The Egyptian Journal of Hospital Medicine (July 2017) Vol.68, Page 929-935

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 autofluorescnce 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 t 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) [(1)]. Accumulation of lipofuscin above a certain threshold can cause functional loss of cells and lead to apoptosis [(2)]. 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 [(3)]. 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 [(4).] 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 [(5).] 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) excitation compared to cSLO (488nm) [(6).]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 [(7).]

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

Received:17/4/2017
Accepted:26/4/2017
DOI: 10.12816/0038193

[8]. 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 people [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 perilesional hyper-autofluorescence, which represent 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 chorioretinal 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 into the deepest retinal layers resulting in detailed images of the choroid, retinal pigment epithelium, and photoreceptors. The green laser focuses on the mid-retinal layers and is strongly absorbed by hemo-globin, thereby imaging blood vessels, hemorrhage, and intraretinal lipid exudation can be seen with it. 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

1- **Schmitz-Valckenberg S, Holz FG, Bird AC, Spaide R F (2008).** Fundus autofluorescence imaging: review and perspectives. Retina,28:385-409.

2- **Sepah YJ, Akhtar A, Sadiq MA, Hafeez Y, Nasir H, Perez B, Mawji N, Dean DJ, Ferraz D, Nguyen QD (2014).** Fundus autofluorescence imaging: fundamentals and clinical relevance. Saudi J Ophthalmol. , 28(2): 111-116.

3- **Delori FC, Dorey CK, Staurenghi G, Arend O, Goger DG, Weiter JJ (1995).** In vivo fluorescence of the ocular fundus exhibits retinal pigment epithelium lipofuscin characteristics. Invest Ophthalmol Vis Sci., 36(3):718–729.

4- **Krebs I, Lois N, Forrester JV (2011).** Fundus autofluorescence. Graefes Arch Clin Exp Ophthalmol., 249(2):309.

5- **Yung M, Klufas MA, Sarraf D (2016).** Clinical applications of fundus autofluorescence in retinal disease. Int J Retina Vitreous. , 8: 2:12.

6- **Park SP, Siringo FS, Pensec N, Hong IH, Sparrow J, Barile G, Tsang SH, Chang S (2013).** Comparison of Fundus Autofluorescence between Fundus Camera and Confocal Scanning Laser Ophthalmoscope–based Systems. Ophthalmic Surg Lasers Imaging Retina, 1; 44(6): 536–543.

7- **Booysen DJ (2013).** A review of fundus autofluorescence imaging. S Afr Optom. , 72(1) 46-53.

8- **Landa G, Rosen RB, Pilavas J, Garcia PM (2012).** Drusen characteristics revealed by spectral-domain optical coherence tomography and their corresponding fundus autofluorescence appearance in dry age-related macular degeneration. Ophthalmic Res., 47(2):81-6.

9- **Delori FC, Fleckner MR, Goger DG, Weiter JJ, Dorey CK (2000).** Autofluorescence distribution associated with drusen in age-related macular degeneration. Invest Ophthalmol Vis Sci., 41(2):496-504.

10- **Batıoğlu F, Demirel S, Özmert E (2015).** Fundus Autofluorescence Imaging in Age-Related Macular Degeneration. Semin Ophthalmol., 30(1):65-73.

11- **Klein R, Klein BE, Knudtson MD, Meuer SM, Swift M, Gangnon RE (2007).** Fifteen-year cumulative incidence of age-related macular degeneration: The Beaver Dam Eye Study. Ophthalmology , 28; 114(2):253-262.

12- **Rudolf M, Vogt SD, Curcio CA, Huisingh C, McGwin G, Wagner A, Grisanti S, Read RW (2013).** Histologic basis of variations in retinal pigment epithelium autofluorescence in eyes with geographic atrophy. Ophthalmology, 120(4):821-828.

13- **Pilotto E, Benetti E, Convento E, Guidolin F, Longhin E, Parrozzani R, Midena E (2013).** Microperimetry, fundus autofluorescence, and retinal layer changes in progressing geographic atrophy. Can J Ophthalmol. , 48(5):386-393.

14- **Burke TR, Duncker T, Woods RL, Greenberg JP, Zernant J, Tsang SH, Smith RT, Allikmets R, Sparrow JR, Delori FC (2014).** Quantitative fundus autofluorescence in recessive stargardt disease. Invest Ophthalmol Vis Sci., 55(5):2841-52.

15- **Boon CJ, Jeroen Klevering B, Keunen JE, Hoyng CB, Theelen T(2008).** Fundus autofluorescence imaging of retinal dystrophies. Vision Res., 48(26):2569-77.

16- **Murthy RK, Haji S, Sambhav K, Grover S, Chalam KV (2016).** Clinical applications of spectral domain optical coherence tomography in retinal diseases. Biomedical Journal, 39(2):107-120.

17- **Srinivasan VJ, Wojtkowski M, Witkin AJ, Duker JS, Ko TH, Carvalho M, Schuman JS, Kowalczyk A, Fujimoto JG (2006).** High-definition and 3-dimensional imaging of macular pathologies with high-speed ultrahigh-resolution optical coherence tomography. Ophthalmology, 113(11): 2054-2065.

18- Hee MR, Izatt JA, Swanson EA, Huang D, Schuman JS, Lin CP, Puliafito CA, Fujimoto JG (1995). Optical coherence tomography of the human retina. Arch ophthalmol. , 113(3):325-32.

19- Yang Z, Tatham AJ, Zangwill LM, Weinreb RN, Zhang C, Medeiros FA (2015). Diagnostic ability of retinal nerve fiber layer imaging by swept-source optical coherence tomography in glaucoma. Am J Ophthalmol. , 159:193-201.

20- Mohler KJ, Draxinger W, Klein T, Kolb JP, Wieser W, Haritoglou C, Kamplik A, Fujimoto JG, Neubauer AS, Huber R, Wolf A (2015). Combined 60° wide-field choroidal thickness maps and high-definition en face vasculature visualization using swept-source megahertz OCT at 1050nm. Invest Ophthalmol Vis Sci., 55(11):6284-6293.

21- Koleva-Georgieva D, Sivkova N (2009). Assessment of serous macular detachment in eyes with diabetic macular edema by use of spectral-domain optical coherence tomography. Graefe's Arch Clin Exp Ophthalmol., 247(11):1461-1469.

22- Helmy YM, Atta Allah HR (2013). Optical coherence tomography classification of diabetic cystoid macular edema. Clin Ophthalmol. , 7: 1731-1737.

23- Badaró E, Novais E, Prodocimo LM, Sallum JM (2014). Spectral-domain optical coherence tomography for macular edema. The Scientific World Journal, 14:201.

24- Grewal DS, Tanna AP (2013). Diagnosis of glaucoma and detection of glaucoma progression using spectral domain optical coherence tomography. Curr Opin Ophthalmol. , 24:150-161.

25- Leite MT, Rao HL, Weinreb RN, Zangwill LM, Bowd C, Sample PA, Tafreshi A, Medeiros FA (2011) . Agreement among spectral-domain optical coherence tomography instruments for assessing retinal nerve fiber layer thickness. Am j ophthalmol. , 151(1):85-92.

26- Park HY, Jeon SH, Park CK (2012). Enhanced depth imaging detects lamina cribrosa thickness differences in normal tension glaucoma and primary open-angle glaucoma. Ophthalmology, 119:10-20.

27- Takayama K, Hangai M, Kimura Y, Morooka S, Nukada M, Akagi T, Ikeda HO, Matsumoto A, Yoshimura N (2013). Three-dimensional imaging of lamina cribrosa defects in glaucoma using sweptsource optical coherence tomography, Invest ophthalmol vis sci., 54(7):4798-4807.

28- De carlo TE, Baumal CR(2016). Advances in Optical Coherence Tomography Angiography. US Ophthalmic Review, 9(1):37–40.

29- Schwartz DM, Fingler J, Kim DY, Zawadzki RJ, Morse LS, Park SS, Fraser SE, Werner JS(2014). Phase-variance optical coherence tomography: a technique for noninvasive angiography. Ophthalmology,121(1):180-187.

30- De carlo TE, Bonini Filho MA, Chin AT, Adhi M, Ferrara D, Baumal CR, Witkin AJ, Reichel E, Duker JS, Waheed NK (2015). Spectral-domain optical coherence tomography angiography of choroidal neovascularization. Ophthalmology, 122(6):1228-1238.

31- Miere A, Querques G, Semoun O, Capuano V, Souied EH (2015). Optical coherence tomography angiography in early type 3 neovascularization. Retina, 35(11):2236-2241.

32- Muakkassa NW, Chin AT, de Carlo T, Klein KA, Baumal CR, Witkin AJ, Duker JS, Waheed NK (2015) . Characterizing the effect of anti-vascular endothelial growth factor therapy on treatment-naive choroidal neovascularization using optical coherence tomography angiography. Retina, 35(11):2252-2259.

33- Ishibazawa A, Nagaoka T, Takahashi A, Omae T, Tani T, Sogawa K, Yokota H, Yoshida A (2015). Optical coherence tomography angiography in diabetic retinopathy: a prospective pilot study. Am J ophthalmol. , 160(1):35-44.

34- Freiberg FJ, Pfau M, Wons J, Wirth MA, Becker MD, Michels S (2016). Optical coherence tomography

angiography of the foveal avascular zone in diabetic retinopathy. Graefe's Arch Clin Exp Ophthalmol. , 254: 1051.

35- **Talisa E, Chin AT, Bonini Filho MA, Adhi M, Branchini L, Salz DA, Baumal CR, Crawford C, Reichel E, Witkin AJ, Duker JS (2015).** Detection of microvascular changes in eyes of patients with diabetes but not clinical diabetic retinopathy using optical coherence tomography angiography. Retina, 35(11):2364-70.

36- **Spaide RF, Fujimoto JG, Waheed NK (2015).** Image artifacts in optical coherence tomography angiography. Retina (Philadelphia, Pa.), 35(11):2163-80.

37- **Alten F, Clemens CR, Heiduschka P, Eter N (2014).**Characterisation of reticular pseudodrusen and their central target aspect in multi-spectral, confocal scanning laser ophthalmoscopy. Graefe's Arch Clin Exp Ophthalmol., 252:715-721.

38- **Pang CE, Freund KB (2014).** Ghost maculopathy: an artifact on near-infrared reflectance and multicolor imaging masquerading as chorioretinal pathology. Am J Ophthalmol .,158:171-178.e2

39- **Tan AC, Fleckenstein M, Schmitz-Valckenberg S, Holz FG (2016).** Clinical Application of Multicolor Imaging Technology. Ophthalmologica, 236(1):8-18.

40- **Sergott RC (2014).** Retinal segmentation using multicolor laser imaging. J Neuro ophthalmol. , 34: S24-28.

41- **Pang CE, Freund KB (2014).** Ghost maculopathy: an artifact on near-infrared reflectance and multicolor imaging masquerading as chorioretinal pathology. Am J ophthalmol. , 158(1):171-8.