearly. (Middle left) Semicircular PED within the SRF seen on OCT appears as a well-defined, semicircular-convex, circular, and translucent prominence with a dark shadow (white arrow) in retromode images. A small PED away from the SRF is also observed in retromode imaging (white arrowhead). (Middle right) RPE protrusion in OCT appears as a relatively ill-defined, flat-convex, irregular, and opaque prominence with a dark shadow in retromode images (white arrow). (Bottom left) No PED is detected in whole OCT scans obtained by a 6 by 6 mm volume scan protocol. However, retro-mode imaging reveals multiple PEDs located at the margin of the SRF (white arrows). (Bottom right) Bullous SRF and small subfoveal PEDs are observed in OCT. Retromode imaging shows the extent of the SRF (white arrowheads) and multiple PEDs alongside the SRF (white arrows). Data are from *Am J Ophthalmol* (Shin et al.[8]).

crescent shadows in the opposite direction of the annular aperture (''DR'' mode or ''DL'' mode).[8] For example, elevated lesions such as PED are composed of lighter portions and shadows such as dark crescents. The dark crescents represent a concave border between the flat RPE area and the elevated PED, while the lighter portions represent the convex area of the elevated PED.[8] Thus, the direction of the deviated aperture and the positions of the dark and light portions of the target lesion should be considered when interpreting retromode images. Depending on whether the ''DR'' or ''DL'' mode is used, convex lesions may appear as convex or concave patterns. In this

way, retromode imaging provides directional information and may enhance subtle features such as low-lying drusen more than infrared SLO indirect imaging.[6,8] Consequently, two consecutive images obtained by the ''DR'' and ''DL'' modes should be analyzed simultaneously. In addition, these shadows are influenced by retinal pigmentation and by lesion convexity and concavity. If abnormally broad, dark shadows that are unrelated to lesions appear in retromode images, verification by fundus photography is necessary to check for the presence of retinal pigmentation.[8]

Advantages of retromode imaging

Retromode imaging has several advantages for the detection of subretinal and RPE alterations. It is a noninvasive, rapid, and simple imaging technique. The imaging process is similar to that of fundus photography. Although FA and indocyanine green angiography (IA) require a long capture time and the injection of intravenous dye, retromode imaging does not. Another advantage is the infrared laser used in retromode imaging. The examination can be performed under

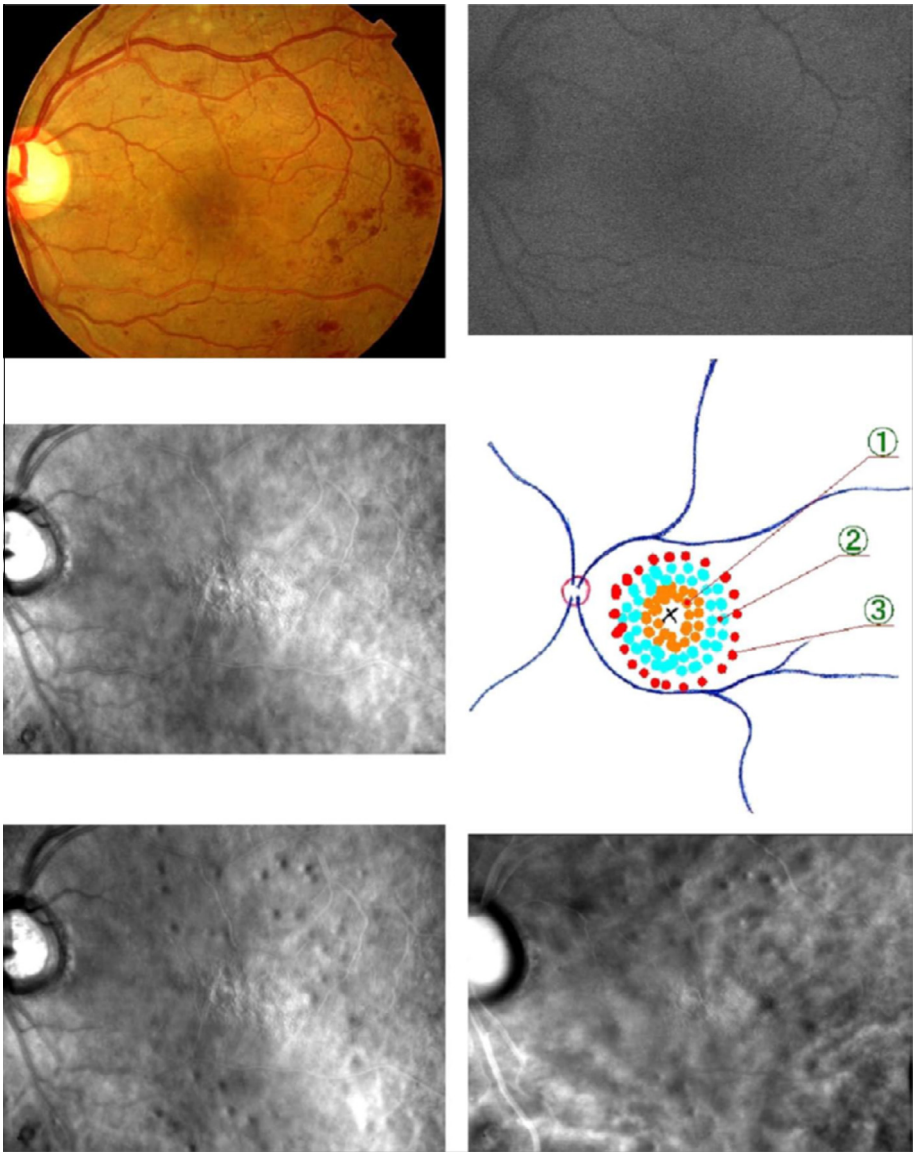

Figure 6. Pictures from a patient with diabetic macular edema treated by subthreshold micropulse diode laser photocoagulation. (Top left) Fundus color photograph immediately after subthreshold micropulse diode laser photocoagulation. Subthreshold photocoagulation was applied to the area of diffuse dye leakage. There was no obvious color change in the treated retina. (Top right) Fundus autofluorescence image immediately after subthreshold diode laser micropulse photocoagulation. There is no change in autofluorescence at the treated area. (Middle left) F-10 retromode images obtained before subthreshold diode laser micropulse photocoagulation. (Middle right) Illustration showing area treated with subthreshold micropulse diode laser photocoagulation. Subthreshold photocoagulation was applied with a 15% duty cycle for 0.2 s at 200% of threshold power (640 mW), creating two circular 200 um spots in the area surrounding the fovea (1). Then, two circular 200 um spots were made at 300% of threshold power (960 mW) outside the first treated area (2). Finally, 125 um spots at 250% of threshold (800 mW) were applied outside the second treated area (3). (Bottom) An F-10 retromode image obtained immediately after subthreshold micropulse diode laser photocoagulation. Several dark spots can be seen after photocoagulation. The spots are mainly visible in the area treated at 300% of threshold or with 125 um at 250% of threshold. The spots seem to be composed of shadow-like dark crescent and lighter portions. (Left) With the left aperture, the image shows dark crescents on the right side. (Right) With the right aperture, the image shows dark crescents on the left side. Data are from *Am J Ophthalmol* (Ohkoshi et al.[10]).

nonmydriatic conditions or even in cases with significant lens opacity, due to the properties of the long-wavelength laser. Moreover, patients may feel more comfortable during the examination because the infrared light is less irritating than the blue light used in FA.[8]

Retromode imaging also provides pseudo-3D images of the lesions on the en face plane in a single image, which helps to evaluate the spatial distribution of lesions in the posterior pole of the fundus.

Limitation of retromode imaging

With respect to the use of retromode imaging for the detection of abnormal features, several issues should be considered. First, retromode imaging is currently available only with use of the F-10 microscope. Second, this technique cannot replace OCT, FA, and IA in evaluating various retinal disorders. OCT is still the gold standard for diagnosing anatomic lesions in retinal and subretinal layers. Unlike FA and IA, retromode imaging cannot be used to describe the disease activity of various retinal disorders, and it is difficult to make treatment decisions using retromode imaging alone. Therefore, retromode imaging may be helpful as an imaging technique that complements OCT, FA and IA. Third, several previous studies with retromode imaging described the relationship between the retromode imaging and that of retinal disorders; however, these experiments were not designed to determine the mechanism causing the appearance of the retinal disorders.[4] Fourth, in the absence of histological confirmation, we cannot necessarily conclude that all abnormalities seen by this new imaging strategy are in fact present and relevant. For example, retromode imaging alone is unable to differentiate flat PED from RPE irregularities.[8] Fifth, this noninvasive imaging technique is helpful in determining both the presence and the extent of abnormal features in the posterior pole, but is not able to localize the exact depth of the lesions within the retinal layers. This might be explained by the optical characteristics of the system, which are unable to separate the back-scattered light reflected from the retina, choroid, and sclera.

Conclusions

Retromode imaging is a new technique capable of providing comprehensive topographic information related to the deep retina and RPE alterations. However, the investigation of retromode imaging is in its earliest stages, and there are shortcomings in the interpretation of these findings. Thus, the combination of retromode imaging and other imaging modalities such as OCT and FA can help to precisely and comprehensively evaluate pathophysiologic features of retinal disorders. This review is expected to help guide future investigations of retromode imaging in various retinal disorders.

Conflict of interest

The authors declared that there is no conflict of interest.

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