Chapter

Optical Coherence Tomography in Diabetic Retinopathy

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Abstract

Optical coherence tomography (OCT) has become an indispensable modality of investigation in the assessment of diabetic retinopathy. It is a non-invasive and reliable imaging tool that provides a comprehensive analysis of the retina. The images are obtained very fast. It is useful for quantitative as well as qualitative assessment of structural changes that occur in diabetic retinopathy. It also enables the detection of subclinical diabetic macular edema. Various imaging biomarkers have been identified on OCT imaging. These markers help prognosticate the case and determine treatment response. The follow-up imaging helps assess the response to treatment and detect recurrence of disease or need for further treatment.

Keywords: spectral-domain optical coherence tomography, swept-source optical coherence tomography, diabetic macular edema, optical coherence tomography angiography, imaging biomarkers

1. Introduction

Diabetes Mellitus (DM) is a disease characterized by elevated blood glucose levels due to its impaired metabolism. It is principally classified into Type 1 DM and Type 2 DM, the former being defined by the absence of insulin secretion whereas resistance to insulin defines the latter. According to the figures analyzed at the global level, diabetes is expected to affect 629 million people by 2045 in the age category of 20 to 79 years [1]. Long-term uncontrolled DM leads to both macrovascular and microvascular complications. Diabetic Retinopathy (DR), a microvascular complication, affects one-third of the population suffering from diabetes [2, 3]. The pathology of DR involves capillary endothelial cell proliferation, thickening of the basement membrane, and loss of pericytes, leading to the formation of microaneurysms, increase in vessel permeability, and the destruction of the blood-retinal barrier. This leads to the accumulation of fluid within and beneath the layers of the retina, causing diabetic macular edema (DME). Diabetic retinopathy is the leading cause of blindness in individuals of the working-age group [4]. In more advanced cases, capillary blockage and ischemia result in the formation of new blood vessels, resulting in proliferative diabetic retinopathy (PDR).

The definition of clinically significant macular edema in diabetes was given by the Early Treatment Diabetic Retinopathy Study (ETDRS) where slit-lamp biomicroscopy or stereoscopic fundus photography was used to identify retinal thickening and hard exudates [5]. However, the use of slit-lamp biomicroscopy or color fundus photography for examining macular edema is subjective and may fail to detect mild changes in retinal thickness. Biomicroscopy does not provide information regarding the exact retinal layer involved. Fundus fluorescein angiography

(FA) is an investigation modality that is used to classify DME into focal and diffuse based on the leakage pattern. This classification helps in guiding focal laser treatment to leaking microaneurysms or grid laser to the leaking capillaries. Ischemic areas and macular ischemia are also well identified on FA. Though FA offers useful information, it is also a subjective test and retinal thickness or morphology cannot be assessed on FA. The advent of optical coherence tomography (OCT), has improved the understanding of DME.

OCT has rapidly grown to become a routine tool of investigation in ophthalmology. Its various advantages lie in the fact that it provides an objective, non-invasive, high resolution, reproducible, and cross-sectional image of the retina [6]. It does not require a highly skilled person for its operation, or pharmacological dilation of the pupil. It is sensitive to identify even mild changes in retinal morphology that are often not visible to the naked eye on clinical examination.

2. Principle and technique

In simple terms, OCT is similar to ultrasound in that a beam of sound or light directed onto a tissue is differentially reflected from structures with different acoustic or optical properties. The time it takes for the sound or light to reflect from the

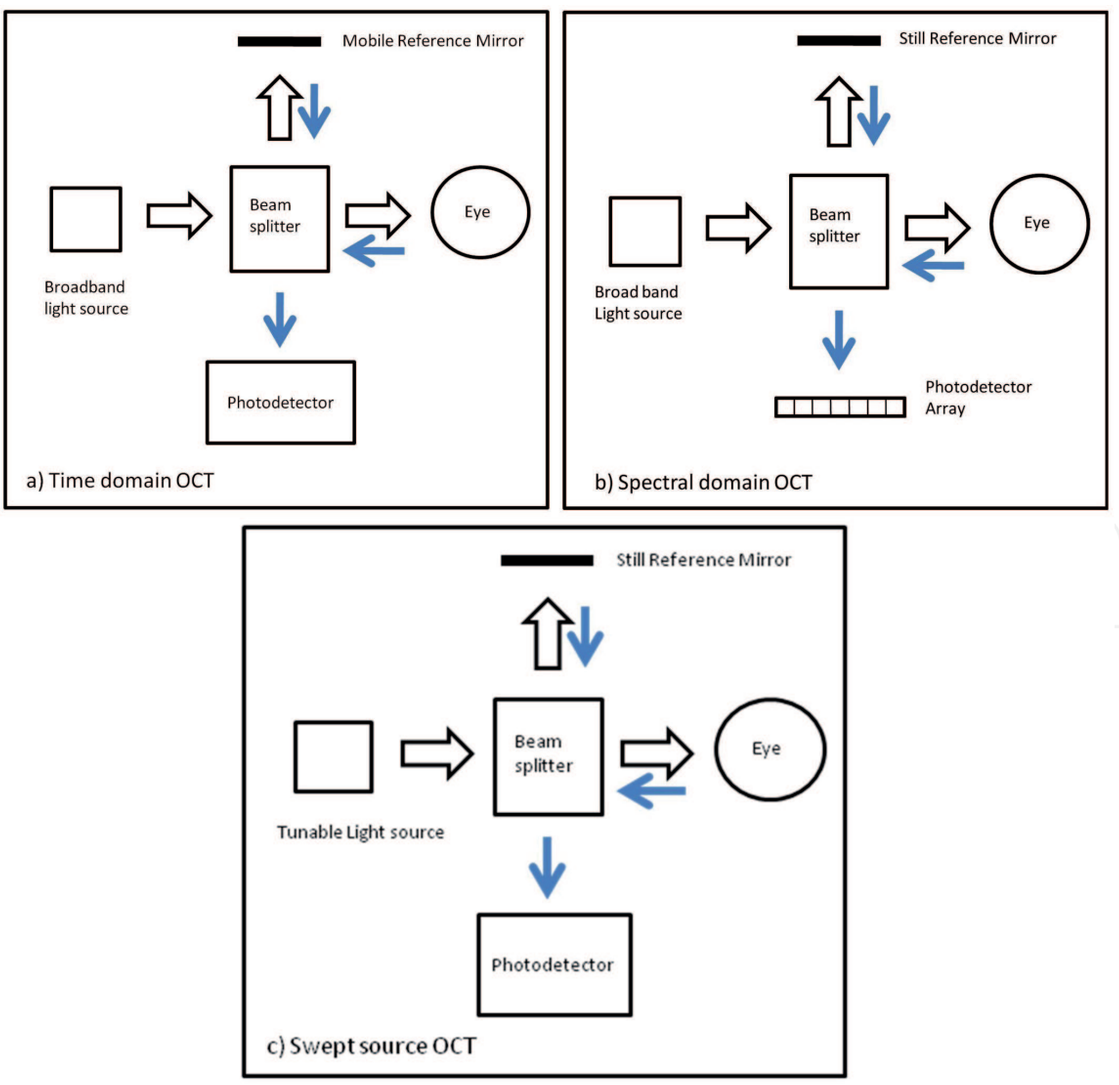

Figure 1.
a) Principle of time domain OCT. b) Principle of spectral domain OCT. c) Principle of swept source OCT.

different structures determines the dimensions of the structures. This provides an image similar to the A-scan or depth scan of ultrasound. Imaging of laterally adjacent depth scans provides a two-dimensional or B-scan image. The time delay involved when using light is in femtoseconds requiring interferometry to do the calculations [7].

The first generation OCT machine or Time-Domain OCT (TD-OCT) uses low time-coherence interferometry to obtain depth scans (**Figure 1a**). A beam splitter splits the light coming from a broadband light source, one directed to the eye and the other to the reference mirror. The position of the reference mirror is changed to mirror the depth of the various layers of tissue being scanned. Light reflected from the two sources is collected and the interferogram is analyzed to give a complete depth scan. TD-OCT involves two scans, one for depth scan and one for lateral scan, thus, resulting in a lesser number of scans acquired per second.

With the use of spectrometer and Fourier-domain technique in the next generation OCT, called Spectral-domain OCT (SD-OCT), the disadvantage of performing a depth scan was avoided. SD-OCT uses an array of photo-detectors to capture the depth scan without having to move the reference mirror (**Figure 1b**). Therefore, only a lateral scan has to be performed [7]. This increased the scan speed enormously. Further refinement of technology led to the change of the broadband near-infrared superluminescent diode light source of wavelength 840 nm in SD-OCT to a tunable swept laser source with a center wavelength of 1050 nm [8]. In conjunction, the array of photodetectors in SD-OCT was replaced with a single photodetector [8]. This led to the evolution of Swept-source OCT (SS-OCT) (**Figure 1c**). SS-OCT provides increased scan speed and denser scans with greater resolution as more A-scan and B scans are acquired per second. The scan area is also increased along with scan depth due to the use of a longer wavelength light source which allows better penetration through retinal pigment epithelium (RPE).

3. Normal retinal morphology on optical coherence tomography

The rapid technological evolution of SD-OCT led to the visualization of different hyperreflective and hyporeflective layers of retina commencing from the innermost vitreoretinal interface to the outermost choroid-scleral interface (**Figure 2**) [9]. The innermost layer visualized is the posterior cortical vitreous which is hyperreflective followed by a hyporeflective preretinal space [10]. The innermost layer of the retina is the hyperreflective internal limiting membrane which overlies the retinal nerve fiber layer (RNFL). The next layer is the ganglion cell layer which is less reflective than the RNFL [11]. Outer to the ganglion cell layer is the hyperreflective inner plexiform layer followed by hyporeflective inner nuclear layer. The outer plexiform layer is hyperreflective. OCT has greatly improved the understanding of human anatomy with the identification of Henle's layer as a component of outer half of the outer plexiform layer [12]. Outer to the outer plexiform layer lies the hyporeflective outer nuclear layer. This is followed by the external limiting membrane (ELM), another hyperreflective layer. Latest OCT machines have also made possible, the identification of outer retinal layers that are anatomic correlates of the myoid and ellipsoid (EZ) zones of the inner segment of the photoreceptors [13]. The myoid zone is hyporeflective and lies next to the ELM followed by EZ layer which is hyperreflective. This is followed by the hyporeflective layer of outer segments of photoreceptor and then a hyperreflective interdigitation zone is noted between cone outer segments and apical processes of RPE [13]. The next layer or the outermost layer of the retina is the hyperreflective RPE-Bruch's membrane complex which can be sometimes visualized as separate layers. OCT also helps visualize the components of the choroid [14]. The innermost layer in the choroid is formed by the choriocapillaris. The Sattler's layer

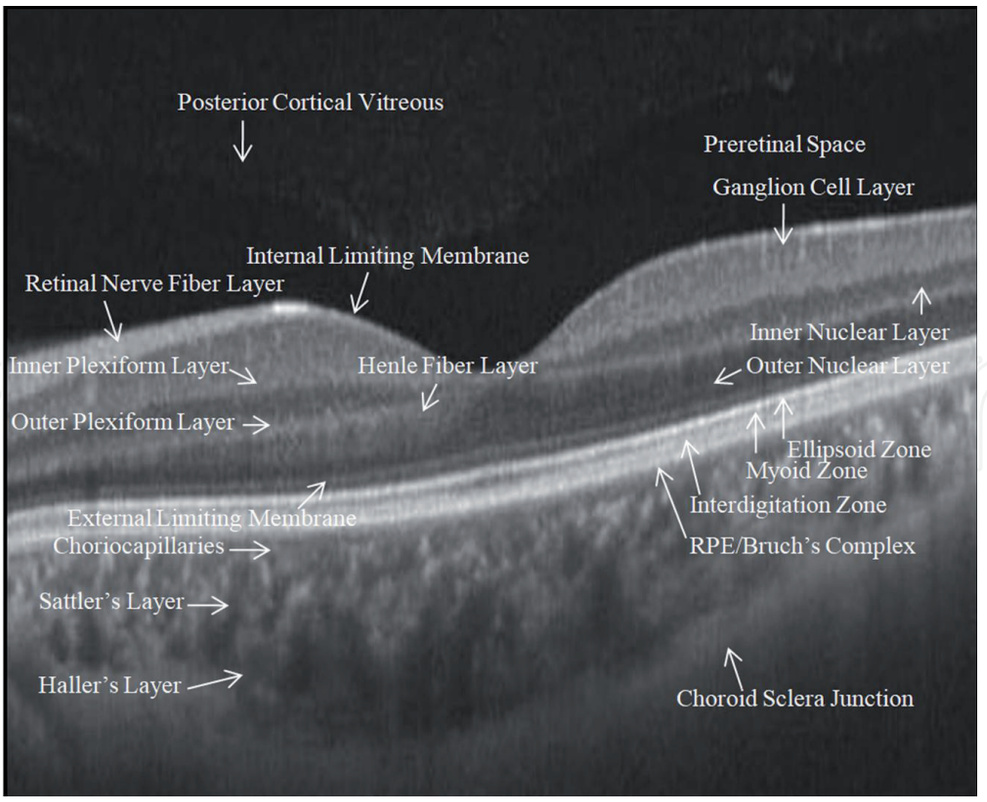

Figure 2.
Normal anatomical landmarks as seen on swept source OCT image.

forms the mid choroid and the Haller's layer forms the outer choroid. The outer boundary of the choroid is the choroidal-scleral junction [14].

Clinically visualized changes of diabetic retinopathy are well delineated on OCT. Hard exudates, cotton wool spots, and epiretinal membrane show hyperreflectivity, edema exhibits hyporeflectivity, and hemorrhages demonstrate backshadowing. Other than these, various discerning features and biomarkers have been identified on OCT which has been discussed later in this chapter.

4. Optical coherence tomography based classification of macular edema

OCT is a sensitive tool to diagnose, quantify, and classify diabetic macular edema. The first OCT-based classification for DME was given by Otani et al [15]. They were the first to identify 3 patterns of fluid accumulation, including sponge-like retinal swelling, cystoid macular edema, and serous retinal detachment (**Figure 3**). They further described that early changes of macular edema were confined to the outer retinal layer mainly the outer plexiform layer when compared to histopathology [15]. With the further accumulation of fluid, the inner retinal layers were involved. The presence of serous retinal detachment in patients with DME is a finding which may not be easily distinguished on biomicroscopy or FA.

In 2004, Panozzo proposed a classification system based on five parameters: retinal thickness, volume, morphology, diffusion, and presence or absence of vitreoretinal traction [16]. They quantified the retinal thickness and volume in three different zones around the fovea. The types of macular edema observed were in agreement with that described by Otani et al., [15] with the only difference being that the size of the cyst was measured to subclassify the grade of the cystoid variety of macular edema. The presence of epiretinal traction and its pattern (tangential or

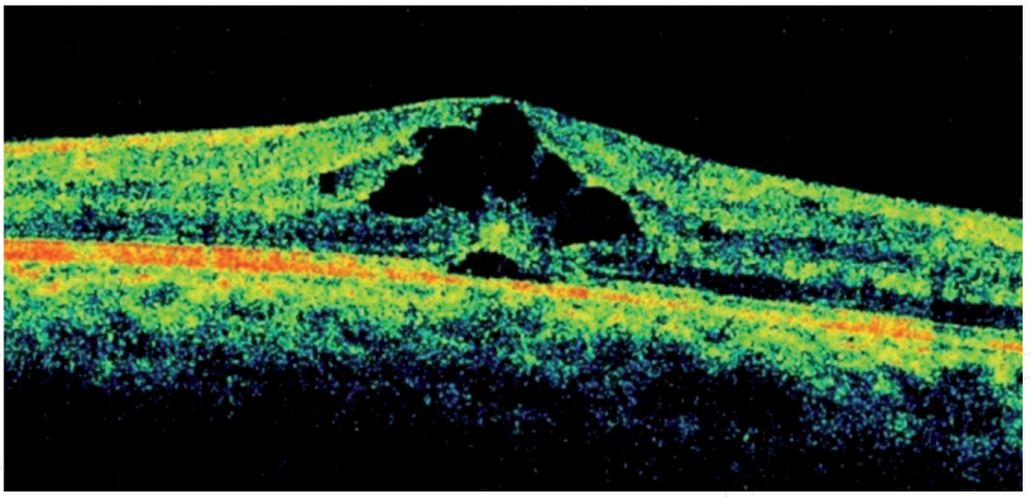

Figure 3.
Cystoid macular edema with presence of serous retinal detachment (spectral-domain OCT).

anteroposterior) were also described. This distinguished cases with an additional component of retinal distortion (**Figure 4**). In 2006, Kim et al. demonstrated similar findings of macular edema and posterior hyaloid traction. In addition, they described tractional retinal detachment as a peak-shaped detachment of the retina [17]. These 3 previous classifications used TD-OCT (**Table 1**).

With the advent of SD-OCT, Murakami et al. for the first time showed that in addition to the morphology of edema, the photoreceptor status played a significant role in the prognosis of visual acuity [18]. They classified edema into serous retinal detachment, cystoid macular edema, and Diffuse type (absence of either cystoid macular edema or serous retinal detachment) with the latter term being used for cases that had retinal thickening but an absence of cysts or serous fluid [18]. Later in 2012, Koleva-Georgieva proposed a classification in which the term early subclinical macular edema was introduced, to describe cases with macular edema which were previously being missed on clinical examination [19]. In addition, they also included the integrity of both the outer retinal layers, the IS/OS (inner segment-outer segment junction, now identified as the EZ layer), and the ELM. Retinal morphology, topography, and presence of traction at macula were also a part of the classification and were similar to the other classifications [19]. In 2013, Helmy et al. further subclassified cystoid macular edema based on the proportion of the largest cyst to the maximum retinal thickness(CME Grade I-IV). The integrity of IS/OS

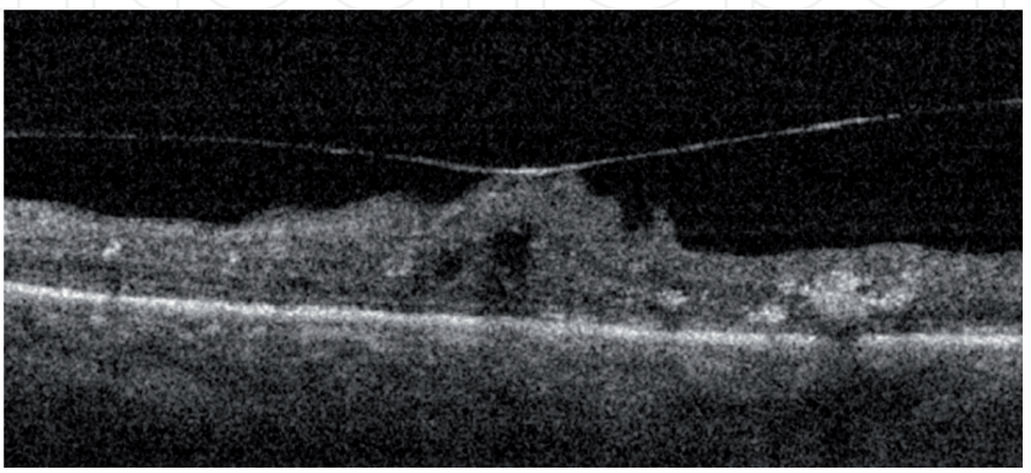

Figure 4.
Vitreomacular traction in a case of diabetic macular edema (captured with SD-OCT).

Classifications based on Time Domain OCT
Otani et al. [15] 1. Sponge-like retinal swelling 2. Cystoid macular edema 3. Serous retinal detachment
Panozzo et al. [16] 1. Retinal thickness 2. Retinal volume 3. Retinal morphology 4. Diffusion 5. Presence of vitreous traction
Kim et al. [17] 1. Diffuse retinal thickening 2. Cystoid macular edema 3. Posterior hyaloidal traction 4. Serous retinal detachment 5. Traction retinal detachment
Classifications based on Spectral Domain OCT
Murakami et al. [18] 1. Serous retinal detachment type 2. Cystoid macular edema type 3. Diffuse type (absence of either cystoid macular edema or serous retinal detachment)
Koleva-Georgieva [19] 1. Retinal thickness 2. Retinal morphology 3. Retinal topography 4. Presence and severity of macular traction 5. Retinal outer layers' integrity (IS/OS and ELM)
Helmy et al. [20] 1. Cystoid macular edema based on the vertical size of the largest macular cyst in proportion to the total macular thickness (CME Grade I-IV) 2. Integrity of External limiting membrane layer and Ellipsoid zone layer (Sub-classification as A-D) [Presence of hyperreflective foci (associated finding)] [Associated neurosensory detachment or vitreomacular traction (associated finding)]
Aiello et al. [21] 1. Center-involved diabetic macular edema 2. Non-center-involved diabetic macular edema

Table 1.
Time domain-OCT and Spectral domain-OCT based classification of Diabetic macular edema.

junction and ELM, presence or absence of neurosensory detachment, or vitreoretinal traction were also included. They extended their classification to include the presence of hyperreflective foci in the outer retina from the ELM to the RPE [20].

5. Role of OCT in treatment of diabetic macular edema

The introduction of intravitreal anti-vascular endothelial growth factor (anti-VEGF) agents significantly changed the treatment of DME a few years ago [22, 23]. Though laser treatment prescribed by the ETDRS study reduced the risk of vision loss significantly, only 20% of laser-treated eyes experienced a gain in visual acuity of at least 3 lines (15 letters) at 2 years [24]. A study by DRCR.net compared the efficacy of anti-VEGF treatment with laser treatment in eyes with DME [25, 26]. Results showed that anti-VEGF therapy was more effective in preventing the loss of visual acuity. In addition, a significant percentage of eyes showed an improvement in mean visual acuity [25, 26].

Monthly injections and follow-up with OCT imaging of the macula have been recommended in various guidelines [27–30]. Monthly treatment till there is no edema on follow-up OCT scan and reinitiating treatment when edema recurs or vision deteriorates is the preferred clinical practice for the management of DME [30, 31].

However, according to the FDA label of Eylea® (aflibercept), 'the recommended dose for eylea (for DME) is 2 mg (0.05 mL) administered by intravitreal injection every 4 weeks (approximately every 28 days, monthly) for the first 5 injections followed by 2 mg (0.05 mL) via intravitreal injection once every 8 weeks (2 months)' [32].

Cases that do not show a response after 3 monthly injections are termed non-responders [31]. Some authorities, however, term a patient nonresponder after the failure of 6 injections [29].

However, other definition of non-responder includes no or minimal reduction in retinal thickness on OCT or no improvement in visual acuity. The study by DRCR.net defined less than 10% decrease in central subfield thickness on OCT and < 5 letter increase in visual acuity as no response to anti-VEGF treatment [21]. Options to treat such cases include other anti-VEGF agents, intravitreal triamcinolone, implantable steroid injection, macular laser, and targeted retinal photocoagulation (TRP) of peripheral capillary nonperfusion areas [30, 31, 33].

Center-involved diabetic macular edema is defined as retinal thickening involving the central subfield zone of the macula that is 1 mm in diameter [34]. The management of center-involved macular edema causing visual decline (visual acuity worse than 20/30) is relatively straightforward and such cases need treatment [28, 35]. The preferred therapy includes intravitreal anti-VEGF agents, steroids, steroid implants, or a combination of these. Cases with center-involved macular edema and good visual function pose a challenge to the treating Ophthalmologist. The dilemma in such cases is whether to start intravitreal therapy or to observe [30, 34]. Such cases have been reported to improve with good control of blood sugar levels alone [31]. The role of anti-VEGF agents in such cases is being explored [36]. These cases have to be monitored at regular intervals to detect deterioration in vision which is an indication to begin anti-VEGF therapy [31, 34].

Non-center involved diabetic macular edema is defined as a retinal thickening in the macula that does not involve the central subfield zone of diameter 1 mm [34]. Laser photocoagulation is still the standard of care for the treatment of cases with non-center involving macular edema [37]. For cases with macular edema with vitreomacular traction, induction of posterior vitreous detachment during pars plana vitrectomy with or without ILM peeling is the recommended choice for treatment [38–40].

6. Biomarkers of DR on OCT

Biomarkers are markers used externally to assess a medical state reliably and accurately [41]. Biomarkers may be physical, chemical, or biological. They are used to assess a physiological state, pathological process, or response to any pharmacological intervention [41]. Imaging biomarkers have the advantage of being non-invasive, reliable, and accurate. Several OCT-based biomarkers have been reported in DME which help in the management of the disease as well as in prognostication [42].

6.1 Disorganization of the retinal inner layers (DRIL)

Earlier studies showed a variable correlation between central retinal thickness measured on OCT and visual acuity achieved post-treatment of DME [43, 44]. A study by DRCR.net revealed that this correlation is modest. They also documented cases with a paradoxical decrease in visual acuity with a decrease in retinal

thickening [45]. Further studies documented the role of OCT-based markers other than the central retinal thickness that affect visual acuity.

These include bridging retinal processes, the integrity of ELM and EZ, the reflectivity of cone outer segment tips, presence of hyperreflective foci, and subretinal fluid [46–49].

Long-standing cystoid macular edema with disturbance in ELM and EZ may suggest a poor visual outcome after treatment (**Figure 5**).

Sun and colleagues evaluated a novel marker in OCT, called disorganization of the retinal inner layers (DRIL), within the central 1 mm area of the fovea [50]. They studied the inner retinal layers in cases with existing DME or resolved DME. DRIL is 'defined as the horizontal extent in microns for which any boundaries between the ganglion cell–inner plexiform layer complex, inner nuclear layer, and outer plexiform layer could not be identified.' [50]. DRIL was found to have a substantial association with visual acuity. The presence of DRIL explained the paradoxical decrease in visual acuity in cases with resolved DME [50]. Later, Joltikov et al. reported the presence of DRIL in diabetics even before the presence of DR, DME, or PDR [51]. Further, Pelosini et al. proposed a theory to explain the negative correlation between retinal volume and visual acuity [52]. They suggested that the accumulation of fluid within the inner retinal layers causes the bipolar cells to stretch. Bipolar cells connect the photoreceptors to the ganglion cells. Fluid exceeding the limit of elasticity of these bipolar cell axons, may break the continuity of these axons and affect the transmission of signals between ganglion cells and photoreceptors. The irreversible destruction of bipolar cells provides a plausible explanation for cases with no improvement in visual acuity even after the resolution of DME [52]. In another study, the presence of retinal tissue between the cystic cavities in cases with DME was found to predict improvement in visual acuity after anti-VEGF therapy. These retinal tissues comprise of Müller and bipolar cells that transmit impulses between inner and outer retinal layers. The absence of these retinal bridging tissues at baseline explains the foveal thinning after the resolution of edema [53].

6.2 Hyperreflective retinal foci

SD-OCT imaging of diabetic retinopathy identified an additional intraretinal pathology which was visualized as hyperreflective dot or foci (HF) in few cases of DME [47]. Bolz et al. reported that the location of these HF on OCT was variable

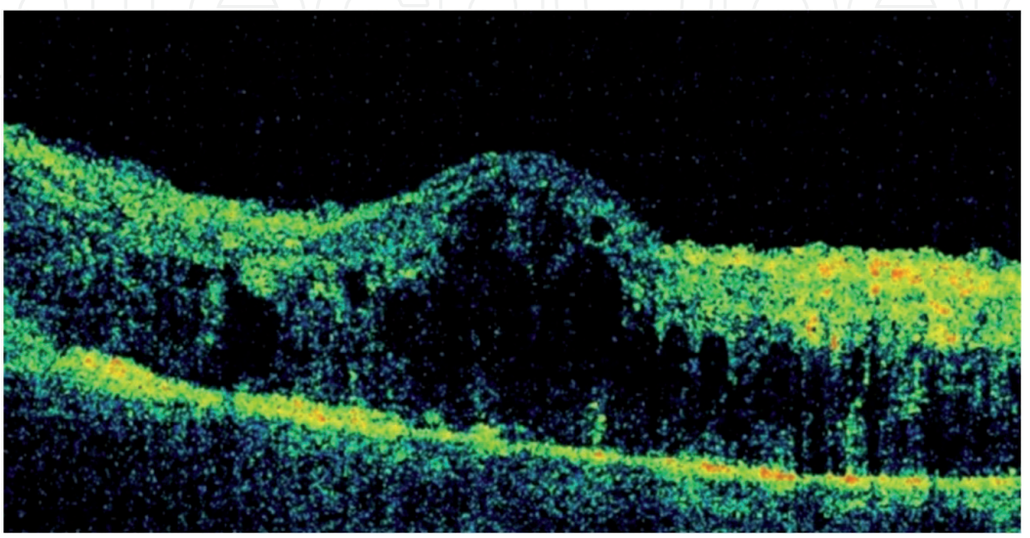

Figure 5.
Long standing cystoid macular edema.

[47]. In some cases, they were noted to be dispersed all through the retinal layers. In other cases, they were observed in the walls of microaneurysms or as confluent plaques at the level of the outer plexiform layer [47]. Bolz et al. hypothesized that the HF represented lipid deposits or precursors of hard exudates [47]. The similarity in the reflective property of HF and hard exudates supported their theory. In contrast, Lee and colleagues proposed that HF corresponded to activated microglial cells [54]. They observed a positive correlation between levels of the cytokine CD14 in the aqueous humor and the number of HF on SD-OCT in patients with DME. Cytokine CD14 is derived from activated microglial cells [55]. Microglial cells are the immune cells in the retina that undergo an inflammatory change in DR [56]. However, further studies are required to establish the origin of HF. Midena et al., described HF as dots with a size less than 30 microns, absence of back shadowing, and reflectivity similar to that of the retinal nerve fiber layer [57]. Their description allowed the distinction of HF from other hyperreflective spots on OCT such as intraretinal hemorrhage and microaneurysm. Intraretinal hemorrhage on OCT has a backshadowing effect such that retinal layers beneath the hemorrhage are not visualized. The microaneurysms on OCT have an external diameter of more than 70 microns in size [58]. Several studies reported a negative correlation between the presence of HF and visual acuity [59–62]. Uji et al. suggested a pathologic association between the presence of HF in the outer retinal layers and disruption of ELM and EZ resulting in photoreceptor dysfunction in cases with DME [59]. The presence of HF has been documented to indicate inflammatory activity or active disease status with studies reporting a significant reduction in HF after treatment with anti-VEGF and steroid implants [60, 61]. HF has also been identified as a predictor of early recurrence of DME after steroid (dexamethasone) implant [62]. HF has also been reported in DME cases that are refractory to anti-VEGF agents [63].

A characteristic arrangement of hyperreflective dots termed as pearl necklace sign in cases of DME was recently reported (**Figure 6**) [64]. It was originally described as HF surrounding the wall of a cyst located in the outer plexiform layer [64]. However, a similar appearance has recently also been described in cystoid spaces in the outer plexiform-outer nuclear layer and the inner wall of the neurosensory detachment [65]. Treatment with anti-VEGF agents in these cases led to the accumulation of hard exudates in the location of HF. A correlation of pearl necklace sign and visual acuity was only described in cases where the cyst or neurosensory detachment involved the fovea [65].

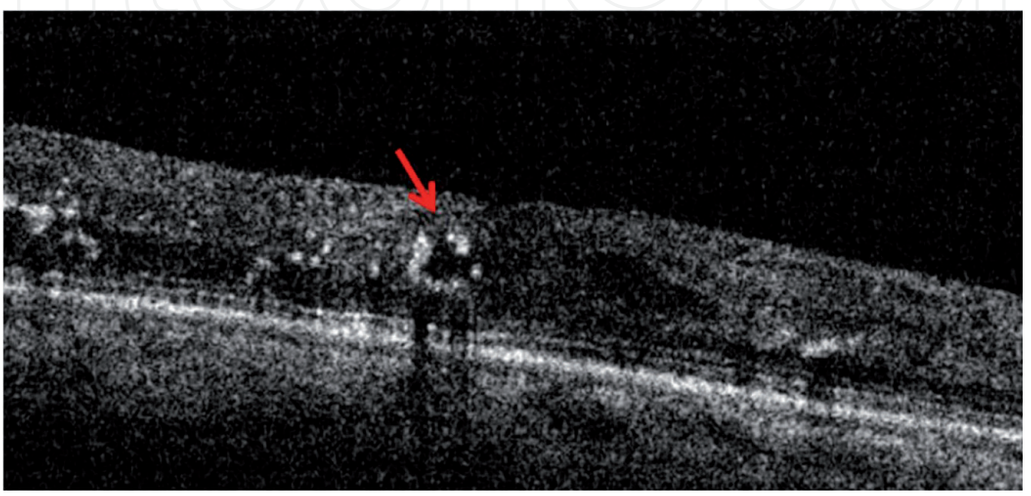

Figure 6.
Pearl necklace sign in a case of diabetic macular edema.

6.3 Hyperreflective material within intraretinal cystoid spaceSolid

Solid appearing cysts with hyper-reflective material within the cyst have been documented in DME (**Figure 7**) [66]. The content of these cysts has been hypothesized to be fibrin or of inflammatory origin [66]. However, no alteration to response to anti-VEGF treatment was reported [66].

Another novel OCT finding that has been recently reported in a patient with DME is a subretinal pseudocyst [67]. Contrary to what has been earlier documented, a cyst-like appearance was observed in the subretinal space and not within the retinal layers. The migration of Müller cells into the subretinal space has been proposed to be the reason for the development of the pseudocyst in that location [67].

6.4 Thickness of photoreceptor outer segment (PROS)

Advancement in technology has allowed the measurement of the thickness of the photoreceptor layer with SD-OCT in patients with diabetes. Patients with DR, DME, or diabetes but no retinopathy, have reported a thin photoreceptor layer in comparison to healthy individuals [46, 68]. Variation in visual acuity has been correlated to the thickness of the outer segment of the photoreceptor (PROS) in eyes with DME. This thickness of PROS is measured from the inner boundary of IS/OS junction to the inner boundary of the RPE layer [69]. The correlation of thickness of PROS with visual acuity is significant particularly when measuring it at the fovea [49].

6.5 Hyperreflective foci within the choroid

Hyperreflective foci within the choroid (HCF) have been recently reported in diabetic eyes [70]. Roy et al. hypothesized that these are intraretinal HF that migrate to the choroid with disruption of ELM and EZ. They documented a negative correlation between visual acuity and the presence of HF in the choroid. The presence of HCF was also observed to have an association with the severity of DR [70].

6.6 Thickness of the choroid

Studies using enhanced depth OCT imaging have evaluated choroidal thickness in eyes with DME and PDR. These studies have reported contradictory results. Kim and associates documented an increase in choroidal thickness with the increase in

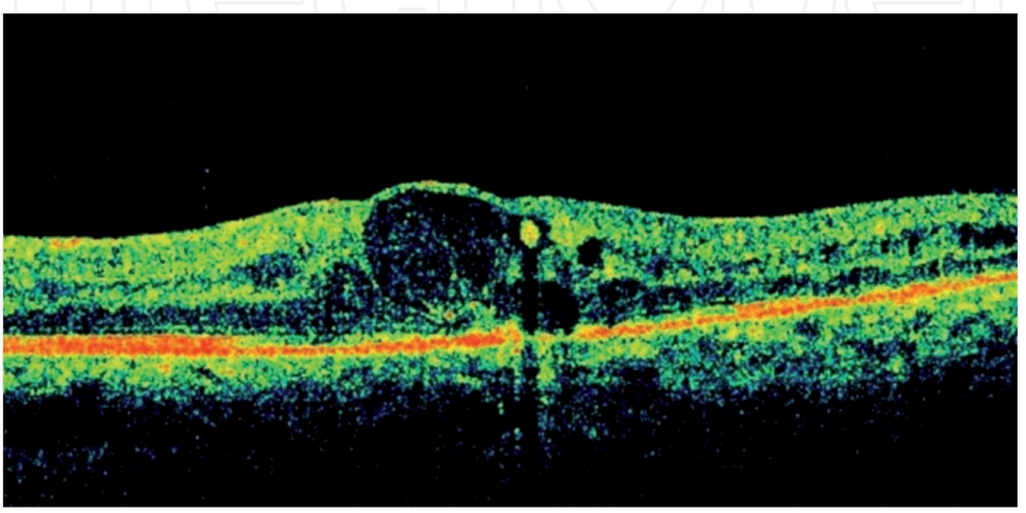

Figure 7.
Hyper reflective material within the cyst in a case of diabetic macular edema.

severity of DR and cases with DME [71]. They also reported a decrease in choroidal thickness in eyes treated with panretinal photocoagulation (PRP) [71]. In contrast, Querques et al. documented thin choroid in diabetic eyes when compared to control [72]. Rayess et al. documented that eyes with thicker choroid at baseline responded better to anti-VEGF treatment [73].

A recent study using swept-source OCT showed that choroidal thickness increased in the early stages of DR and then decreased as the severity of DR progressed [74]. The study proposed several mechanisms to explain choroidal thickening in early DR. Diabetic choroidopathy resulting in dysfunction of RPE and increased vascular permeability was implied as one of the mechanisms. Inflammation and oxidative stress-induced increase in cytokines was also suspected to be associated with choroidal thickening. In contrast, a decrease in blood flow and hypoxia was probably associated with thinning of the choroid with the progression of DR. However, whether choroidal thinning is primary or secondary to retinal ischemia remains to be established [74].

6.7 Choroidal vascularity index (CVI)

Choroidal vascularity index (CVI), another OCT-based marker enables the assessment of vascularity of the choroid [75]. Unlike choroidal thickness, this marker does not vary with physiological factors [75]. The choroid has two main components, the stroma, and the vascular layer. CVI is the proportion of the vascular component to the total choroidal area. A positive correlation has been documented between CVI and the status of choroidal blood supply [75]. Studies evaluating the CVI in diabetes have suggested that reduction in choroidal blood flow occurs as an early manifestation in diabetes even before retinopathy developed [76]. The thickening of choroid noted in the early stages of DR is probably explained by an increase in the stromal component of the choroid. As retinopathy progresses, the choroidal blood vessel further reduces in density [76]. However, further studies are required to confirm these theories.

7. Role of OCT in PDR

7.1 Neovascularization on OCT

High-resolution OCT imaging allows the evaluation of details of neovascularization in patients with PDR [77, 78].

Neovascularization of the retina was observed to breach the internal limiting membrane and protrude into the vitreous cavity [77]. The posterior hyaloid was attached or partially detached around the neovascularization [77]. Neovascular loops were seen as hyperreflective loops protruding into the vitreous with back-shadowing obscuring the retina at the points of attachment [77].

Thick neovascularization of the disc (NVD) was noted to grow along the posterior hyaloid which serves as a scaffold [77]. NVD appeared as hyperreflective tissue over the disc protruding into the vitreous cavity in cases with detached posterior hyaloid, which is uncommon in eyes with NVD [77]. Vaz-Pereira et al. in their study identified SD-OCT-based features that can distinguish active neovascularization from quiescent neovascularization [79]. They observed the presence of hyperreflective dots in the vitreous cavity in cases with active neovascularization. These hyperreflective dots were theorized to represent increased vascular permeability. Features such as the presence of epiretinal membrane, inner retinal tissue contracture, vitreous invasion, and protrusion towards the vitreous were found

in cases of quiescent or inactive neovascularization [79]. Another finding in PDR that is observed on OCT is vitreoschisis [80]. This is defined as the splitting of the posterior vitreous which leaves a layer of vitreous attached to the retina when vitreous detachment occurs. These can cause traction on the neovascular vessels and complicate surgery in PDR [80].

In contrast, intraretinal microvascular abnormalities (IRMA) are intraretinal, hyperreflective areas that were observed to distort the inner retinal layers. They do not breach the overlying ILM or vitreous. There is no thickening of the posterior hyaloid [77].

7.2 Wide-field OCT imaging in PDR

Mishra et al. have recently described a novel technique to facilitate wide-field imaging of the retina beyond the posterior pole. These images provide a better assessment of the vitreoretinal interface and therefore help in surgical planning in eyes with PDR [81].

8. Optical coherence tomography angiography (OCTA)

OCT angiography (OCTA) provides non-invasive imaging of the retinal vasculature parallel to images provided by FA [82]. The advantage over FA is that it circumvents the need for dye injection and therefore forestalls the risk of incidents like anaphylaxis. With the help of OCTA, people with contraindications to FA, can also undergo imaging of the retinal vasculature. OCTA uses the split-spectrum amplitude decorrelation algorithm [82]. In simple terms, it analyzes the light signals reflected from various tissues on repeated B scan imaging of a particular location. The mobile blood cells of the retinal or choroidal vasculature are the only structures responsible for providing a signal of different intensity or phases on repeated B scans [82]. The other tissues being stationary will not show any difference. It provides high-resolution images of both superficial and deep capillary plexus [83]. It provides better visualization of retinal capillary non-perfusion areas including capillary drop-out areas and foveal avascular zone [84]. Swept source-OCTA systems provide better imaging of the choroidal vasculature compared to SD-OCTA [85]. OCTA enables delineation of the morphology of microaneurysm into saccular or fusiform swelling [86]. Unlike FA, OCTA does not evaluate hyperpermeable pathological vessels. It does not show leakage (as seen on fundus fluorescein angiography) to indicate retinal edema or neovascularization [87]. OCTA also helps to estimate the activity status of the neovascularization [86]. Various quantitative measures have also been described using OCTA [88, 89]. Further details of OCTA are beyond the scope of this chapter.

9. Newer modalities in OCT

Adaptive optics OCT improves the transverse resolution of OCT images. Adaptive optics OCT provides microscopic images of the vasculature. It has been used to quantitatively analyze the lumen of retinal capillaries and microaneurysms in diabetic retinopathy [90, 91]. Based on the Doppler principle, Doppler OCT is a functional imaging technique that allows for visualization and measurement of blood flow [92]. Studies have observed reduced retinal blood flow in patients with DR compared to healthy individuals [93].

10. Conclusion

OCT has become a very valuable tool in the imaging of diabetic retinopathy. It is useful in the diagnosis of DME as well as decision-making regarding the treatment of DME. It is also helpful in following up the cases with DME after treatment with anti-VEGF therapy. It helps in diagnosing non-responders to treatment. It also provides information regarding the vitreoretinal interface and therefore helps decide the need for surgical intervention. It provides reliable qualitative information regarding retinal thickness. Various OCT-based classifications of DME have helped in better understanding of the disease pathogenesis. The evaluation of retinal layers on OCT explains the correlation between the retinal thickness at baseline and the final visual acuity achieved after treatment. The arrival of OCTA has further enhanced the imaging process. It adds to the information provided by SD-OCT or SS-OCT. It gives information regarding the blood supply of the retina, the density of the vessels, changes in the foveal avascular zone and helps to identify neovascular networks. It precludes the use of the invasive fundus fluorescein angiography and hence can be used in people with contraindications to fundus fluorescein angiography.

Thus, OCT has become a vital tool to diagnose and monitor the response of DME to various intravitreal pharmacotherapies including anti-VEGF agents.

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