F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries. Lancet 2004; 364:937-52.
27 Iacobellis G. Imaging of visceral adipose tissue: an emerging diagnostic tool and therapeutic target. Curr Drug Targets Cardiovasc Haematol Disord 2005; 5: 345-53.
28 Iacobellis G,Willens HJ, Barbaro G, Sharma AM. Threshold values of high risk echocardiographic epicardial fat thickness. Obesity (Silver Spring). 2008; 16:887-92.
29 Jeong JW, Jeong MH, Yun KH, Oh SK, Park EM, Kim YK. Echocardiographic epicardial fat thickness and coronary artery disease. Circ J 2007; 71:536-9.
30 Natale F, Tedesco MA, Mocerino R, de Simone V, Di Marco GM, Aronne L, et al. Visceral adiposity and arterial stiffness: echocardiographic epicardial fat thickness reflects, better than waist circumference, carotid arterial stiffness in a large population of hypertensive. Eur J Echocardiography 2009; 10:549-55.
31 Wang TD, Lee WJ, Shih FY, Huang CH, Chang YC, Chen WJ, et al. Relations of epicardial adipose tissue measured by multi detector computed tomography to components of the metabolic syndrome are region-specific and independent of anthropometric indexes and intra abdominal visceral fat. J Clin Endocrinol Metab 2009; 94:662-9. 52.
32 Abbara S, Desai JC, Cury RC, Butler J, Nieman K, Reddy V. Mapping epicardial fat with multi-detector computed tomography to facilitate per cutaneous transepicardial arrhythmia ablation. Eur J Radiol 2006; 57:417-22.
33 Greif M, Becker A, von Ziegler F, Lebherz C, Lehrke M, Broedl UC, et al. Pericardial adipose tissue determined by dual source CT is a risk factor for coronary atherosclerosis. Arterioscler Thromb Vasc Biol 2009; 29:781-6.
34 Dey D, Nakazato R,LiD, Berman DS, Epicardial and thoracic fat - Noninvasive measurement and clinical implications. J Cardiovascular and Diagnosis Therapy 2012; 2(2):85-93.
35 35 Shemirani H, Khoshavi M. Correlation of echocardiographic epicardial fat thickness with severity of coronary artery disease-an observational study. Anadolu kardiyoloji dergisi : AKD = the Anatolian journal of cardiology. 2012;12(3):200-5.
36 Nabati M, Saffar N, Yazdani J, Parsaee MS. Relationship between Epicardial Fat Measured by Echocardiography and Coronary Atherosclerosis: A Single-Blind Historical Cohort Study. Echocardiography. 2013;30(5):505-11.

REVIEW ARTICLES

OCT – A WINDOW TO RETINA

Sahrish Mukhtar[1], Nuzhat Hassan[2], Zafar Dawood[3]
[1]Department of Anatomy, Ziauddin University, Karachi, Pakistan.
[2]Department of Anatomy, Ziauddin University, Karachi, Pakistan.
[3]Department of Ophthalmology, Ziauddin University, Karachi, Pakistan.

ABSTRACT

Optical coherence tomography (OCT) is a non-contact, non invasive imaging modality that helps diagnosing a variety of diseases involving the eye. It provides quantitative measurements of retinal nerve fiber layer (RNFL), optic nerve head and macular thickness parameters [1, 2] and can be used as a valuable tool in many intraocular surgeries.
This article discusses the applications of different OCT systems available commercially for diagnosing and managing various ophthalmic conditions. Furthermore, future directions of OCT technology, clinical uses and benefits are also discussed.

Different articles published till year 2014 majorly in between 2005 to 2014, obtained from online search engines Pubmed and Google Scholar were used in preparation of this review. Those articles were included that contained information regarding OCT and its uses in various ophthalmologic conditions and its future advancements. We excluded those articles that did not contain relevant information regarding OCT and its uses.

Due to advancements in OCT technology, it is now possible to reveal the structural changes associated with retinal diseases that help in improving early analysis and monitoring of disease progression and response to treatment.

Three generations of OCT have been introduced till date. Early versions of this technology i.e. OCT 1 and OCT 2 are relatively slow, limiting both the amount of data to be captured and the quality of image. The older versions required dilation of the pupil but the latest version, the Stratus OCT can be used without dilating the pupil.[3]

Commercially, OCT is employed in diverse applications including diagnostic medicine, interventional cardiology and art conservation. Ophthalmology is still the most important field of OCT application because of transparent ocular structures.

KEY WORDS: Optical Coherence Tomography (OCT), Retinal Nerve Fiber Layer (RNFL) thickness, Glaucoma, Diabetic Retinopathy.

INTRODUCTION

In the medical field, optical techniques are of great importance because these are low cost and safe, offering good therapeutic prospective. Advancements in OCT technology have made it possible for its relevance in an extensive diversity of applications but its medical application is still dominating.[4-6]

OCT was first introduced by Huang et al. in 1991. [7] It allows in vivo imaging of ocular tissue to a very high magnification, making it an easy method of assessment of internal eye structures. It helps in obtaining retinal images from which retinal estimates can be made which have been proved to be helpful in diagnosing various diseases.[8, 9]

SD-OCT known as OCT-3, is 100 times faster than older versions. This increased rate diminishes the possibility of motion artifacts, decreases the chance of missing lesions and enhances the resolution. Advancements in SD-OCT also permit precised choroidal thickness measurements that was not possible with older versions. The choroidal changes observed by SDOCT are now being appreciated. As a result it is now the emerging point of interest for research. [10-13]

Apart from commercially available OCT systems, prototype OCT systems have added to an ever-growing research body. It includes ultra high-resolution OCT (UHR-OCT), SD-OCT with longer wavelength light making deep tissue penetration easy, and swept-source OCT (SSOCT). [14]

It is quoted in a paper that the SS-OCT is 5 to 10 times faster than that of the SD-OCT, and can achieve more accurate axial resolutions in tissue. [14]

OCT – PRESENT APPLICATIONS

By using ultra-speed high-resolution OCT, three-dimensional OCT imaging can be obtained providing wide-range mapping and visualization of retinal microstructure. The high-data obtaining speeds allow data sets of high-density with large numbers of slanted positions on the retina reducing the possibility of missing any focal pathologies.[15, 16]

OCT is used widely to obtain high-resolution images of both the anterior and posterior eye segments. Nowadays, various diseases are evaluated by using OCT. It also provides assessment of axonal integrity as in macular degeneration and multiple sclerosis. Many researches indicate that OCT may be used as a consistent tool for observing the disease progression involving the eye. Differ-

ential diagnosis is made easy by imaging structures at such levels that were not possible previously such as in differentiating retinal detachment from retinoschisis. [17]

Estimates of retinal thickness is significant in monitoring various diseases such as macular edema, glaucoma, macular holes, optic disc pit maculopathy etc. OCT plays an important role in recognizing retinal nerve fiber layer (RNFL) loss long before the appearance of symptoms leading to better prognosis of the disease.[18, 19] The early detection of changes in retina helps clinicians to identify the cause potentially before the patient suffers objective limitations.
Measurements of RNFL thickness is dependent on transparency of the anterior and posterior retinal planes. The OCT software has a predefined algorithm that identifies the outer limits of retina at the inside of a greatly reflective layer possibly the retinal pigment epithelium (RPE) and the choriocapillaries. Two laminae are seen at the interface. The internal streak may signify the reflective part or the neurosensory retina whereas the outer line is considered to relate histologically with RPE. [20]

OCT & glaucoma:
Glaucoma shows gradual loss of retinal ganglion cells (RGCs) leading to reduced retinal thickness. [21] It has been found that before the visual field defect is clinically symptomatic, 30% or more of RGCs are already lost. Significant loss in thickness may lead to visual field defects and optic disc cupping. [22] It is reported that thinning of retina starts in the initial stages of glaucoma, therefore, it can be used as a predictive indicator for glaucomatous damage.

OCT was found to be more sensitive to detect early nerve fiber layer loss than other techniques such as visual fields or red-free photography.[23] It has the ability to spot focal defects in the RNFL occuring in early glaucoma with high accuracy.[24]

It is now possible to perform automatic measurements of circumpapillary RNFL thickness with the recent development of OCT. [1425] Kafieh et al. in their study have suggested that even earlier than noticeable changes in the visual field occur, there is reduction of RNFL thickness in diseased eyes which is observed by using OCT.[26]

OCT & maculopathy:
OCT can help in diagnosing and quantifying various macular diseases, including idiopathic macular hole, maculopathies, macular pits etc. [27, 28] While talking about macular diseases the first thing coming to mind is macular edema in which macular thickness can be easily assessed by OCT rather than by biomicroscopy which has a limited extent to which edema can be detected.

For visual loss, macular edema is found to be one of the major causes in which there is abnormal fluid buildup within the retina with increase in retinal thickness usually from the break in blood-retinal barrier.[29, 30] This is found in diabetic retinopathy, retinal vein occlusion, uveitis etc.

Conventional methods for evaluating macular edema, like slitlamp biomicroscopy, stereoscopic photography and fluorescein angiography, are found to be relatively insensitive to tiny changes in retinal thickness. OCT has facilitated the clinicians to spot and assess even minute changes in macular thickness.[31]

Imaging of macular holes and other pathologies in the vitreofoveal interface has also become feasible with high-speed OCT offering three dimensional images to facilitate further precision and minute observations of the intraretinal structural changes.[32] OCT has also shown its significance in differentiating neurosensory layer and retinal epithelial layer detachment. [33] Measurements by this technique are found to be highly accurate. [34, 35]

Owing to the defined resolution of OCT, it may possibly be a supportive device to track anatomical features of idiopathic macular holes longitudinally over time. Recently, OCT has been used to follow the sequence of events leading to macular hole formation. In a research by Shimozono et al. in 2011, it is stated that due to vitreofoveal traction, the anteroposterior powers result in splitting of retina, following full-thickness macular hole documented longitudinally by OCT. [36]

OCT may aid discriminating actual holes from partial thickness holes, macular pseudo-holes and cysts. It helps in staging the hole and quantifying the diameter of the hole and in assessing the risk of hole formation in the fellow eye. [37]

In age-related maculopathy, retinal thinning and an increased reflectivity of the choroid due to lack of pigment in the retinal pigment epithelial layer is identified easily by OCT. These areas are seen as regions of increased reflectivity on the tomogram. [38]

Thus, OCT is able to validate the anatomical configurations. Macular examination by using OCT helps in the diagnosis and allows follow-up of the macular pathologies after surgical repair.[37]

OCT & diabetic retinopathy:
OCT can detect significant variation of retinal thickness in patients with diabetic retinopathy even when macular edema is not clinically significant. [39] Goebel et al. in their study suggested that OCT plays major role in evaluating retinal thickness of diabetic patients with excellent reproducibility and great reliability.[40] Another study by Roy Beck et al. concluded that OCT was found to be very helpful in evaluating the three crucial changes in diabetes which include macular edema, retinal swelling and detachment of retina.[41]

Furthermore, OCT is stated to be useful for diagnosing and differentiating tractional retinoschisis from retinal detachment in patients with proliferative diabetic retinopathy and macular elevation.[42]

OCT & retinal vascular diseases:
A detailed analysis of retinal structure is obtained by 3D cross-sectional retinal levels at high resolution.[43] Retinal vessels can be visualized because of the high resolution imaging leading to more objective diagnosis in retinal vascular diseases including retinopathy of prematurity, hypertensive retinopathy etc. Moreover, vessel visualization also allows to follow fundus color changes for better understanding of the structure and localizing retinal lesions.[44]

Preeclampsia and eclampsia cause retinopathy similar to hypertensive retinopathy with papilloedema, hemorrhages, cotton wool spots, retinal detachment, and lesions of the retinal pigment epithelium (RPE) which can be easily detected by using OCT.[45]

OCT & optic neuritis in multiple sclerosis (MS):
Optic neuritis (ON) is a very common presentation of multiple sclerosis (MS). It occurs often as the initial symptom of CNS demyelination. RNFL is that part of brain where nerve fibers are not enclosed with myelin sheath because it develops from optic cup, thus making the OCT examination particular for demyelinating nerve injury contrasting to brain MRI changes, which reflect a range of various types of tissues in the brain.[46]

The measurement of RNFL thickness represents a feasible way of monitoring axonal loss in MS patients as RNFL comprises of unmyelinated axons.[47, 48] Studies have suggested that eyes with a history of optic neuritis revealed reduction in RNFL thickness, showing occurrence of axonal loss. [49-51]

OCT & visual disorders in Alzheimer's Disease (AD):
Visual disorders are usually noted in patients with Alzheimer's disease affecting the visual field. Many studies have suggested that the visual field defects are probably due to nerve degeneration in the visual cortex.[52, 53] Recent studies have suggested that retina and optic nerve degeneration also add to the occurrence of such disorders in AD patients.[54, 55]

In an OCT based study by Yan Lu et al. in 2010, the RNFL thickness was measured in normal individuals and patients with Alzheimer's disease and was found to be reduced in patients with Alzheimer's disease. Reduction in RNFL thickness might be due to loss of nerve leading to neuronal cell body loss.[54] It is suggested that OCT is a simple method and this technique could be used in improving the diagnosis of individuals who are affected clinically by memory disturbances.[56]

Miscellaneous:
In Parkinson's disease, visual impairment is due to loss in dopaminergic neurons in retina. This loss is believed to alter visual process by altering the axons that form the RNFL. OCT is found to be an efficient tool in ruling out such disorders.[57]

The choroidal tumor appears similar to normal choroid when the overlying retina is normal and appears less reflective than normal when the overlying retina is not normal. These small alterations in tumor appearance can easily be diagnosed by using OCT. [58, 59]

OCT also accomplished its name in localizing laser scars, disciform scars, chorioretinal atrophy, and choroidal neovascularization and many other retinal disorders. Other retinal diseases like X-linked retinitis pigmentosa, juvenile macular retinoschisis, idiopathic polypoidal choroidal vasculopathy, idiopathic juxtafoveolar retinal telangiectasis and pigment epithelial hyperplasia can also be diagnosed by OCT.

Comparison of OCT with older modalities:
Comparing the Retinal Thickness Analyzer (RTA) and OCT Scanners for retinal thickness measurements in macular diseases, it is noted that media opacities produce less hindrance for OCT than for RTA which is helpful in a way that in populations with frequent occurrence of media opacity, images can be achieved in a larger fraction of eyes by OCT than by RTA. [60]

Ophthalmoscope, the most commonly used instrument showed many limitations while compared with OCT. Different researches were conducted to compare its validity and it was found to be inferior than OCT.[61, 62] Another study by Hibbs et al. stated that OCT alongwith fundoscopy is valueable.[63]

OCT is different from ultrasound B-scan which uses sound waves rather than light rays in providing higher resolution. It is also found to be helpful in detecting the detachments of retinal layers which are not easily observed by biomicroscopy.

Oct & Its Future:
While talking about the future of OCT, it is an excellent option to be used in medical diagnosis. It can be fiber optic based, allowing inexpensive incorporation with endoscopes and catheters. It is compact and portable and can be done without direct contact with the tissue. It is comparatively fast, allowing real time imaging of tissues at a rate not available with MRI or CT scan. [17, 64]
Recent advancements in SD-OCT have now helped imaging the choroid which was not possible earlier.[10] Further advancements are expected to offer enhanced understanding of choroid involvement in retinal diseases using various techniques.

SS-OCT & Longer wavelength OCT
An exact choroid estimation by OCT should be made by measuring upto the interface of choroid and sclera.(59) Studies using Cirrus OCT suggested almost accurate revelation of the choroid by looking upto choroid–sclera interface in just 70–75% of included eyes. [10, 12, 13] Eyes with even clear choroid–sclera interface have not been reported with Spectralis OCT but prototype OCT using longer wavelength have verified an improved estimation of the choroid, also through opaque media . SS-OCT is also anticipated to be of great help in visualizing the choroid.[14]

The visualization of choroid–sclera interface is expected to improve because of longer-wavelength OCT systems including SS-OCT. This can be helpful in conditions in which the choroid is thicker than normal, and it is difficult to assess the entire thickness

Doppler optical coherence tomography
Traditional examinations like, indocyanine green (ICG) and fluorescein angiography are now taken inferior to Doppler OCT which is a promising technology that localizes the accurate position of vascular abnormalities using cross-sectional imaging. Doppler OCT can assess the flow and volume of blood and evaluate the abnormalities in retinal and choroidal vasculature [65].

CONCLUSION

Modifications in OCT software, enhancement and competent data processing are essential for valuable assessment of retinal and choroidal changes in posterior segment diseases. OCT technology offers enhanced understanding, proper monitoring of disease progression and its response to various treatment modalities employed in eye diseases especially chorioretinal diseases. This expansion has updated the ophthalmic practice over the period of last ten years. Further advancements in OCT technology are expected to be of greater help in assessing diseases more easily and in more depth.

REFERENCES

[1] Mwanza J-C, Oakley JD, Budenz DL, Anderson DR, Group COCTNDS. Ability of cirrus HD-OCT optic nerve head parameters to discriminate normal from glaucomatous eyes. Ophthalmology. 2011;118(2):241-8. e1.

2 Rao H, Babu J, Addepalli U, Senthil S, Garudadri C. Retinal nerve fiber layer and macular inner retina measurements by spectral domain optical coherence tomograph in Indian eyes with early glaucoma. Eye. 2012;26(1):133-9.

3 Kanamori A, Nakamura M, Tomioka M, Kawaka Y, Yamada Y, Negi A. Agreement among three types of spectral-domain optical coherent tomography instruments in measuring parapapillary retinal nerve fibre layer thickness. British Journal of Ophthalmology. 2012;96(6):832-7.

4 Fercher AF, Drexler W, Hitzenberger CK, Lasser T. Optical coherence tomography-principles and applications. Reports on progress in physics. 2003;66(2):239.

5 Kyono H, Guagliumi G, Sirbu V, Rosenthal N, Tahara S, Musumeci G, et al. Optical coherence tomography (OCT) strut-level analysis of drug-eluting stents (DES) in human coronary bifurcations. EuroIntervention: journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology. 2010;6(1):69-77.

6 Vakoc BJ, Fukumura D, Jain RK, Bouma BE. Cancer imaging by optical coherence tomography: preclinical progress and clinical potential. Nature Reviews Cancer. 2012;12(5):363-8.

7 Huang D, Swanson EA, Lin CP, Schuman JS, Stinson WG, Chang W, et al. Optical coherence tomography. Science. 1991;254(5035):1178-81.

8 Podoleanu AG. Optical coherence tomography. 2014.

9 Leite MT, Zangwill LM, Weinreb RN, Rao HL, Alencar LM, Sample PA, et al. Effect of disease severity on the performance of Cirrus spectral-domain OCT for glaucoma diagnosis. Investigative ophthalmology & visual science. 2010;51(8):4104-9.

10 Adhi M, Duker JS. Optical coherence tomography–current and future applications. Current opinion in ophthalmology. 2013;24(3):213.

11 Regatieri CV, Branchini L, Fujimoto JG, Duker JS. Choroidal imaging using spectral-domain optical coherence tomography. Retina (Philadelphia, Pa). 2012;32(5):865.

12 Regatieri CV, Branchini L, Carmody J, Fujimoto JG, Duker JS. Choroidal thickness in patients with diabetic retinopathy analyzed by spectral-domain optical coherence tomography. Retina (Philadelphia, Pa). 2012;32(3):563.

13 Manjunath V, Goren J, Fujimoto JG, Duker JS. Analysis of choroidal thickness in age-related macular degeneration using spectral-domain optical coherence tomography. American journal of ophthalmology. 2011;152(4):663-8.

14 Grulkowski I, Liu JJ, Zhang JY, Potsaid B, Jayaraman V, Cable AE, et al. Reproducibility of a long-range swept-source optical coherence tomography ocular biometry system and comparison with clinical biometers. Ophthalmology. 2013;120(11):2184-90.

15 Wojtkowski M, Srinivasan V, Fujimoto JG, Ko T, Schuman JS, Kowalczyk A, et al. Three-dimensional retinal imaging with high-speed ultrahigh-resolution optical coherence tomography. Ophthalmology. 2005;112(10):1734-46.

16 Wakabayashi T, Fujiwara M, Sakaguchi H, Kusaka S, Oshima Y. Foveal microstructure and visual acuity in surgically closed macular holes: spectral-domain optical coherence tomographic analysis. Ophthalmology. 2010;117(9):1815-24.

17 Hrynchak P, Simpson T. Optical coherence tomography: an introduction to the technique and its use. Optometry & Vision Science. 2000;77(7):347-56.

18 Gordon-Lipkin E, Chodkowski B, Reich D, Smith S, Pulicken M, Balcer L, et al. Retinal nerve fiber layer is associated with brain atrophy in multiple sclerosis. Neurology. 2007;69(16):1603-9.

19 Garas A, Vargha P, Hollo G. Diagnostic accuracy of nerve fibre layer, macular thickness and optic disc measurements made with the RTVue-100 optical coherence tomograph to detect glaucoma. Eye. 2011;25(1):57-65.

20 Spaide RF, Curcio CA. Anatomical correlates to the bands seen in the outer retina by optical coherence tomography: literature review and model. Retina (Philadelphia, Pa). 2011;31(8):1609.

21 Na JH, Sung KR, Baek S, Kim YJ, Durbin MK, Lee HJ, et al. Detection of glaucoma progression by assessment of segmented macular thickness data obtained using spectral domain optical coherence tomography. Investigative ophthalmology & visual science. 2012;53(7):3817-26.

22 Leung CK, Choi N, Weinreb RN, Liu S, Ye C, Liu L, et al. Retinal nerve fiber layer imaging with spectral-domain optical coherence tomography: pattern of RNFL defects in glaucoma. Ophthalmology. 2010;117(12):2337-44.

23 Guedes V, Schuman JS, Hertzmark E, Wollstein G, Correnti A, Mancini R, et al. Optical coherence tomography measurement of macular and nerve fiber layer thickness in normal and glaucomatous human eyes. Ophthalmology. 2003;110(1):177-89.

24 Springelkamp H, Lee K, Ramdas WD, Vingerling JR, Hofman A, Klaver CC, et al. Optimizing the information yield of 3-D OCT in glaucoma. Investigative ophthalmology & visual science. 2012;53(13):8162-71.

25 Cvenkel B, Kontestabile AŠ. Correlation between nerve fibre layer thickness measured with spectral domain OCT and visual field in patients with different stages of glaucoma. Graefe's Archive for Clinical and Experimental Ophthalmology. 2011;249(4):575-84.

26 Kafieh R, Rabbani H, Abramoff MD, Sonka M. Intra-retinal layer segmentation of 3D optical coherence tomography using coarse grained diffusion map. Medical image analysis. 2013;17(8):907-28.

27 Imamura Y, Zweifel SA, Fujiwara T, Freund KB, Spaide RF. High-resolution optical coherence tomography findings in optic pit maculopathy. Retina. 2010;30(7):1104-12.

28 Freeman SR, Kozak I, Cheng L, Bartsch D-U, Mojana F, Nigam N, et al. Optical coherence tomography-raster scanning and manual segmentation in determining drusen volume in age-related macular degeneration. Retina. 2010;30(3):431-5.

29 Choi W, Baumann B, Liu JJ, Clermont AC, Feener EP, Duker JS, et al. Measurement of pulsatile total blood flow in the human and rat retina with ultrahigh speed spectral/-Fourier domain OCT. Biomedical optics express. 2012;3(5):1047-61.

30 Quellec G, Lee K, Dolejsi M, Garvin MK, Abramoff MD, Sonka M. Three-dimensional analysis of retinal layer texture: identification of fluid-filled regions in SD-OCT of the macula. Medical Imaging, IEEE Transactions on. 2010;29(6):1321-30.

31 Chan A, Duker JS, Ko TH, Fujimoto JG, Schuman JS. Normal macular thickness measurements in healthy eyes using Stratus optical coherence tomography. Archives of Ophthalmology. 2006;124(2):193-8.

32 Hangai M, Ojima Y, Gotoh N, Inoue R, Yasuno Y, Makita S, et al. Three-dimensional imaging of macular holes with high-speed optical coherence tomography. Ophthalmology. 2007;114(4):763-73.

33 Spaide RF. Enhanced depth imaging optical coherence tomography of retinal pigment epithelial detachment in age-related macular degeneration. American journal of ophthalmology. 2009;147(4):644-52.

34 Bowd C, Weinreb RN, Williams JM, Zangwill LM. The retinal nerve fiber layer thickness in ocular hypertensive, normal, and glaucomatous eyes with optical coherence tomography. Archives of Ophthalmology. 2000;118(1):22-6.

35 Bowd C, Zangwill LM, Berry CC, Blumenthal EZ, Vasile C, Sanchez-Galeana C, et al. Detecting early glaucoma by assessment of retinal nerve fiber layer thickness and visual function. Investigative ophthalmology & visual science. 2001;42(9):1993-2003.

36 Shimozono M, Oishi A, Hata M, Kurimoto Y. Restoration of the photoreceptor outer segment and visual outcomes after macular hole closure: spectral-domain optical coherence tomography analysis. Graefe's Archive for Clinical and Experimental Ophthalmology. 2011;249(10):1469-76.

37 Munuera JM, García-Layana A, Maldonado MJ, Aliseda D, Moreno-Montañés J. Optical coherence tomography in successful surgery of vitreomacular traction syndrome. Archives of Ophthalmology. 1998;116(10):1388-9.

38 Salinas-Alamán A, García-Layana A, Maldonado MJ, Sainz-Gómez C, Alvárez-Vidal A. Using optical coherence tomography to monitor photodynamic therapy in age related macular degeneration. American journal of ophthalmology. 2005;140(1):23. e1-. e7.

39 Schaudig UH, Glaefke C, Scholz F, Richard G. Optical coherence tomography for retinal thickness measurement in diabetic patients without clinically significant macular edema. Ophthalmic surgery and lasers. 1999;31(3):182-6.

40 Goebel W, Kretzchmar-Gross T. Retinal thickness in diabetic retinopathy: a study using optical coherence tomography (OCT). Retina. 2002;22(6):759-67.

41 EDEMA M. Three-year follow-up of a randomized trial comparing focal/grid photocoagulation and intravitreal triamcinolone for diabetic macular edema. Arch Ophthalmol. 2009;127(3):245-51.

42 Imai M, Iijima H, Hanada N. Optical coherence tomography of tractional macular elevations in eyes with proliferative diabetic retinopathy. American journal of ophthalmology. 2001;132(1):81-4.

43 Bonin T, Franke G, Hagen-Eggert M, Koch P, Hüttmann G. < i> In vivo</i> Fourier-domain full-field OCT of the human retina with 1.5 million A-lines/s. Optics letters. 2010;35(20):3432-4.

44 Niemeijer M, Garvin MK, van Ginneken B, Sonka M, Abramoff MD, editors. Vessel segmentation in 3D spectral OCT scans of the retina. Medical Imaging; 2008: International Society for Optics and Photonics.

45 Braaf B, Vermeer KA, Vienola KV, de Boer JF. Angiography of the retina and the choroid with phase-resolved OCT using interval-optimized backstitched B-scans. Optics express. 2012;20(18):20516-34.

46 Serbecic N, Aboul-Enein F, Beutelspacher SC, Vass C, Kristoferitsch W, Lassmann H, et al. High resolution spectral domain optical coherence tomography (SD-OCT) in multiple sclerosis: the first follow up study over two years. PLoS One. 2011;6(5):e19843.

47 Sergott RC, Frohman E, Glanzman R, Al-Sabbagh A. The role of optical coherence tomography in multiple sclerosis: expert panel consensus. Journal of the neurological sciences. 2007;263(1):3-14.

48 Garcia-Martin E, Pueyo V, Pinilla I, Ara J-R, Martin J, Fernandez J. Fourier-domain OCT in multiple sclerosis patients: reproducibility and ability to detect retinal nerve fiber layer atrophy. Investigative ophthalmology & visual science. 2011;52(7):4124-31.

49 Ratchford JN, Saidha S, Sotirchos ES, Oh JA, Seigo MA, Eckstein C, et al. Active MS is associated with accelerated retinal ganglion cell/inner plexiform layer thinning. Neurology. 2013;80(1):47-54.

50 Saidha S, Sotirchos ES, Oh J, Syc SB, Seigo MA, Shiee N, et al. Relationships between retinal axonal and neuronal measures and global central nervous system pathology in multiple sclerosis. JAMA neurology. 2013;70(1):34-43.

51Talman LS, Bisker ER, Sackel DJ, Long DA, Galetta KM, Ratchford JN, et al. Longitudinal study of vision and retinal nerve fiber layer thickness in multiple sclerosis. Annals of neurology. 2010;67(6):749-60.

52 Kirbas S, Turkyilmaz K, Tufekci A, Durmus M. Retinal nerve fiber layer thickness in Parkinson disease. Journal of Neuro-Ophthalmology. 2013;33(1):62-5.

53 Hajee ME, March WF, Lazzaro DR, Wolintz AH, Shrier EM, Glazman S, et al. Inner retinal layer thinning in Parkinson disease. Archives of Ophthalmology. 2009;127(6):737-41.

54 Lu Y, Li Z, Zhang X, Ming B, Jia J, Wang R, et al. Retinal nerve fiber layer structure abnormalities in early Alzheimer's disease: evidence in optical coherence tomography. Neuroscience letters. 2010;480(1):69-72.

55 Anders ME, Turner L, Freeman J. Evaluation of Clinical Decision Rules for Bone Mineral Density Testing among White Women. Journal of osteoporosis. 2013;2013.

56 Paquet C, Boissonnot M, Roger F, Dighiero P, Gil R, Hugon J. Abnormal retinal thickness in patients with mild cognitive impairment and Alzheimer's disease. Neuroscience letters. 2007;420(2):97-9.

57 Inzelberg R, Ramirez JA, Nisipeanu P, Ophir A. Retinal nerve fiber layer thinning in Parkinson disease. Vision research. 2004;44(24):2793-7.

58 Chen W-L, Hu P-S, Ghazaryan A, Chen S-J, Tsai T-H, Dong C-Y. Quantitative analysis of multiphoton excitation autofluorescence and second harmonic generation imaging for medical diagnosis. Computerized Medical Imaging and Graphics. 2012;36(7):519-26.

59 Adhi M, Bryant JS, Alwassia AA, Chen C, Duker JS. De-novo Appearance of a Choroidal Osteoma in an Eye with Previous Branch Retinal Vein Occlusion. Ophthalmic surgery, lasers & imaging retina. 2013;44(1):77.

60 Polito A, Shah SM, Haller JA, Zimmer-Galler I, Zeimer R, Campochiaro PA, et al. Comparison between retinal thickness analyzer and optical coherence tomography for assessment of foveal thickness in eyes with macular disease. American journal of ophthalmology. 2002;134(2):240-51.

61 El-Ashry M, Hegde V, James P, Pagliarini S. Analysis of macular thickness in British population using optical coherence tomography (OCT): an emphasis on interocular symmetry. Current eye research. 2008;33(8):693-9.

62 Xu L, Burke TR, Greenberg JP, Mahajan VB, Tsang SH. Infrared imaging and optical coherence tomography reveal early-stage astrocytic hamartomas not detectable by fundoscopy. American journal of ophthalmology. 2012;153(5):883-9. e2.

63 Hibbs S, Smith A, Chow L, Downes S. Response to 'Combined OCT and colour fundus photography in virtual clinic assessments of wet AMD patients'. Eye. 2012;26(4):620.

64 Potsaid B, Baumann B, Huang D, Barry S, Cable AE, Schuman JS, et al. Ultrahigh speed 1050nm swept source/-Fourier domain OCT retinal and anterior segment imaging at 100,000 to 400,000 axial scans per second. Optics express. 2010;18(19):20029-48.

65 Miura M, Makita S, Iwasaki T, Yasuno Y. Three-dimensional visualization of ocular vascular pathology by optical coherence angiography in vivo. Investigative ophthalmology & visual science. 2011;52(5):2689-95.