Recent Trends in Retinal and Choroidal Imaging

Tarek A. El-M’amon, Abdel-rahman G. Salman, Safaa S. Mahmoud, Alyaa B. Mohammed
*Department of ophthalmology, Ain Shams University, college of medicine, Cairo, Egypt

Abstract

The last decade have witnessed a tremendous advancement in retinal and choroidal imaging technologies thanks to improved light sources, detectors and high speed computers which are continuously improving. There are many examples as Fundus autofluorescence is a relatively novel imaging method that allows topographic mapping of lipofuscin distribution in the retinal pigment epithelium cell monolayer as well as of other fluorophores that may occur with disease in the outer retina and the subneurosensory space. Optical coherence tomography is a method of using low-coherence interferometry to determine the echo time delay and magnitude of backscattered light reflected off an object of interest. This method can be used to scan the retina with very high axial resolution. Optical coherence tomography angiography (OCTA) is a new non-invasive imaging technique that employs motion contrast imaging to get high-resolution volumetric blood flow information generating angiographic images in just a few seconds. OCT is undergoing another transformation with Multicolor technology by combining with confocal scanning laser ophthalmoscope to acquire images using data from three simultaneous lasers red, green and blue taking advantage of the different wavelengths of each of these colors to image 3 different zones of the retina.

Keywords: Fundus autofluorescence (FAF) – Age related macular degeneration (AMD) – Optical coherence tomography (OCT) - Optical coherence tomography angiography (OCTA) –Multicolor imaging (MCI)

Introduction

Retinal pigment epithelium (RPE) is a single layer of polygonal shaped cells, which separates the choroid from the neurosensory retina. It is responsible for phagocytosis and lysosomal breakdown of pigmented outer segments of photoreceptors. Over the course of a lifetime, each RPE cell will phagocytose 3 billion outer segments. With aging, incomplete or partial breakdown of these segments in the post-mitotic RPE cells causes the accumulation of lipofuscin (LP). Accumulation of lipofuscin above a certain threshold can cause functional loss of cells and lead to apoptosis. Fundus autofluorescence (FAF) is a non-invasive imaging technique that detects ocular fluorophores, which is naturally occurring molecules that absorb and emit light of specified wavelengths. Lipofuscin is a dominant ocular fluorophore that absorbs blue light with a peak excitation wavelength of 470nm and emits yellow-green light at a peak wavelength of 600-610nm. FAF utilizes blue-light excitation, then collects emissions within a preset spectra to form a brightness map reflecting the distribution of lipofuscin, FAF may use other excitation wavelengths to detect additional fluorophores, such as melanin with near-infrared autofluorescence. Commercially available FAF systems include fundus cameras (FC), confocal scanning laser ophthalmoscopes (cSLO), and ultra-wide field technologies. Fundus camera systems often utilize longer wavelength (530 to 580nm) compared to cSLO (488nm). Near infra-red fundus autofluorescence can be recorded using excitation wavelengths of 790 nm with emissions above 800 nm using a cSLO. Its emission corresponds to areas of higher density melanin in the retinal pigment epithelium and choroidal pigment.

FAF in AMD

FAF is highly valuable in age-related macular degeneration (AMD) as RPE damage is a hallmark of the disease, patients with early AMD, characterized by sub RPE deposits called drusen. Drusen have a variable appearance on FAF depending on size, composition, and health of the overlying RPE
Large drusen are more likely to result in FAF changes, while small drusen may be iso-autofluorescent and remain undetected. Intermediate drusen (63-125 µm in diameter) demonstrate a pattern of central hypo-autofluorescence with an annulus of hyper-autofluorescence, likely due to central RPE atrophy surrounded by abnormal RPE (9). Description of different autofluorescence patterns of drusen is helpful in determining the prognostic factors, characterization of high risk patients, and follow-up of the course of the disease (10). Geographic atrophy is the end stage of AMD in 35% of patients and will become more prevalent with the aging population (11). Lesions mostly occur parafoveally, with foveal sparing, RPE atrophy and consequent absence of lipofuscin results in a patchy atrophic area with a low FAF signal with sharply demarcated borders (12). Geographic atrophy may be surrounded by perilerial hyper-autofluorescence, which repesent areas of ongoing RPE cell dysfunction and variable progression to atrophy (13). An excessive accumulation of Lipofuscin, and therefore an increased FAF in the junction are highly suggestive of the appearance or progression of pre-existing GA (10).

**FAF in Stargardt Disease:**

It is the most common form of juvenile macular degeneration (5). It presented clinically by foveal atrophy surrounded by yellow flecks with peripapillary sparing. The flecks are deposit of lipofuscin, which builds up abnormally in patients with Stargardt disease and progressive vision loss may occur due to death of specialized, light-sensitive photoreceptor cells in the macula. With FAF Early stages may demonstrate a general increase in lipofuscin and thus increased autofluorescence (14). Then a pattern of chorioretinal atrophy as the disease progresses resulting in macular hypo-autofluorescence, surrounded by hyper-autofluorescent flecks, in end stages, complete degeneration and diffuse RPE atrophy and photoreceptor cell death result in hypo-autofluorescence and vision loss (15). Limitations of FAF include a low signal strength (two orders of magnitude less than the peak signal of fluorescein angiography), autofluorescence artifact from anterior segment structures. In addition, the blue-light excitation beam may cause patient discomfort. cSLO imaging cannot be preceded by fluorescein angiography, which has a similar excitation and emission spectra (5).

**Optical Coherence Tomography**

Optical coherence tomography (OCT) is considered one of the investigative tools which made a revolution in ophthalmology and helped ophthalmologist a lot in diagnosis, treatment and follow up of many posterior segment diseases. It is a noninvasive noncontact imaging modality that provides a high-resolution cross-sectional image approaching that of histological sections of the cornea, retina, choroid and optic nerve head, its noninvasive nature and high resolution images has made OCT particularly useful in the detection and management of retinal and choroidal pathologies (16). Spectral domain OCT uses near-infrared light to produce cross-sectional or three dimensional (3D) images of the retina. With scan Speed ranging from 29,000 to 80,000 scans per second and an axial resolution up to 2µm (17). During SD-OCT imaging, a beam of low coherence light from a superluminescent diode is split through a beam splitter into a sample and a reference beam. Both reflected beams of light are simultaneously detected, compared and combined into an interference pattern and converted into depth profile by combining many A-scans which is the intensity of reflected light at various retinal depths at a single retinal location, Entire A-scan created at a single time Process repeated many times to create B-scan using a modified Michelson interferometer, called the spectral interferogram or spectrometer (18). SWEPT-SOURCE OCT (SS-OCT) uses a frequency swept laser with a tunable wavelength of operation instead of the diode laser used in spectral-domain OCT (19). The SS-OCT has improved image penetration using a wavelength of 1050nm and has an axial resolution of 1 µm and an axial scan rate of 100,000 scans per second (20).

**OCT in Diabetic Maculopathy**

OCT enables precise measurement of macular thickness. Thus, it facilitates detecting macular oedema which is the main pathologic feature of diabetic maculopathy (21). With rise of era of OCT, new classifications of DME appeared in addition to the traditional classification based
on Fluorescein Angiography \(^{(16)}\), Helmy and Atta Allah \(^{(22)}\) made a study in 2012, using the Cirrus HD-OCT and including 104 eyes from 86 patients to propose a new classification of diabetic cystoid macular edema (CME) based on (OCT) findings. They classified patients into four groups based on the ratio of vertical size of the largest macular cyst in relation to the size of maximum macular thickness, with the use of OCT. Patients with cysts less than \((30\%)\) of macular thickness were considered to have CME I, while those between 30% and 60% of macular thickness were considered to have CME II. Patients with cysts between 60% and 90% of macular thickness were considered to have CME III and CME IV was diagnosed when the size of the cyst became more than 90% of the macular thickness. OCT not only has a role in classification of DME but also has an important role in prognosis of visual acuity (VA) in patients with DME. Presence of foveal exudates may contribute to poor prognosis, various studies have reported that the integrity of the outer retinal layer is linked to a good visual prognosis but, disruption of the hyperreflective photoreceptor inner segment/outer segment junction on OCT, located just above the RPE, may reveal damage to the macular photoreceptors and subsequent poor prognosis \(^{(23)}\).

**OCT in Glaucoma**

SD-OCT are able to outline the retinal nerve fiber layer (RNFL) with much accuracy, so, it enables a comprehensive assessment of all the retinal ganglion cell (RGC) axons as they approach the optic nerve head (ONH) \(^{(24)}\). OCT has three main parameters relevant to the detection of glaucoma: retinal nerve fiber layer (RNFL), optic nerve head (ONH), and the “ganglion cell complex.” (Comprised of RNFL, ganglion-cell layer (GCL), and inner plexiform layer (IPL), the numeric values for all parameters are presented in colors as white, green, yellow, or red, with the yellow representing, < 5% and red representing < 1%, compared to the normative database \(^{(25)}\). It was demonstrated with EDI-OCT that Lamina Criprosa in glaucoma patients is thinner than in normal subjects \(^{(26)}\). However, the posterior laminar surface is not visualised clearly using SD-OCT. SS-OCT enables detailed analysis of the optic disc including LC. Focal LC defects, which corresponded with neuroretinal rim thinning and with visual field defects, were observed in glaucoma patients. \(^{(27)}\).

Because OCT utilizes light waves, media opacities can interfere with optimal imaging. As a result, the OCT will be limited the setting of vitreous hemorrhage, dense cataract or corneal opacities. In addition Patient movement can diminish the quality of the image \(^{(16)}\).

**Optical Coherence Tomography Angiography OCTA**

Optical coherence tomography angiography (OCTA) is an exciting new imaging technology that allows for non-invasive non-dye-based visualization of blood flow in the posterior pole. The technology has been used to image a variety of choriorretinal disorders including choroidal neovascularization in age-related macular degeneration, diabetic retinopathy, retinal arterial occlusion, retinal vein occlusion, and macular telangiectasia type 2. Continued advances in the software will improve the quality of OCTA and reduce image artifacts \(^{(28)}\). It employs motion contrast imaging to high-resolution volumetric blood flow information generating angiographic images in a few seconds. OCTA compares the decorrelation signal (differences in the backscattered OCT signal intensity or amplitude) between sequential OCT b-scans taken precisely at the same cross-section in order to construct a map of blood flow \(^{(29)}\).

**OCTA in Choroidal Neovascularization**

Segmentation of the outer retina and/or choriocapillaris shows type 1 and 2 CNV as either a well-circumscribed sea-fan network or a poorly-circumscribed filamentous vascular tree while type 3 CNV appears as a vascular tuft or ball above a retinal pigment epithelial detachment (PED) \(^{(30)}\). The feeder vessel to the choroid in type 1 and 2 CNV and to the retinal vasculature in type 3 CNV may be visible when there is good signal and scan quality \(^{(31)}\). OCTA can be used to monitor CNV after anti-vascular endothelial growth factor (anti-VEGF) treatment with reduced CNV density and size, vascular rarefication, and loss of smaller or peripheral capillaries after therapy \(^{(32)}\).
**OCTA in Diabetic Retinopathy**

OCTA in DR may demonstrate capillary non-perfusion, microaneurysms, irregular and/or enlarged Foveal avascular zone (FAZ), intraretinal microvascular abnormalities (IRMA), diabetic macular edema, and preretinal neovascularization (33). The normally ovoid and regular shape of a normal FAZ may become irregular and enlarged in DR, which is more notable in the deep inner retina (34). The FAZ is enlarged in diabetic eyes compared with age-matched controls, and increases with each stage of progression of retinopathy (35). Segmentation of the OCTA above the internal limiting membrane in proliferative DR allows for visualization of preretinal neovascularization, which often occurs adjacent to capillary non-perfusion and/or IRMA (36).

Multiple OCTA image artifacts may affect image quality. Motion artifact due to blinking or gross eye movement appear as horizontal or vertical black and white lines, respectively, and motion correction software can create vessel doubling, stretching of the image, quilting, or loss of detail in the attempt to compensate for these motion artifacts (37).

**Multicolor Retinal Imaging**

Multicolor laser imaging (MCI) performed with OCT represents the most recent advance for in vivo retinal imaging, uses the confocal scanning laser ophthalmoscope cSLO to capture three simultaneous reflectance images using three monochromatic laser sources: (1) blue reflectance (BR; 488nm), (2) green reflectance (GR; 515nm) and (3) infrared reflectance (IR; 820nm). With this technology, the retina and optic nerve are scanned simultaneously with 3 laser beams of different wave lengths (38). Each colored laser focuses on a different depth within the retina. Because of these different depths of penetration, unique localizing information is obtained from 3 discrete levels of the retina in a topographic map. The infrared laser penetrates to the shallowest depth and provides detailed images of the retinal nerve fiber layer, ganglion cells, macular pigment, and any structures on the surface of the retina, such as an epiretinal membrane (39).

The blue laser penetrates to the shallowest depth and provides detailed images of the retinal nerve fiber layer, ganglion cells, macular pigment, and any structures on the surface of the retina, such as an epiretinal membrane (39).

**Multicolor Imaging in Choroidal Tumors**

Fundus imaging in retinal and choroidal tumors is important for accurate documentation and to detect changes in the appearance and size. The depth of the lesion, the degree of pigmentation and surrounding changes like blood, fluid or atrophy all influence the appearance of lesion on multicolor imaging (40).

**Artifacts in Multicolor Imaging**

Artifacts with multicolor laser occur predominantly in the center of the image. Because the lens surfaces are curved, light reflected from the peripheral retina during scanning is scattered out of the beam path and is not captured in the fundus image. However, if a patient has a significant cataract and/or if the camera is improperly aligned an artifact appears. In these cases, the sensitivity of the detector will be increased to obtain a clearly illuminated retinal image, and the light reflected on the lens surface is visible. Patients with corneal opacities, optically significant cataracts, poor papillary dilation, and high myopia are prone to demonstrate artifacts with multicolor imaging (41). Ghost maculopathy is an imaging artifact appearing at the macula specially or nasal or superonasal to the fovea on near-infrared reflectance and MultiColor imaging that occurs predominantly in pseudophakic patients and may be mistaken for true chorioretinal pathology. Ghost maculopathy showed large interindividual variability in size, shape, location, and reflectivity between different eyes (41).

**Conclusion**

Investigative ophthalmological tools witnessed tremendous improvement which helped the ophthalmologists a lot in diagnosis, treatment and follow up of most of retinal and choroidal diseases and these tools are continuously improving.
References


