Optical Coherence Tomography Assessment of Macular Oedema

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Neither of the authors has a financial interest in any product mentioned in this paper

Core Messages

- Optical coherence tomography (OCT) is a novel non-contact examination technique of the macula
- The high resolution of 10 µm is achieved by using the physical mechanism of coherence interferometry
- OCT allows new diagnostic criteria to be defined for macular oedema without subjecting the patient to fluorescein angiography
- Therapeutic decisions can be taken on the basis of OCT images, and macular oedema may be monitored very easily after medical or surgical treatment
- OCT is particularly useful in the assessment of diabetic macular oedema and of macular oedema associated both with age-related macular degeneration and with vitreomacular traction syndromes
- In the future, ultrahigh-resolution OCT, which uses a titanium-sapphire laser light source, may give an image resolution of up to 3 µm
- Ultrahigh-resolution OCT will be especially useful in the exact localization of subfoveal or sub-RPE choroidal neovascular membranes with important consequences for their medical or surgical management

1.1 Introduction

Optical coherence tomography (OCT) is a new medical diagnostic technology, which can perform micron resolution tomographic cross-sectional imaging of biological tissues [8, 17, 28, 33]. The initial development of the technology was pioneered at the Massachusetts Institute of Technology in Boston, USA, and the first OCT machines became available for widespread clinical use around 10 years ago. After the first two generations of scanners, the latest type has been available on the global market since 2002. Apart from its use in ophthalmology, OCT technology has also been applied in many other medical subspecialties such as urology, dermatology and cardiology, but also in non-medical fields such as engineering.

1.2 Principles of Operation and Instrumentation

1.2.1 Optical Tomography Versus Ultrasound

Cross-sectional imaging of the posterior pole has for many years been only possible with ultrasound, whose resolution depends directly on the frequency or wavelength

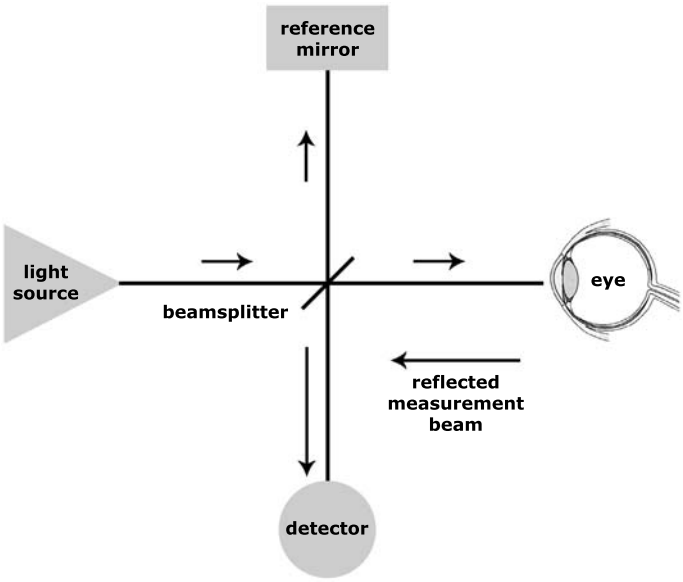

Fig. 1.1. Schematic diagram depicting the optical pathways of the OCT machine. The central beam splitter sends one part to the reference mirror, and the other part to the imaged tissue. If the two light pulses coincide when they are reflected back to the detector, they produce a phenomenon known as interference. This is measured by a light-sensitive detector, which then transforms the signal into the OCT image on the screen

of the sound waves. It yields a spatial resolution of approximately 150 µm at the posterior pole. Recently, high-resolution ultrasound imaging systems have been developed, which use higher frequency sound waves and which have resolutions on the 20-µm scale. However, due to strong attenuation in biological tissues this type of imaging can only be performed in depths of 4–5 mm, limiting the application to the anterior segment of the eye.

Imaging with OCT is analogous to ultrasound B-mode imaging, except that *light* is used rather than acoustic or radio waves. The primary difference between ultrasonic and optical imaging is speed. The velocity of propagation of light is nearly a million times faster than the speed of sound, which allows measurements with a resolution of 10 µm at the posterior pole. In contrast to ultrasound, there is no need for physical contact with the eye during examination, which reduces patient discomfort.

1.2.2 Low Coherence Interferometry

The OCT scanner uses low-coherence interferometry to create an image (Fig. 1.1). An optical beam from a superluminescent diode laser emitting at 830 nm is directed onto an optical beam-splitter, which functions as the interferometer [17]: Half the beam is reflected from a reference mirror and the other is transmitted to the imaged tissue. The operation of the system can be understood qualitatively if one thinks of the light beam as being composed of short pulses of light. The pulse of light reflected from the reference mirror will only coincide with the pulse of light reflected from a given structure in the patient's eye if both pulses arrive at the same time. This will occur only if the distance that the light travels to and from the reference mirror precisely matches the distance that the light travels when it is reflected from a given structure in the patient's eye. When the two light pulses coincide, they produce a phenomenon known as interference, which

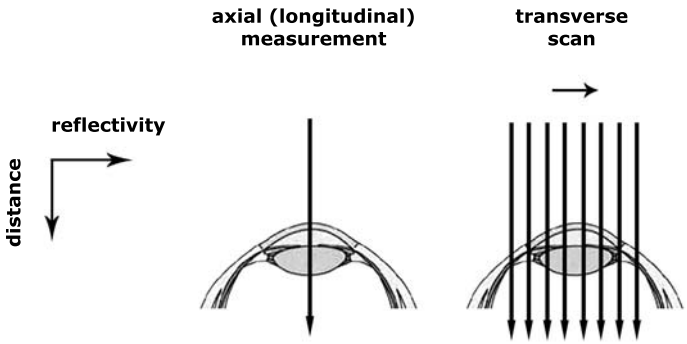

Fig. 1.2. Schematic diagram illustrating the optical pathways for the image acquisition by OCT. Successive longitudinal measurements at sequential transverse points (A-scans) are performed. As the light source moves across the retina, optical reflection and backscatter from retinal structures are detected. A two-dimensional set of data is collected and the cross-sectional image is composed

is measured by a light-sensitive detector. To facilitate transmission of light, high-quality fibre optics and optical communications technology are used in the OCT set-up.

1.2.3 Tomographic Imaging and Volumetry

Successive longitudinal measurements at sequential transverse points (A-scans) are performed. As the light source moves across the retina, optical reflection and backscatter from retinal structures are detected. A two-dimensional set of data is collected and a cross-sectional map is obtained (Fig. 1.2).

The map is displayed in false colours whereby each colour corresponds to a defined degree of reflectivity: Red and white represent highly reflective structures, whereas black and blue describe feebly reflective structures. Green structures represent intermediate reflectivity. Higher reflectivity thus corresponds to a higher cellularity. For example, fibrosis, hard exudates, haemorrhages, inflammatory infiltrates or pseudovitelliform material all appear hypereflective.

Retinal layers can be defined on linear scans, and data on retinal thickness can be obtained by measuring the distance between the vitreoretinal interface and the retinal pigment epithelium based on their different reflectance patterns. A surface map where different colours represent attributed retinal thickness can also be displayed by using six linear scans at a 30° interval. Red and white colouring corresponds with voluminous retinal structures, whereas blue and black colouring indicates areas of thinned retina (Fig. 1.4b).

1.2.4 Image Resolution

A main determinant of OCT resolution is the coherence length of the light source [17]. For the commercially available system, OCT provides an axial resolution of approximately 10–15 µm [8]. Penetration through clear media is excellent, but optical penetration through a thick haemorrhage is usually less than 100 µm. The recent ultrahigh-resolution ophthalmic OCT, which uses a titanium-sapphire laser as light source, can reach a resolution of up to 3 µm [7].

1.2.5 Image Processing and Correction for Eye Motion

Since the resolution of OCT imaging is extremely high, it is essential to compensate for motion of the eye during an image acquisition, which usually takes 1–2 s. Eye motion triggered by microsaccades and tremor can cause image blurring, and image-processing techniques have been developed to correct for this problem [33].

1.2.6 Instrumentation for Retinal Imaging

Generally speaking, the instrument operates as a fundus camera (Fig. 1.3). A high-powered condensing lens (+78 Dpt) is used so that the retina may be imaged onto a plane within the instrument. The magnification of the retinal image is determined by the refractive power of the condensing lens and the magnification of the ocular. A typical field of view at lowest magnification is 30°. The fundus image can be viewed either directly through the ocular, or via a television screen linked to a video camera. The diode beam produces a scan pattern on the retina that is visible to the operator as well as to the patient. Thus the exact location of the tomographic scan in the fundus can be determined at all times. Instrument magnification can be adjusted depending on the examination that is being performed, and on the degree of refractive error of the examined eye. If the visual acuity of the examined eye is very low and central fixation is not possible, a guiding light can be placed in front of the non-examined eye, which can stabilize the eye position for image acquisition. Dilatation of the pupil has usually been required to obtain high-resolution images, although the latest generation of OCT machines can obtain good-quality pictures with a minimal pupil dilation of 3 mm. Media opacities such as cataract or vitreous or subretinal haemorrhages and lack of foveal fixation or nystagmus can impede the image acquisition and thus represent important limitations of OCT technology.

Fig. 1.3. Photograph of the latest generation Stratus OCT (Carl Zeiss Meditec Inc., Dublin, CA, USA). Both the table and the chin rest are adjustable to the patient's height. The movable fixation light can be placed in front of the contralateral eye to help the examination of eyes with loss of central fixation

Summary for the Clinician

- **Optical coherence tomography (OCT) is a novel non-contact examination technique of the macula, which shows cross-sectional images of the retina**
- **The high resolution of 10 μm is achieved by using the physical mechanism of coherence interferometry**
- **Image acquisition lasts for about 1 s and only minimal pupil dilatation of about 3 mm is necessary**
- **OCT images may be obtained both as cross-sections and as retinal thickness maps**

1.3 Clinical Use of OCT

1.3.1 Retinal Disease

Since its discovery in 1991 [17], OCT technology has become a valuable tool for rapid imaging of the eye, particularly of the retina [13, 28, 33]. It has allowed for the first time the performance of quantitative cross-sectional analysis of the retinal layers. Comparisons of histological and OCT images of human and animal eyes have shown reliable correlation [35]. Minute details of retinal diseases such as macular holes, epiretinal membranes, vitreoretinal traction syndrome or choroidal neovascular membranes can now be accurately visualized, while cell layer thickness measurements provided by OCT have found interest among many glaucoma and cornea specialists. The cross-sectional images obtained by OCT can, in some instances, have a higher sensitivity than other current imaging tools, especially fluorescein angiography, and avoid at the same time the potential allergic manifestations inherent in fluorescein angiography use. The reliability and reproducibility of OCT in healthy and diseased retinal tissues have added to its diagnostic power [23].

1.3.2 Macular Oedema

Macular oedema is caused by a breakdown of the blood-retinal barrier with consecutive accumulation of fluid in the extracellular and subretinal space of the retina. It can be generated by several mechanisms such as ischaemia, inflammation or traction. The diagnosis of macular oedema is often difficult to establish solely by fundus examination, and ophthalmoscopic thickness assessment of the macula is highly examiner dependent. Although fluorescein angiography can confirm the diagnosis in most instances, only OCT can definitively measure the retinal thickness, allowing a more precise and reproducible assessment. Furthermore, the classic petaloid pattern is not always seen on fluorescein angiography (Fig. 1.4 a), and it is often difficult to ascertain the exact origin of the leakage in the outer layers of the retina since it can be obscured by inner retinal leakage. The rate of detection of macular oedema by means of OCT has been described as higher than by means of fluorescein angiography [4, 15], and early detection of macular oedema without perceptive functional loss may help to accelerate appropriate therapeutic management.

Mean foveal thickness in healthy subjects has been determined at between 170 and 174 µm [15, 24]. Common features of macular oedema on OCT consist of a pathognomonic increase in retinal thickness of up to 1,000 µm with a concomitant hyporeflective signal corresponding to fluid accumulation in the extracellular space. The latter can appear in different shapes; it can either accumulate into intraretinal cystoid cavities (Fig. 1.4 c) or it can constitute an optically clear layer under the neurosensory retina, above the highly reflective retinal pigment epithelium (Fig. 1.6 e). Evaluation of macular oedema by OCT has become particularly useful in cases of diabetic maculopathy, retinal vein occlusions, uveitic and postoperative inflammations, as well as in age related macular degeneration and in vitreomacular traction syndromes. The most recent OCT aided studies have helped a great deal both to classify different subtypes of macular oedema, to guide therapeutic decisions and in particular to document treatment response during clinical follow-up.

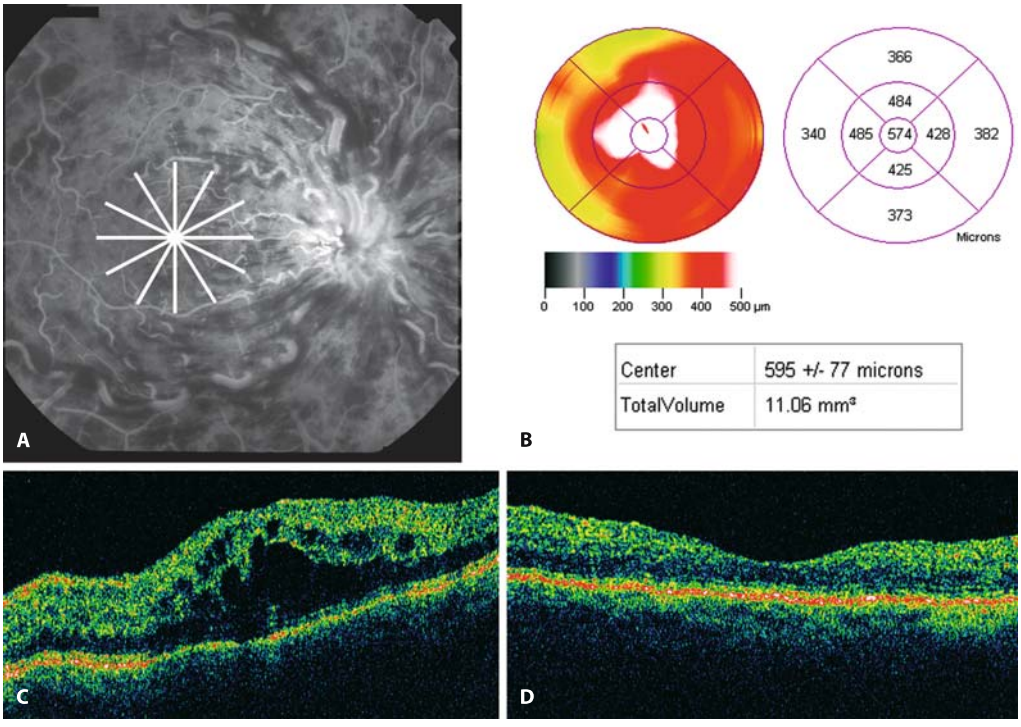

Fig. 1.4 A–D. Right eye of a 58-year-old patient with a central retinal vein occlusion. **A** Fluorescein angiography showing engorged optic disc, but there is no fluorescein leakage at the level of the fovea. The superimposed pattern corresponds to the six scans, which have to be performed in order to obtain the OCT macular thickness map. **B** Retinal thickness map and macular volume measurements using six radial scans (every 30°) of 6 mm length. **C** OCT showing macular oedema with typical cystoid hyporeflective spaces in the outer retinal layers. Fluid accumulation is intraretinal in its entirety since the reflectivity of the RPE is present. **D** Resolution of macular oedema 5 weeks after vitrectomy and radial optic neurotomy with restitution of the foveal depression

Summary for the Clinician

- **The clinical assessment of retinal thickness in the macula using OCT scanning is more reliable than biomicroscopy**
- **OCT scanning is more reliable than fluorescein angiography in the detection of intraretinal or subretinal fluid, since leakage in the inner retina may mask fluid in the outer retina on angiography**
- **OCT gives less information than angiography on the geographic extent of the fluid leakage within the macula**

1.3.2.1 Diabetic Macular Oedema

Diabetic macular oedema, which occurs both in the proliferative and non-proliferative forms of diabetic retinopathy, is the major cause of visual impairment among diabetic patients. The primary permeability changes occur at the level of the inner blood-retinal barrier, while the outer blood-retinal barrier may be secondarily affected: Leakage into the extracellular space can be either focal, diffuse or multifocal when coming from both retinal vessels and retinal pigment epithelium.

Clinically significant diabetic macular oedema has been defined using Goldmann contact-lens slit-lamp biomicroscopy and stereoscopic fundus photographs. Both these methods are, however, qualitative and poorly sensitive to small retinal thickness changes. Because of these diagnostic difficulties, severity of macular thickening and its extent within the different retinal layers have hitherto not been taken into account by the ETDRS for the management of diabetic maculopathy.

OCT appears to be more sensitive than fundus examination in diagnosing diabetic macular oedema [13], both when compared with the 78-diopter non-contact lens [6] and with the Goldman contact lens fundus examination, which has been described as having a 10 % higher sensitivity than the non-contact lens fundus examination [5]. This higher sensitivity of OCT is particularly improved when thickening is mild on OCT [5, 13, 15]. Recently, a new entity, the *subclinical foveal oedema,* has been proposed for these cases [5], with its potential therapeutic implications. Comparing the sensitivity of OCT with stereofundus photography, OCT assessment of diabetic macular oedema corresponds well with stereofundus photography for both extent and location of the oedema [32]. Reproducibility of OCT has been proven to be high between observers for diabetic maculopathy [24].

For clinical purposes a topographic map of macular thickness based on six radial tomograms equally spaced at 30° and centred on the fovea has been developed [13, 15]. It divides the macular area into nine regions, allowing a precise localization of retinal thickening in the centre of the fovea as well as in the areas surrounding it (Fig. 1.4 b). There appears to be an accurate correlation between OCT retinal thickness measurements and best corrected visual acuity [13, 15], which confirms previous work which concluded that retinal thickness increase is a better indicator of visual acuity loss than the amount of leakage on fluorescein angiography [26]. Nevertheless, fluorescein angiography still plays an important role in the evaluation of diabetic macular oedema since the ischaemic form cannot be determined by OCT.

The three most important structural patterns of diabetic macular oedema seen by OCT are the following: (a) sponge-like retinal swelling, (b) cystoid macular oedema, and (c) serous retinal detachment [27]. Apart from macular thickening, which is always present in the three patterns, additional specific features can be observed. In the sponge-like retinal swelling, OCT imaging reveals diffuse, homogeneous intraretinal reduced reflectivity due to fluid accumulation throughout the neurosensory retina (Fig. 1.6 c). Cystoid macular oedema appears as optically clear cystic cavities predominantly in the outer layer of the retina with bridging elements between the cysts, which correspond to Müller cells. Serous retinal detachment shows an optically clear layer under the neurosensory retina above the highly reflective retinal pigment epithelium. Different patterns can coexist in the same eye, and posterior hyaloid traction may be concomitant, appearing as a hypereflective band connected to the retina.

Functional analyses of the OCT subtypes in diabetes using multifocal electroretinograms (ERG) have highlighted the correlation between foveal thickness and macular ERG response. A recent report confirms that visual loss due to cystoid macular oedema is the worst compared to the two other subtypes [39]. A recent retrospective study [19] examined the correlation of different patterns of diabetic macular oedema on fluorescein angiography and on OCT. Focal leakage on fluorescein angiography appears to be related to the sponge-like

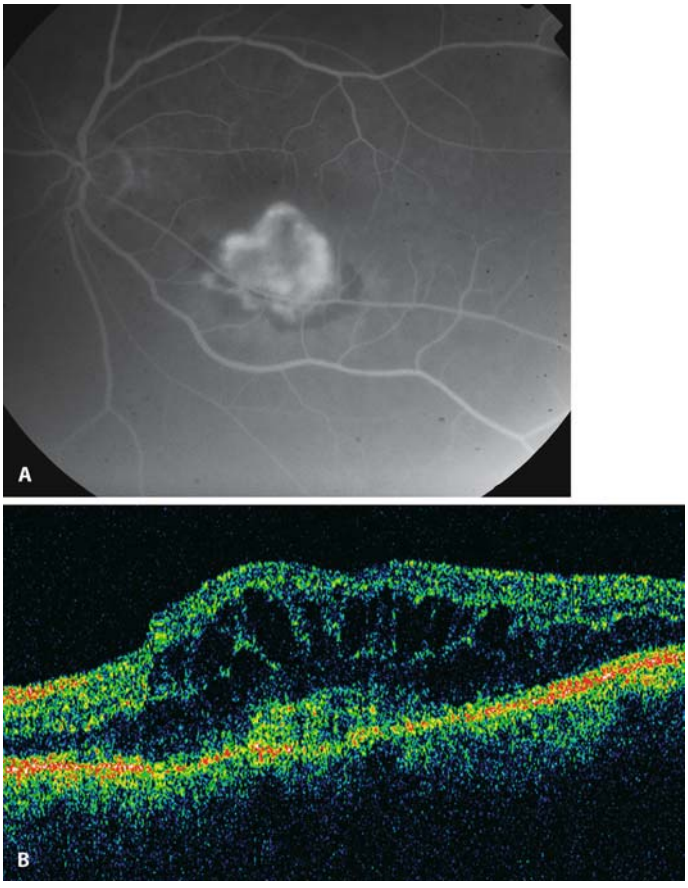

Fig. 1.5 A, B. Massive cystoid macular oedema associated with classic choroidal neovascularization. Visual acuity is limited to 5/60. **A** Fluorescein angiography showing well-defined dye leakage with a hypofluorescent ring corresponding to the neovascular membrane. **B** OCT image showing the multiple cystoid hyporeflective spaces of cystoid macular oedema. Bridging reflective elements between the cysts correspond to Müller cells. The hyperereflective subretinal structure corresponds to the neovascular membrane, whose borders are merging with the reflectivity of the RPE

type on OCT, while diffuse or diffuse cystoid leakage is correlated with cystoid macular oedema or serous retinal detachment with or without hyaloid traction on OCT. The importance of the three OCT subtypes mentioned above is reinforced by the fact that there exists the same correlation between subtypes and best corrected visual acuity [19], which had already been suggested by others [39]. Indeed, the OCT sponge-like subtype is associated with a better best-corrected visual acuity than serous retinal detachment or cystoid macular oedema [19]. It has been hypothesized that subretinal serous detachment may precede cystoid macular oedema since the latter corresponds to a worse visual acuity and a thicker retina on OCT [19]. Identification of OCT subgroups with specific patterns and corresponding retinal function can thus help both to identify at-risk patients and to choose suitable treatment modalities.

One of the major contributions of OCT to the understanding of diabetic macular oedema is its capacity to highlight the presence or absence of posterior hyaloid traction, which has been identified as a key element in the decision-making process of whether to treat patients with pars plana vitrectomy [21]. The poor or absent response to laser treatment of diabetic macular oedema in certain instances has been attributed to posterior hyaloid traction, and surgical peeling of this tissue has been shown to treat macular oedema successful-

ly in the majority of cases (Fig. 1.5c, d). In some instances, visual acuity loss has been attributed not only to increased macular thickness but also to tractional macular detachment, which could only be diagnosed by OCT [18]. As OCT has a higher sensitivity than fundus examination for the identification of small retinal thickness changes, it is expected to be similarly helpful in revealing subclinical posterior hyaloid traction in patients who may ultimately benefit from surgical hyaloid separation [24]. In contrast, vitrectomy may not be beneficial in the long term for patients with diabetic macular oedema, which does not respond to laser treatment, and which does not present posterior hyaloid traction on OCT [24].

Summary for the Clinician

- **The major contribution of OCT to the understanding of diabetic macular oedema is its capacity to highlight the presence or absence of posterior hyaloid traction**
- **Indication of surgical treatment of posterior hyaloid traction can be based on OCT images**
- **OCT allows the detection of subclinical diabetic macular oedema, a new disease entity, which has not yet been included in the ETDRS criteria for clinically significant macular oedema**
- **There is a correlation between macular thickness measured by OCT and visual acuity in diabetic macular oedema**

1.3.2.2 Central and Branch Retinal Vein Occlusion

Cystoid macular oedema may accompany central or branch retinal vein occlusion (CRVO, BRVO). In all cases, a breakdown of the inner blood-retinal barrier at the venous arm of the retinal circulation is implicated with loss of the vascular endothelial barrier. This may lead to leakage of fluid and lipids. Macular oedema associated with CRVO usually carries a poor prognosis and ends more often than not in a central RPE atrophy or a lamellar macular hole. The long-term clinical prognosis appears to be better in BRVO.

Most of the ophthalmoscopic features of central or branch retinal vein occlusion, such as retinal oedema, retinal haemorrhages, and cotton-wool spots, are well visualized on OCT. Qualitative OCT analysis can reveal fluid accumulation in the outer retina appearing as a hyporeflective area (Fig. 1.4c). A macular hole may form if the retina ruptures at the roof of a cyst, interrupting the reflectivity of the inner retina with variable depth. As in diabetic macular oedema, serous subretinal detachment can occur in central retinal vein occlusion and will be revealed on OCT by a regular hyporeflective band lying above the hyperreflective retinal pigment epithelium. It is important not to confuse the hyporeflectivity of the fluid itself with the shadowing effect produced by a retinal haemorrhage, which appears as hypereflective as the retina. Cotton-wool spots will appear as elevated hyperreflective structures disrupting the retinal layers leading to an attenuation of underlying reflectivity. Progression of macular oedema can be evaluated by repeated retinal thickness measurements. However, there appears to be no correlation between macular thickness measured by OCT and visual acuity as reported for diabetic macular oedema [20]. This lack of correlation has been attributed to the fact that a substantial drop of visual acuity occurs rapidly in central retinal vein occlusion and that residual visual acuity relies on the state of the remaining circulation rather than on retinal thickness as in diabetic macular oedema. Although OCT is not required to identify cotton-wool spots

and retinal haemorrhages, which can be easily seen on fundus examination, it may still be of value in determining the evolution of retinal thickness before and after surgical interventions for CRVO and BRVO (Fig. 4 c, d).

In an OCT study of 14 eyes with branch retinal vein occlusion, 4 eyes were seen to have cystoid macular oedema by fluorescein angiography, whereas 10 eyes were detected by OCT. Serous retinal detachment involving any portion of the macula was found on 10 of the 14 eyes (71.4 %), and serous detachment extending into the fovea was found in 6 patients (42.9 %). Only two of these were detected by ophthalmoscopy. Two of 14 patients (14.3 %) also showed subfoveal haemorrhage that appeared to have gravitated inferiorly through the serous retinal detachment to the dependent portion of the detachment [31]. The results of this study may help explain why it is difficult for the treating physician to get nice crisp laser treatment spots during photocoagulation in some of these patients. The presence of a subclinical retinal detachment prevents typical laser photocoagulation spots from forming. The finding of the subclinical retinal detachment in patients with branch retinal vein occlusion may also account for the presence of subretinal haemorrhage out of the region of involvement with the vein occlusion, something not previously explainable.

Summary for the Clinician

- **There is no correlation between macular thickness measured by OCT and visual acuity in CRVO associated macular oedema**
- **This has been attributed to a substantial drop in visual acuity, which occurs early and rapidly. Residual visual acuity relies on the state of the remaining circulation rather than on retinal thickness as in diabetic macular oedema**

1.3.2.3 Uveitis

OCT appears to be as sensitive as fluorescein angiography for detecting uveitic macular oedema and may give a more detailed image of fluid distribution within the retina than fluorescein angiography, particularly when subretinal fluid accumulation is present [1]. Furthermore, OCT has shown higher sensitivity than fundus biomicroscopy in the identification of active inflammatory lesions in posterior uveitis and of secondary neovascular membranes [11], allowing early treatment of these lesions. In a prospective study, which assessed intravitreal injection of triamcinolone for uveitic macular oedema, OCT was chosen to monitor macular oedema evolution because of its reproducibility and safety [2]. As previously described for macular oedema associated with CRVO, there is a poor correlation between visual acuity and retinal thickness in uveitic macular oedema [1, 2]. This observation has been attributed to the irreversible retinal damage induced by chronic cystoid macular oedema. OCT appears to be particularly useful for imaging uveitic cystoid macular oedema as these patients can have important posterior synechiae that impede sufficient dilation for fundus examination or fluorescein angiography. As mentioned before, the latest generation of Humphrey-Zeiss OCT machines requires only a 3-mm dilation to obtain good-quality images. Furthermore, uveitis patients may have multiple allergies and the use of OCT can prevent idiosyncratic reactions to the fluorescein dye.

Summary for the Clinician

- **There is no correlation between macular thickness measured by OCT and visual acuity in uveitis associated macular oedema**

- **This has been attributed to the irreversible retinal damage induced by chronic cystoid macular oedema**

1.3.2.4 Age-Related Macular Degeneration

In the majority of cases the exudative form of age-related macular degeneration (AMD) is complicated by intraretinal fluid accumulation and detachments of the retinal pigment epithelium. Fundus examination, fluorescein angiography, and indocyanine green angiography remain the main diagnostic tools for exudative AMD, and treatment eligibility has been assessed on the basis of these examinations. However, treatment of choroidal neovascularization (CNV) remains unsatisfactory in many circumstances and new imaging techniques such as OCT may help to better visualize and thus define anatomical subtleties, which may improve therapeutic success.

Like other hypercellular structures, the CNV will appear as a hyperreflective band on OCT. The identification of a CNV often relies on the reflectivity of the adjacent structures and on the CNV's localization in relation to the latter. Some authors have suggested that OCT is more sensitive than biomicroscopic examination in identifying retinal oedema and also small neurosensory or pigment epithelium detachments in AMD [14]. OCT may indeed also have some advantages over fluorescein angiography in AMD. In addition to the structural definition of the CNV, OCT allows the identification of an underlying CNV obscured by pooling of dye or by thin haemorrhages on fluorescein angiography [14]. Furthermore, while the source of dye leakage on fluorescein angiography has to be active to suspect retinal oedema, OCT can objectify and quantify even minimal oedema whether the source is leaking or not. The latter advantage of OCT also applies to other causes of retinal oedema and is of major interest for the comparison between natural evolution versus treatment monitoring. Although intraretinal fluid accumulation occurs often, cystoid macular oedema has not been classically described in association with exudative AMD, probably because of its difficult visualization on fluorescein angiography when dye leakage from the CNV predominates and the accumulation of dye in the inner retina is obscured.

Using OCT, Hee et al. [14] have proposed a simple classification of exudative AMD into three categories: (a) well-defined CNV, (b) poorly defined CNV or (c) fibrovascular pigment epithelium detachment. A poorly defined CNV appears as a zone of diffusely increased choroidal reflectivity associated with hyporeflective subretinal or intraretinal fluid accumulation. The presence of hyporeflective fluid or of small disruptions at the level of the retinal pigment epithelium and the choriocapillaris help distinguish the poorly defined CNV from increased choroidal reflectivity due to pigment epithelium atrophy (Fig. 1.5a, b). The proposed CNV classification does not necessarily correlate with fluorescein angiography findings. Thus well-defined CNVs or fibrovascular pigment epithelium detachments, which appear with relatively well-demarcated boundaries on OCT, were classified in some cases as angiographically occult CNVs, while poorly defined CNVs corresponded to angiographically occult CNV in most cases. This suggests that OCT provides anatomical details that are not obvious on fluorescein angiography. Since angiographically classic and occult CNVs imply different therapeutic approaches and prognosis, OCT may help to optimize treatment in these patients.

The prevalence of cystoid macular oedema in patients with subfoveal CNV secondary to AMD has been estimated to be around 46 % in a recent retrospective study

[34]. Cystoid macular oedema showed a statistically significant higher average foveal thickness, and it was statistically strongly associated with the classic form of choroidal neovascularization, while absence of cystoid macular oedema was correlated to occult CNV. Surprisingly, the presence of neither submacular nor subfoveal fluid showed any statistically relevant impact on visual acuity. Intraretinal fluid accumulation has been described with several types of exudative AMD [14, 29, 34], including retinal angiomatous proliferation [4].

Imaging by OCT has also been used to assess the treatment response after photodynamic therapy [29]. There appear to be five stages of evolution to which different degrees of fluid accumulation correspond. While a mild fluid accumulation is described in a first stage corresponding to an acute inflammatory response after the photodynamic therapy, the most important stage occurs at 4 weeks after the first treatment. When fluid accumulation predominates in this stage and active leakage is present on fluorescein angiography, re-treatment is suggested [29]. The shape of fluid accumulation in this stage is described as subretinal, causing a neurosensory detachment. Cystoid macular oedema appears only in the penultimate stage, on average 5 months following photodynamic therapy, which is associated with important subretinal fibrosis on OCT. The ultimate stage takes place when complete resolution of retinal fluid is concomitant with subretinal fibrosis and retinal atrophy. The study concluded that subretinal fluid after PDT is correlated with an active CNV, while cystoid macular oedema is associated with a hypoactive fibrotic stage of CNV for which re-treatment will not necessarily give better results than natural evolution.

Recently, ultrahigh-resolution OCT, which uses a titanium-sapphire laser light source, has been shown to give a resolution of approximately 3 µm, which allows choroidal thickness measurement in the presence of retinal pigment epithelium atrophy [7]. This technique seems also to be able to partially visualize a CNV underneath a retinal pigment epithelium detachment [7]. This has proven impossible using the current commercially available OCT (Humphrey-Zeiss Inc., San Leandro, CA). The novel ultrahigh-resolution technique could play a role in the future for better understanding macular oedema and exudative CNV pathogenesis by improving knowledge about the precise location of the retinal oedema and about the interaction between CNV type, activity and degree of fluid accumulation.

Because cross-sectional images cannot delineate the limits of the entire CNV, OCT can still not replace fluorescein and indocyanine green angiography assessment. It does, however, add a considerable amount of valuable information, which aids in the optimization of treatment, and in particular the re-treatment of CNVs.

Summary for the Clinician

- **OCT may allow the localization of a choroidal neovascular membrane (CNV) to be identified in relation to the retinal pigment epithelium and the neurosensory retina**
- **OCT can be particularly helpful if the CNV is obscured by pooling of dye or by thin haemorrhages on fluorescein angiography**
- **Cystoid macular oedema on OCT is strongly associated with the classic form of choroidal neovascularization**
- **Imaging by OCT may also be used to assess the treatment response after photodynamic therapy, and in case of fluid persistence, re-treatment may be advocated**

- **Because cross-sectional images cannot delineate the limits of the entire CNV, OCT cannot replace fluorescein and indocyanine green angiography**

1.3.2.5 Retinitis Pigmentosa

In patients with retinitis pigmentosa (RP), OCT appears to be more sensitive than contact lens or ophthalmoscopic fundus examination in the detection of macular oedema [10, 15, 16]. A prevalence of 13 % of cystoid macular oedema in patients with RP has recently been reported [16]. Some eyes in which cystoid macular oedema was observed on OCT interestingly did not show any leakage on fluorescein angiography. Unlike diabetic macular oedema but similarly to epiretinal membrane-related macular oedema, macular thickness does not seem to correlate either with best-corrected visual acuity or with fluorescein angiography grading. However, using the surface of the total area of the cystoid lesions for analysis the authors found that this correlates well with both best-corrected visual acuity and the degree of dye leakage on fluorescein angiography. In contrast, in a study of a small group of 12 patients with retinitis pigmentosa and cystoid macular oedema treated by vitrectomy, foveal thickness and visual acuity were used as main outcome measures and good correlation between the two was recorded [10].

1.3.2.6 Vitreoretinal Interface and Macular Oedema

The aetiology of vitreomacular traction syndrome, macular hole, epiretinal membranes and cystoid macular oedema has been attributed to different types of vitreoretinal adhesions and traction. In conjunction with macular oedema, traction exerted on the retina has been shown to produce retinal thickening and fluid accumulation that appears as leakage on fluorescein angiography. Contact lens fundus examination has classically been used to assess pathologies of the vitreous, but this is made difficult by the optical transparence of many of the vitreous structures and this technique may thus underestimate the incidence of vitreous pathologies. In a similar fashion, fluorescein angiography does not visualize epiretinal membranes, macular holes or vitreomacular adhesions clearly, rendering the diagnosis difficult.

OCT appears to offer many advantages for the diagnosis of vitreoretinal traction. OCT has been proven to be more sensitive than Goldmann contact lens biomicroscopy in identifying vitreoretinal adhesions. Two distinct patterns were defined using OCT and consisted of either a focal adhesion to the foveal or parafoveal retina associated with an incomplete posterior vitreous detachment (Fig. 1.6 e) or of multifocal adhesions to the macula separated by areas of posterior vitreous detachment appearing as optically clear on OCT [9]. Focal vitreoretinal adhesions appear to be associated with vitreoretinal traction syndrome and macular holes while multiple adhesions were seen in association with epiretinal membranes. The discontinuity of a reflective interface at the vitreoretinal junction in obliquely placed vitreous strands represents a limitation in the OCT image acquisition since it requires angular alignment [17]. This may lead to an underestimation of vitreoretinal adhesions using OCT. To improve visualization of vitreomacular adhesions, it may often be necessary to perform multiple vertical and horizontal single scans between 3 and 7 mm long across the retina.

Epiretinal membranes are cellular and contain collagen and appear thus as a relatively reflective thin band above the reflec-

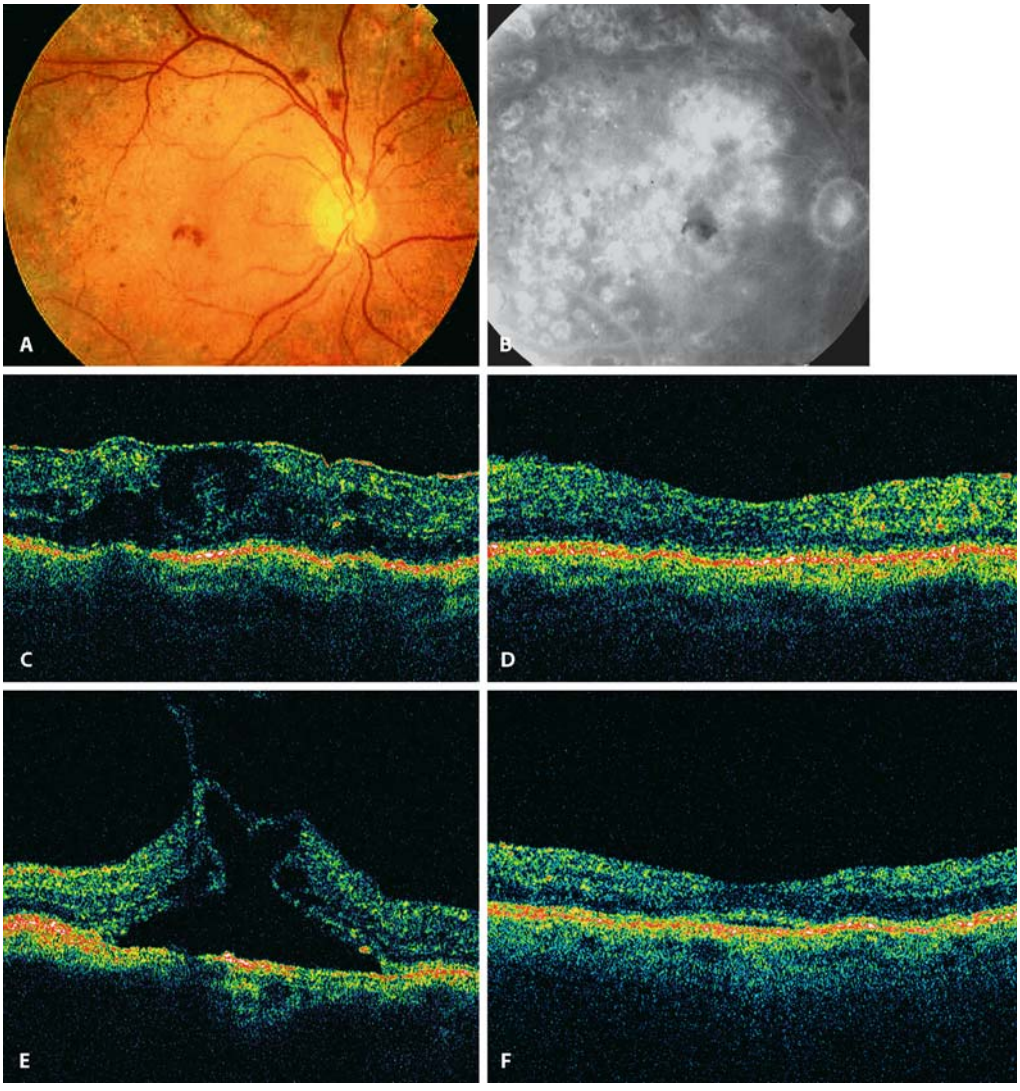

Fig. 1.6 A–F. Diffuse macular oedema in the right eye of a 54-year-old diabetic patient. **A** Fundus photography showing a few macular haemorrhages. **B** Late phase fluorescein angiography showing very diffuse and partly cystoid dye leakage. **C** OCT scan showing diffuse retinal swelling with intraretinal hyporeflectivity due to fluid accumulation. Please note the thickened posterior hyaloid visible on the retinal surface. **D** OCT image of the same eye 2 months after vitrectomy and peeling of the posterior hyaloid showing important regression of the oedema with restitution of the foveal depression. **E** A 68-year-old patient showing well-defined macular oedema and subretinal fluid on OCT due to massive vitreomacular traction. **F** OCT scan taken of a 48-year-old patient 1 month after encircling buckle for a macula-off retinal detachment. There is a small, circumscribed area of residual subfoveal fluid, which was visible neither on fundus biomicroscopy nor on fluorescein angiography

tive neurosensory retina with or without optically clear spaces between the two structures. The membrane should not be mistaken for the posterior hyaloid, which has a lower reflectivity and is usually thinner. When an epiretinal membrane is highly adherent to the retina, OCT shows a pseudo-thickening of the whole retina [36]. Epiretinal membranes may be confused on OCT with the highly reflective retinal fibre layer, particularly when scans are taken vertically, due to the anatomical configuration of the fibre layer [36]. Increased macular thickness and loss of the foveal pit are the more common OCT finding in patients with epiretinal membranes [22, 25]. Cystoid macular oedema has been proposed as a potential indicator of visual acuity following vitrectomy and epiretinal membrane removal. Preoperative visual acuity shows good correlation with macular thickness in patients with epiretinal membranes [22, 25, 36]. Surprisingly, such a correlation was not present after vitrectomy: visual acuity improves but macular thickness tends to remain increased [22]. It has been proposed that this may be associated with intraretinal gliosis, which prevents the macula from regaining its normal structure during the postoperative phase [22, 25].

Summary for the Clinician

- **OCT is more sensitive than Goldmann contact lens biomicroscopy in identifying vitreoretinal adhesions and associated macular oedema**
- **Two distinct patterns can be seen on OCT: focal adhesion to the foveal or parafoveal retina associated with an incomplete posterior vitreous detachment or multifocal adhesions to the macula separated by areas of posterior vitreous detachment**
- **To improve visualization of vitreomacular adhesions, it may often be necessary to perform multiple vertical and horizontal single scans between 3 and 7 mm long across the retina**
- **Although preoperative visual acuity shows good correlation with macular thickness on OCT in patients with epiretinal membrane, such a correlation does not exist after vitrectomy and peeling**

1.3.2.7 Postoperative Macular Oedema

Cystoid macular oedema can occur after any type of ocular surgery, but it is mostly associated with cataract surgery. In most cases postoperative macular oedema resolves with medical treatment, but in rare cases it is refractory and visual loss persists. For these cases, new treatments have been proposed such as intravitreal triamcinolone acetonide injection. Fluorescein angiography has been used routinely for the diagnosis of postoperative macular oedema, but the introduction of OCT has rendered the monitoring of medical and surgical treatment of these patients much easier [3]. Changes in macular thickness can even be detected after uneventful cataract surgery and without associated visual loss [30].

An intriguing aspect of pre- and postoperative macular changes after retinal detachment surgery has been discovered recently using OCT [38]. In a prospective study preoperative OCT imaging of the detached macula showed extensive cystoid macular oedema in the majority of patients, and there was a trend for these patients to have a worse postoperative final visual acuity. Postoperative OCT findings at 1 month showed in almost two-thirds of patients a very shallow area of subfoveal fluid accumulation, which could not be seen either on fundus biomicroscopy or on fluorescein angiography (Fig. 1.6 f). Further studies on this phenomenon have shown

that encircling buckles appear to be associated with such residual subfoveal fluid whereas patients with macula-off retinal detachments operated on with vitrectomy and gas showed no such fluid on OCT [37]. The pathogenesis of this fluid retention remains speculative.

Summary for the Clinician

- **Changes in macular thickness can be detected on OCT after uneventful cataract surgery and without associated visual loss**
- **Subclinical subfoveal fluid, which can only be seen on OCT, may persist for several months after buckle surgery for macula-off retinal detachment**

1.4 Summary

The introduction of OCT for the clinical examination of the macula has opened up several new avenues in the diagnosis and monitoring of cystoid macular oedema. This novel technique has become of particular importance in the assessment of diabetic macular oedema and of macular oedema associated both with age-related macular degeneration and with vitreomacular traction syndromes. It has added new diagnostic criteria as well as more objective data both to make informed therapeutic decisions and to monitor macular oedema after applied treatment.

Novel technologies such as ultrahigh-resolution OCT, which uses a titanium-sapphire laser light source, may play an important role in the future by providing much needed increased image resolution of up to 3 µm. This technology will be particularly useful in the exact localization of subfoveal or sub-RPE choroidal neovascular membranes with important consequences for their medical or surgical management.

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