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Between flesh and what's fantasy

B. Springsteen

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ABBREVIATIONS

AMD: age-related macular degeneration ART: automatic real time

BM: Bruch's membrane BRAO: branch retinal artery occlusion BRVO: branch retinal vein occlusion

C: choroid

CC: choriocapillaris CNV: choroidal neovascularization CRAO: central retinal artery occlusion CRVO: central retinal vein occlusion CSCR: central serous chorioretinopathy CSJ: choroid scleral junction cSLO: confocal scanning laser ophthalmoscope

EDI: enhanced depth imaging ELM: external limiting membrane ERM: epiretinal membrane

FA: fluorescein angiography FAF: fundus autofluorescence FCE: focal choroidal excavation FP: color fundus photo

GCL: ganglion cells layer

HD: high definition HS: high speed ICG: indocyanine green angiography ILM: inner limiting membrane INL: inner nuclear layer IPL: inner plexiform layer IR: infrared reflectance image IS/OS: inner segment/outer segment

MAC TEL: macular telangiectasia MC: multicolor image

NFL: nerve fiber layer

OCT: optical coherence tomography ONL: outer nuclear layer OPL: outer plexiform layer

PCV: polypoidal choroidal vasculopathy PED: pigment epithelium detachment

RAP: retinal angiomatous proliferation RF: red-free/blue reflectance image RPE: retinal pigment epithelium

SCL: sclera SD: spectral domain SRD: serous detachment of the neurosensory retina / sub retinal fluid TD: time domain

VMA: vitreomacular adhesion VMT: vitreomacular traction

INTRODUCTION

Optical coherence tomography (OCT) is a recently introduced imaging technique which provides high resolution images of eye tissues sections. It signals a new era in the field of non-invasive diagnosis and in follow-up of several ophthalmological pathologies.

The revolution caused by these instruments is a result of their capability to study eye structures which are vitally important for vision, such as the optical nerve, the choroid, the retina and in particular the macula, in much greater detail than is possible with other methods.

Since the OCT is mainly used for studying the macular region, this manual will essentially focus on the correct acquisition and interpretation of OCT images in this area of the retina.

This is essential given the increasing use of OCT in daily clinical practice, and the differences existing between the several commercially available instruments. especially nowadays , when the lack of a common software and standard acquisition protocols creates difficulties while comparing images and measurements produced with different machines.

Starting from these considerations the aim of this publication is to provide clinicians and technicians a practical support when using this fascinating imaging technique and to overcome the aforementioned difficulties with a thorough evaluation and comparative examination of different instruments

An introduction to OCT methodology, its evolution and basic working principles are presented in the first part of the manual. A comparison between four OCTs models is presented by a series of images collected from the same patients with different instruments to better appreciate similarities and differences.

Finally we will present a large quantity of examples with B-scan OCT describing pathological findings and pathological conditions most commonly founded in everyday OCT clinical practice.

An assessment chapter with interactive quiz questions is available at the end of the book. This is made up 80 scans each one includes 4 multiple choices. An enjoyable way to learn and check your knowledges.



Alessandro Invernizzi, Mariano Cozzi, Carlo D. Bianchi, Alessandro Pagani

A Brief History



The use of optical interferometry was first described by Simonsohn et al. in 1969.¹

Following this, experiments to measure bulb length using interferometry were carried out in the early 1980s. From this point on advances in technology and further researches led to the development of OCT in the early 1990s.

The first in vivo images of eye tissue using OCT were published in 1993 by independent groups in Boston and Vienna.²⁻⁴

The first system available on the market was produced by Humphrey (Humphrey Instruments, Inc., San Leandro, California, USA in 1995 (OCT 1). Image acquisition was based on the so called Time Domain technology (OCT-TD) which will be discussed at greater length later. With this instruments the low resolution of the images made it impossible to distinguish fine anatomical detail.

OCT using the same technology were became later available for clinical practice, the most famous being the Stratus OCT (Carl Zeiss Meditec, Inc., Dublin, California, USA). This machine made OCT extremely common and actually part of everyday clinical practice. Nowadays, many years later, Stratus OCT can still be found in a large number of clinics worldwide. The images provided by this instrument allow a good view of retinal tissues associated with a good repeatability so that was used in several clinical trials for the evaluation of drugs and treatments for diabetic macular edema and age-related macular degeneration.⁵

This model of OCT dominated the market for approximately ten years with practically no competitors, although some technical limitations connected with scan acquisition speed, prevent it from collecting images beyond a certain resolution and make it vulnerable to moving artifacts,

However in the 2004 the introduction of a radically different technique for OCT signal analysis, the so called Spectral Domain method, which will be analyzed in coming pages, generated a real revolution in the OCT world.⁶

This new technology drastically reduces image acquisition time resulting in lower susceptibility to moving artifacts and in the creation of scans with much higher resolution and quality.

Currently, Spectral Domain OCTs have supplanted the old Time Domain technology thank to the evident advantages they offer. Despite this some clinical trials still require the use of Stratus OCT.

Today there are several models available for purchase, produced by the sector's market leaders: Carl Zeiss Meditec, Heidelberg Engineering, Nidek, OPKO, Optopol Technology, Optovue, Canon, Optos, Tomey and Topcon Medical System.

This has pushed producers towards healthy competition in developing machines which are constantly improving. On the other hand the existence of several instruments has been responsible for difficulties in interpretation when comparing images. In fact, as we noted earlier, the lack of uniformity in image acquisition and analysis software often causes discordant results between different machines and makes a definition of common guidelines more difficult.⁷

Basic Working Principles



Figure 1.1 Multiple A-Scans and B-Scans representation

From Signal to Image⁸

In this section we will examine some concepts frequently referred to during the course of the manual. These informations are needed in order to understand how light waves can give rise to retinal sections similar to histological ones (tomograms).

Like other imaging techniques such as ultrasound, OCT sends a wave beam through tissues and analyses the signal reflected back, transforming it into an image.

However a single beam can only provide information about the portion of tissue it has travelled through; hence it will generate a one-dimensional image made up of variations in tissue reflectivity along the propagation axis of the signal itself. Only when a certain number of one-dimensional images is collected these can be computed into the form of a two-dimensional scan.

These concepts are behind both TD and SD technology, and form the basis of a good understanding of these methods; therefore it as well to be thoroughly familiar with them before we go any further.

<u>A-scan</u>

A one-dimensional longitudinal scan that exploits the phenomenon of tissue reflectivity. For each A-scan reflectivity-versus-depth curve is built up and then converted by software into a scale of false colors or shades of grey.



<u>B-scan</u>

A two-dimensional section obtained by A-scans flanking. To obtain a B-scan software must integrate the different A-scans onto one plane with the aim of building up a single image. When the extension of tissue explored remains equal, a higher number of A-scans generates a B-scan with greater detail.



Figure 1.2 B-scan arrangement starting from single a-scans

Movie 1.1 Volume process creation



Volume

This visualization modality represents a 3-D reconstruction of the anatomical portion studied through a series of B-scan.

The software computes B-scan sections, uniting them to create a 3-dimensional representation of the studied tissue, thus providing the possibility of exploring the volume along X, Y and Z axes. Obviously, the greater the number of B-scans the more precise the volumetric analysis obtained. This visual reconstruction is a good study aid in localizing lesions of the retina.

Figure 1.4 OCT volume obtained with Spectralis OCT. One of the Bscans composing the volume is highlighted.



Figure 1.3 3D visualization of different macular cube scan respectively collected with Cirrus OCT (A);Spectralis OCT (B); RTVue (C).

En Face Images

Besides conventional tomography, the three Spectral Domain instruments examined in the following pages also generate other supplementary images.

En face technology allows us to analyze coronal retinal scans, some perfectly flat and others adapted to the depth and the concavity of the posterior pole.

During analysis the software builds up a 3-D model of the retina from which it extrapolates en face sections.

Depending on the software we can visualize:

<u>C-scan</u>: (Coronal scanning) perfectly flat frontal sections, which cut across the different retinal layers.

<u>T-scan</u>: (Transverse scanning) the software builds up a curved surface adapting it to the layers of the retina.



Figure 1.5 En-face reconstruction obtained by SD-OCT. The yellow line overlapped to the B-scan in the left image represents the level of the retina we are visualizing by enface modality on the right.

<u>C-scan</u>

Cross-section images, obtained with perfectly flat coronal sections, reconstructions provided by software which process the scans on a

frontal plane, at an angle of 90° to the B-scan. The concave profile of the retina limits this type of analysis. C-scans are perfectly flat and as a consequence they cut across the different layers of the retina, sometimes making it difficult to interpret results.



Gallery 1.1 A case of epiretinal membrane examined with HRA-Spectralis through different visualization modalities.

Infrared Image



<u>T-Scan</u>

In this last type of retina visualization, the software (found in RTVue, Cirrus and Spectralis) creates a 3D reconstruction of the various tissues and adapts them to the profile of the analyzed structure. All the layers of the retina follow and adapt to the curve of

the posterior pole, creating an ideal parabola that uses a layer of the retina chosen by the technician as a reference point.



Figure 1.6 T-scan reconstruction obtained by SD-OCT in a patient affected by a detachment of retinal pigmented epithelium. The four images show the T-scan visualization of the same volume at different depth levels. ILM: inner limiting membrane. IPL: inner plexiform layer. RPE: retinal pigmented epithelium. RPE Ref: section reconstructed by following the RPE profile.

Time Domain OCT 9

The light source on which OCT is based is a superluminescent diode which emits low coherence light with a wavelength of approximately 800 nanometers (this varies from model to model).

The signal emitted is split into two beams by a partially reflecting mirror.

The transmitted beam (sample beam) enters the eye. The other beam (reference beam) is directed towards a moving reference mirror.

The first beam is reflected by eye tissue onto which it has been projected and returns to the instrument altered by its interaction. The amplitude of the reflected beam depends on the degree of light absorption and reflectivity in the eye tissue.

The second beam is reflected, unchanged, by the reference mirror.

When the two beams meet they generate an interference signal which is intercepted, measured and transmitted by a photodetector to a computer micro-processor.

This transforms information on interference between the "pure" reference beam and the sample beam altered by its passage through eye tissue into an A-scan image.

As we noted in the previous chapter an A-scan gives us information about the reflectivity of study tissue at different depths. That is to say it is built on a reflectivity-versus-depth curve.

In OCT Time Domain, depth information is obtained by mechanically shifting the mirror in the reference arm during each scan acquisition. This technological characteristic, the mechanical shifting of the reference mirror, prevents any reduction of the image acquisition speed beyond a certain point. Finally, the computer assigns a corresponding color or shade of grey to each reflectivity value, and unites the single A-scans in order to generate a two-dimensional image: the B-scan seen on the screen. (see the interactive scheme)

Movie 1.2 TD-OCT image acquisition process



Click on the screen to play the movie

Spectral Domain OCT 10



This new generation of OCT uses a broad band light source (superluminescente diode).

As with TD-OCT the beam is split in two: sample arm and reference arm.

The first beam, as in the previous technology, is reflected by the tissue it travels through whereas the second is sent back "pure" to the instrument by the reference mirror.

However, differently from what happens with time domain technology, shifting the reference mirror is not necessary in SD-OCTs for the reflectivity-depth curve construction.

By the use of a spectrometer, Spectral Domain OCT is capable of analyzing the interferometric signal which is generated from the comparison of the tissue-probing beam and the static reference beam. The signal is divided into its different component parts through the Fourier equation and since a higher frequency corresponds to greater depth, a reflectivity-depth curve can be directly obtained.

This means that in order to generate an A-scan it is sufficient to send a single signal, and not a repetitive series of pulses connected to the shifting mirror.

As with TD-OCT the computer then assigns a gray scale or false colors to the different reflectivity values and generates an image (see the interactive scheme).

Movie 1.3 SD-OCT image acquisition process



Click on the screen to play the movie

Time Domain vs. Spectral Domain 11,12





Considering what discussed in the previous chapters, it can be easily understood how the development of OCT imaging was revolutionized by the arrival of Spectral Domain technology. The possibility of acquiring images up to one hundred times faster than TD-OCT not only drastically reduced examination times, it also brought a surprising improvement in the quality of scans.

No less important, as discussed earlier, was the market liberalization associated with the new technology which led to healthy competition between the different manufacturers and resulted in the development of increasingly innovative software and acquisition techniques.

Compared with Time Domain OCT, Spectral Domain presents several advantages:

- greater acquisition speed
- greater axial and transverse resolution
- better signal to noise ratio
- greater diagnosis accuracy

Greater acquisition speed (from the approximately 400 A-scans per second of a TD-OCT to 40,000 scans per second of the HRA-Spectralis,Heidelberg Engineering, Heidelberg, Germany, i.e. one hundred times faster) is the key to the success of spectral technology. But what does the reduction in A-scan acquisition speeds mean in practical terms?

In order to generate a B-scan (made up of 512 A-scans) a TD-OCT takes 1-1.2 seconds. This makes the image acquisition very susceptible to moving artifacts owing to eye blinking or gazing losses. An SD-OCT obtains the same result in 0.014 seconds, reducing the ac-

quisition speed of a B-scan approximately seventy-fold. This means it is possible to considerably increase the number of A-scans for each single B-scan (going up to 4,000-8,000 A-scans per single B-scan), resulting in images containing more information on the probed tissue; thus higher resolutions and greater detail.

Since B-scans can also be generated more rapidly by reducing the acquisition speed of A-scans, it is possible to increase the area of the scan and the number of B-scans without risk of encountering motion artifacts.

This has led to three dimensional imaging.



Figure 1.8 3D OCT

A 3D reconstruction of a Macular Cube obtained with a SD-OCT

In fact if a high number of consecutive two dimensional images is collected (B-scans), by moving along the Z axis parallel to the reti-

nal surface it is possible to extrapolate a 3D reconstruction of the studied tissue through software processing.

These "cubes" of reconstructed tissue can then be "explored", rotated and sectioned by the operator along the three axes, X,Y and Z, to provide a global vision and unprecedented diagnostic possibilities.

One of the fundamental characteristics of OCT's in evaluations of the macular region is the extrapolation of a map representing retinal thickness. This can also be done using TD-OCT; however it is easy to understand how the greater number of scans obtainable with an SD-OCT focusing on the same area of the retina, also makes these instruments much more reliable in the map elaboration.

Another great advantage of the higher SD-OCT speed consists in the fact of being able to repeat several times the same retinal scan during acquisition phase. This makes it possible to generate a "mean" image formed from the mean of the single B-scans carried out in a certain area of tissue. In generating the mean, the computer highlights details with a constant presence in single images at the expense of elements varying in position in each single scan (for example the small signal dots caused by background noise). The resulting mean image is therefore cleaner and better defined than the single B-scans it is based on (Fig. 1.9).

The search for increasingly detailed images and three dimensional reconstructions, which require a greater number of A- and B-scans and therefore higher acquisition times, is potentially a source of motion artifacts in Spectral Domain OCT. In order to overcome this problem the latest generation of instruments is equipped with another important function: the eye-tracking system.

Figure 1.9 SD-OCT: single B scan vs Mean B-Scan



SD-OCT: the same retina scan obtained with a single b-scan and with an averaged image obtained by the mean of 20 single B-scans.

There are several variations of eye-tracking technology and detailed analysis of how they work is beyond the scope of this manual. However all the systems work to protect images from motion artifacts. Before, during, and after acquisition depending on the model used, the machine attempts at least in part, to compensate for eye movement during scanning, by aligning images with reference points such as retinal blood vessels. Comparative studies have been carried out on the different eye-tracking systems adopted in different models of OCT and results show the Heidelberg TruTrack system, capable of literally following eye movement during the image acquisition phase, to be the most reliable method to date. Spectral Domain OCT's use a light source with a slightly higher wavelength (870 nm in the Heidelberg Spectralis) than Time Domain (820 nm) giving a higher penetration of the signal through the probed tissues.

Moreover in the last few years the introduction of a new imaging modality called Enhanced Depth Imaging (EDI) has allowed to take advantage of a reverse hidden image generated by SD OCTs during the scan acquisition which better visualize deeper structures.^{13,14}

Figure 1.10 SD-OCT: standard modality vs EDI



HRA-Spectralis OCT: The same retina scan obtained with standard acquisition and with EDI function activated. Note how the details of the vitreous appreciable in the standard image (top) are lost in favor of a better visualization of the deeper structures with EDI modality (bottom). To conclude; differences between TD-OCT and SD-OCT have resulted in a slow decline of Time-Domain in favor of the more advanced SD-OCT technology. However, since Stratus OCT's are still widely used, as well as being required in certain clinical trials, it is advisable to have a good understanding of the potential advantages and limits of both systems.

CHAPTER 2

OCT in Clinical Practice

Alessandro Invernizzi, Mariano Cozzi, Carlo D. Bianchi

As we have already noted, OCT is an imaging technique which allows to obtain tomographic images similar to histological sections of the eye structures This technique can be considered as an "optical biopsy" allowing analysis of in vivo and in situ tissues. It is a contact less, repeatable and, no less importantly, economical technique.

OCT is part of the daily clinical practice both for the study of the anterior and posterior segment of the eye.

Several anterior structures including the cornea, the anterior chamber, the iris, the iridocorneal angle, and the sclera can be imaged by OCT although some instruments require adjunctive lenses for anterior segment imaging.

Posterior segment study can be carried out in mydriasis or miosis (when dioptric media are transparent) and allows to visualize the vitreoretinal interface, the retina, the choroid, and sometimes the sclera and retro-bulbar fat. $\frac{15}{2}$

Although OCT is a method that offers a wide range of uses, this manual will focus, as we said earlier, on the use of OCT for studying the posterior segment, in particular the macular region.

OCT and the Retina: in vivo histology ¹⁶

Figure 2.1



Spectral Domain OCT allows us to obtain an in vivo histological section of the retina and choroid (Fig 2.1)

Moving from the upper portion to the lower, or from interior to exterior, in a healthy retina we can recognize the following:

- ILM (inner limiting membrane): a membrane marking the limit of the inner retinal surface. It is formed at the extremity of the Muller cells and borders the vitreous humor, thus forming a diffusion barrier between neural retina and vitreous humor. Often a physiological thickening of the ILM is visible by OCT in younger subjects.
- NFL (nerve fiber layer): corresponding to ganglion cell axons without a myelin sheath, which reach the optic disc from different regions of the retina to form the optic nerve.
- GCL (ganglion cell layer): represented by the cell bodies of ganglion cells and some rare amacrine cells.
- IPL (inner plexifrom layer): made up of interlaced axons and dendrites coming from adjacent layers. Bipolar cell neurites are also present, arranged in synaptic relation to multipolar cell dendrites and amacrine cells.
- INL (inner nuclear layer): containing the cell bodies of bipolar cells, horizontal cells, amacrine cells and Muller cells.
- OPL (outer plexiform layer): made up of the synapses between photoreceptors, bipolar cells and horizontal cells. Photoreceptor axons, the synaptic organs of their terminals, and the dendrites of bipolar cells are present in this layer. The dendrites and axons of horizontal cells are also present.

- ONL (outer nuclear layer): represented by the photoreceptors. cell bodies.
- ELM (external limiting membrane): corresponding to the transition zone between the photoreceptor inner segment and their cell bodies, and houses the end-feet of Muller cell (cells with a support function).
- Ellipsoid Zone: mitochondria rich, this is the most external constituent of the inner segment photoreceptor.
- Interdigitation Zone: hyper-reflective band corresponding to the interdigitation of the photoreceptor outer segment with the retinal pigment epithelium.
- RPE (retinal pigmented epithelium): a single layer of prismatic cells with hexagonal base resting on the Bruch's Membrane (BM) which separates them from the choriocapillaris(CC). The cells vary in shape depending on age and site.With age the cells, which are unable to reproduce, significantly decrease in number. The apical surface has several microvilli arranged between the photoreceptor external segments which increases the exchange surface with photoreceptors themselves.
- BM (Bruch's Membrane): not normally visible in OCT in healthy subjects, it can be visualized in case of RPE detachment.
- CC (Choriocapillaris): the capillary layer of the choroid, equipped with multiple fenestrations, an anatomical structure that makes it unique.
- C (choroid): histologically composed by two vascular layers besides the choriocapillaris. The outermost layer is made up of larger diameter blood vessels and is called Haller's layer. More internally, between the choriocapillaris and Haller's layer, is a

layer made up of medium diameter blood vessels called Sattler's layer. This sub-classification cannot be appreciated in the OCT scan, even when using the EDI function.

- ScSJ: choroid sclera junction.
- SCL (sclera): completely visible by OCT in eyes with transparent optical media and little pigmentation of the fundus (albino subjects for example) and/or in cases of retinal or choroidal thinning (myopic subjects or geographic atrophy).

Interattivo 2.1 Graphic scheme of the retinal structure (Courtesy of S. Sciarini).





The correlation between what is visualized in an OCT section and the anatomical-histological equivalent has always stimulated interest and debate in the scientific community. In fact what appears in the quasi-histological images obtained with these machines is not always easily identifiable in corresponding anatomical structures. In order to understand this discrepancy we need to think that color/brightness changes in an OCT image, and subsequent identification of a structure compared to its surroundings (i.e. a layer of the retina) is not necessarily caused by the presence of a distinct cellular element but to a change in the reflectivity of a certain structure with respect to the OCT signal.

This determines the identification of hyper and hypo-reflective lines or elements without an anatomical "cellular" equivalent, but which refer, for example, to the passage between a cell body and its continuation, rather than the interface between two adjacent cell layers.

In this respect while the inner "histological" retina almost perfectly corresponds to what is visualized in OCT, deeper layers closer to the pigmented epithelium have caused several interpretation problems. A common agreement was present on what is visible with TD-OCT. In particular, at the level of the outer retina two hyper-reflective bands are identifiable: the first was considered to correspond to the connection between photoreceptor inner segment and outer segment, the second deeper band to correspond to the retinal pigment epithelium.

However with the advent of Spectral Domain technology four distinct hyper-reflective bands, situated between the photoreceptor layer and the pigmented epithelium, have been highlighted. This has set off a debate on interpreting anatomical equivalents of what is visible using these new instruments.



Figure 2.3 Graphic Scheme of a cone (Courtesy of S. Sciarini).

It is a common opinion that the innermost band can be attributed to the External Limiting Membrane (ELM). The idea that the outermost band represents the retinal pigment epithelium (RPE) has similarly become consolidated. Bruch's membrane (BM) is most likely part of the choriocapillaris. (CC) Of the two central bands, the innermost is commonly described as the junction between the photoreceptor inner and outer segments (IS/OS). However comparative analyses by Spaide and Curcio have cast doubt on this idea. In order to understand the hypothesis of the authors it is essential to have a deeper understanding of the histology of the photoreceptor inner segment. This portion of the cell is itself divided into an exter-



Figure 2.4 A case of Central Serous Chorioretinopathy (CSCR) that demonstrates the third line of outer retina disappearing during the neuroretinal detachment (Courtesy of Prof. Staurenghi).

nal part called the ellipsoid which is mitochondria rich and adjacent to the outer segment of the photoreceptor itself (OS), and a more internal part called the myoid, close to the external limiting membrane (ELM), which contains the endoplasmic reticulum.

On the basis of this anatomical information the hypothesis of the authors is that the second band cannot be attributed to the IS/OS junction, but that it corresponds to the ellipsoid portion of the photoreceptor inner segment.

The anatomical correlation with the third band which causes the greatest disagreement. Three hypotheses have been proposed on its nature.

For some Authors this band corresponds to the Verhoeff membrane, currently identified as the network of tight junctions between the cells of the retinal pig-
ment epithelium.

A second theory, proposed by W. Drexler, suggests the third line corresponds to the granules of melanin present in the RPE

Finally, a third hypothesis identifies the third hyper-reflecting band as the interdigitation of the external portion of the photoreceptor external segment with apical processes of the RPE cells.

To support this latter theory we propose a clinical observation. During detachment of the neuro-epithelium the photoreceptor outer segments disconnect from the microvilli of the retinal pigment epithelium causing the loss of the third hyper-reflective band; the line reappears when detachment disappears, most probably as an effect of re-interdigitation between the two cellular layers. (Fig. 2.4

It is evident from this brief analysis how the interpretation of the four bands visualized with SD-OCT has been the subject of strong debate. Despite the fact that certain authors disagree, and perhaps technological progress will again raise doubts about what we know, the majority of experts recently came to an agreement on no-menclature to be referred to in imaging analysis.

A summary of this long debate was recently published in an Ophthalmology editorial.¹⁸

CHAPTER 3

Comparison of different OCT instruments

Alessandro Pagani, Carlo D. Bianchi, Mariano Cozzi, Alessandro Invernizzi

The following chapter reports seven cases, examined, on the same day, using the four different OCT machines we have discussed.

The aim of this comparison is to highlight similarities and differences existing between the scans obtained by different equipment, applying the same imaging method to the same patients.

The comparison of ETDRS grids (Early Treatment Diabetic Retinopathy Study) shown by the side of corresponding scans is particularly interesting. In fact there is an obvious difference in the calculation of retinal thickness. As described in the introduction, this difference in value is caused by different segmentation algorithms used by different types of OCT software.

The Stratus OCT positions the line which identifies the outer limit of the retina more internally than the other machines, at the level of the hyper reflective inner/outer segment band. Spectral Domain OCTs align the outer limit at a deeper level usually corresponding to the retina pigment epithelium (RPE). However there are also differences between the various SD-OCT. For example the Heidelberg Spectralis identifies the outer retina limit in correspondence with Bruch's Membrane (BM).^Z

Case 1

Gallery 3.1 Normal retinal with physiological foveal profile. Note the presence of a retinal vessel on the left side of the scan producing a back shadowing effect (See Artifacts Section).



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Case 2

Gallery 3.2 Subfoveal neuroretinal detachment. In higher resolution (HR) images photoreceptor outer segment and Ellipsoid zone interruption can be appreciated.



Case 3

Gallery 3.3 Subfoveal deposits of medium reflective material in a patient affected by Pattern Dystrophy



• •

Case 4

Gallery 3.4 Retinal pigmented epithelium detachment (PED) with subfoveal deposits of mixed material.



• •

Case 5

Gallery 3.5 Macular hole with a small operculum and vitreomacular traction (VMT). In some images the presence of intraretinal cysts can be appreciated



• •

Case 6

Gallery 3.6 Hyper-reflective plaque with well defined margins in a patient affected by late stage age related exudative macular degeneration with inactive lesion. Note the presence of small intraretinal structural cysts



• •

Case 7

Gallery 3.7 Full thickness macular hole (Stage IV) with intraretinal cysts at the edges. The automatic segmentation lines have been maintained in the four scans. Note the differences between the ETDRS maps and the segmentation errors produced by the different instruments



CHAPTER 4

OCT Interpretation: Pathological findings

Mariano Cozzi, Alessandro Invernizzi

After becoming familiar with the necessary information for acquiring and analyzing OCT images, we come to the most difficult as well as most fascinating part of the diagnostic exam: interpretation.

A detailed analysis of all the information gathered in an OCT exam of the retina is beyond the scope of this manual, given the many conditions and shades of difference confronted in clinical practice each day. However, in order to perform exams as personalized as possible, with the best visualization of the most relevant clinical information, a good knowledge of the main clinical signs that can be found on an OCT image is mandatory.

The following chapter can be considered as a sort of "photographic dictionary" presenting a collection of pathological alterations as they appear on OCT images.

Drusen 19



Drusenoid RPE detachments or large soft drusen

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Drusen are represented by the accumulation of extracellular material usually located between the Bruch's membrane and the RPE. Hallmark sign of age related macular degeneration, they are classified according to their clinical appearance and size. In OCT scans they can appear as:

- multiple small bumps of the RPE fulfilled with hyper-reflective homogeneous material (hard drusen/cuticular drusen)
- multiple medium to confluent RPE bumps/detachments fulfilled with hyper reflective homogeneous material (soft drusen)
- multiple small accumulations between just above the RPE (reticular pseudodrusen/subretinal drusenoid deposits)

Pigment Epithelium Detachment (PED) 20



Serous PED

Retinal pigmented epithelium detachment (PED) is typical of several pathologies such as age related macular degeneration and central serous chorioretinopathy to name a few.

In OCT scans it appear as a detachment of the RPE from the Bruch's membrane. It can be classified as serous (when its content gives no OCT signal appearing uniformly black) or fibrovascular (when fulfilled by a structure of various reflectivity usually represented by a neovascular membrane)

Serous Detachment of the Neurosensory Retina (SRD)



Laminar longstanding SRD

• • • • •

Neuroretinal Detachment is a pathological condition that can be found in several eye diseases. It is characterized by the presence of fluid accumulation in a virtual space created by the separation of the neuroretina from the RPE. In OCT the fluid appears as an hypo reflective space that can vary in shape from a laminar thin layer typical of chronicle conditions to a round shape pocket in acute diseases. SD-OCT is also able to show the elongation of photoreceptor outer segment in SRD. ²¹

Edema²²

Cystoid macular edema

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Intraretinal edema is represented by the accumulation of extracellular fluid within the retinal tissue. It can be found in all the pathological conditions characterized by the presence of a blood retinal barrier breakdown (i.e. diabetes, retinal veins occlusions, inflammatory conditions, etc).

In OCT it is represented by multiple round shaped hypo reflective spaces within the retina (usually located in the macular area or nearby a damaged capillary net). According to the distribution pattern it can be classified as cystoid, sponge-like macular swelling, diffuse.

Microaneurysms 23



Iuxtafoveal microaneurysm without edema

Microaneurysms are capillary dilations. They are typical of diabetic retinopathy and appear early in the disease history. In OCT they look like small round-shaped/ovular lesions located in the inner plexiform/inner nuclear layers. In bigger lesions a hyper-reflective border corresponding to the vessel walls can be identified. The lumen is usually inhomogeneous and mid/low reflective. A back shadowing effect is visible beneath the lesion. As soon as the blood retinal barrier brakes down intraretinal edema starts to form around the microaneurysms.

Hard Exudates ²⁴



Multiple smaller Hard exudates (yellow arrows)

Hard exudates are the result of proteins accumulation within the retina in case of pathological exudation. They appear as hyper reflective dots/round-shaped formations usually disposed around an edematous area of the retina generating a back shadowing effect on the underlaying retinal layers.

Cotton Wool Spots 25



A cotton wool spot superior the optic disc

Cotton wools exudates are the clinical expression of NFL ischemic damage. They appear as hyper reflective thickened areas of the inner retinal layers generating backshadowing on the underlaying retinal layers.

Vitreo-Retinal Interface 26



Posterior premacular vitreous pocket

In a normal young subject vitreous cortex is so tightly adherent to the inner retinal surface that it cannot be visualized by OCT. With the progressive separation of the vitreous from the retinal surface occurring with aging the cleavage plan becomes visible. Pathological thickenings of the inner limiting membrane and the posterior cortical vitreous are visible as well. In case of clear optic media OCT also allows a good visualization of the vitreous composition (i.e. premacular vitreous pockets²⁷, debris etc.)

Atrophy



Large outer retinal layers and RPE atrophy (yellow dotted line) in a patient affected by Stargardt disease. Note the increased transmission effect (white arrowheads) allowing an enhanced visualization of the choroid and the choroidal scleral interface. A residual RPE tissue is visible at the center of the scan (yellow arrow).

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Generated by the loss of retinal tissue, atrophy results in a thinning of the retina accompanied by a better visualization of the underlaying structures. The most common atrophic conditions involve the outer retinal layers along with the RPE and are usually characterized by an increased transmission effect on OCT signal which allows a good visualization of the choroid and the choroid sclera junction.

Structural Cysts



Structural cysts in Macular Telangiectasia type 2

This alteration can be found in several chronic diseases. Differently from intraretinal cysts related with edema these lesions are not signs of an active exudation. On the contrary they represent a structural evolution with apoptotic retinal cell loss. Contrary to edema-tous cysts hypo-reflective spaces of structural cysts are typically not round shaped and can be found within the inner retinal layers.

Outer Retinal Tubulations²⁸



Two outer retinal tubulations in a patient affected by advanced exudative AMD

Visualized by OCT as small round-shaped formations with an hyper-reflective margin surrounding an hypo-reflective core, these lesions can be considered as a sign of clinical stability. Although the similarities with intraretinal fluid this formations represent invaginations of the photoreceptor layers evolving to apoptotic death.

Choroidal Folds



Multiple choroidal folds

Choroidal folds appear as multiple bumps in the Bruch's membrane, in the RPE and in the overlaying retina. They are typical of inflammatory/exudative conditions, hypotony and choroidal masses.

Retinal Pigment Epithelium Tear 29



RPE tear: the yellow arrow indicates the retracted and folded RPE whereas the brake is marked by the yellow dotted line

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When a retinal pigment epithelium detachment stretches the RPE so much to exceed its deformation capability the result is an RPE brake/tear (rip).

This condition has a typical double appearance in OCT consisting of an elevation and a retracted and folded RPE on one side and an

OCT Artifacts & Pitfalls



Moving/multiple blinking appear as multiple vertical black lines or shifting in the OCT retinal image

1 von 12

Despite the increased acquiring speed and the eye tracking systems, OCT images can be affected by several artifacts caused by patient movements, technician mistakes or pathological conditions. Moreover some unusual clinical entities can resemble different and more common conditions on OCT scans leading to mistakes and misdiagnosis.

CHAPTER 5

OCT Interpretation: Pathological conditions

Alessandro Invernizzi, Mariano Cozzi

Central Serous Chorioretinopathy (CSCR)³⁰



CSCR with subfoveal SRD (yellow arrow) and a small PED (white arrow)

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Central serous chorioretinopathy is characterized by the presence of one or more neuroretinal detachments usually involving the posterior pole. In most of the cases it is associated with stress or with systemic steroid assumption. It can resolve spontaneously within 3 months, recur or become chronic. Typical OCT signs of CSCR are SRD (acute/chronic), small PEDs which usually correspond to a leaking point on fluorescein angiography and a thickened choroid.

Choroidal Neovascularization (CNV) 31,32



Occult CNV characterized by a fibrovascoular PED (white arrow) and subfoveal SRD (yellow arrow)

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Choroidal neovascularizations are represented by the pathological growth of new formed vessels sprouting from the choroid. They can characterize several pathological conditions such as pathological myopia, posterior uveitis and more commonly the wet form of age related macular degeneration (AMD). In OCT they can appear as fibrovascoular PED when the new vessels develop between the Bruch's membrane and the RPE (occult CNV) or as a PED associated with RPE disruption and medium reflective exudative material between the RPE and the retina when the new vessels grow in this space (classic CNV). The evidence of SRD, blood, intraretinal edema and intraretinal flecks are considered as signs of lesion activity.

Retinal Angiomatous Proliferation (RAP) 33



A stage I RAP lesion (yellow arrow) with intraretinal alterations and cystic intraretinal spaces. Small reticular pseudodrusen are visible on the left side of the image. On ICG Angiography the lesion corresponds to the hyper fluorescent spot.

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Retinal Angiomatous proliferation represent a particular type of lesion found in a small amount of patients affected by wet AMD. They are the result of a pathological growth of new vessels within the retina which result in an anastomosis between retinal and choroidal vasculature. According to the current classification they are divided in 4 progressive stages: STAGE I: intraretinal neovascularization originating from the deep capillary plexus

STAGE II: intraretinal neovascularization progresses posteriorly generating intraretinal hemorrhages and SRD

STAGE III: intraretinal neovascularization associates with a neovascularized PED

STAGE IV: choroidal and retinal neovascularization anastomize each other into a retinochoridal anastomosis

Polypoidal Choroidal Vasculopathy (PCV)^{34,35}



PCV associated with occult CNV. Note the PCV lesion within the PED (yellow arrow) and the SRD aside (blue arrow)

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PCVs are pathological dilations of choroidal vasculature causing subretinal exudation and consequent retinal damage. They can develop as isolated lesions more likely found close to optic nerve head or in association with choroidal neovascularization at the posterior pole. In OCT they appear as round-shaped lesions with hyper-reflective margins and mid/low reflective core located between the Bruch's membrane and the RPE. As for CNVs, the presence of SRD and/or intraretinal edema is considered as a sign of active exudation. Hard exudates can be seen at the margins of SRD.

Dry Age-related Macular Degeneration (AMD) <u>36</u>



Drusen and RPE mottling as sign of dry AMD

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Dry AMD consists of a series of non-neovascular alterations that can affect retinal tissue of patients older than 55 years old. The early stages are characterized by the presence of RPE mottling and drusen. Progressively photoreceptors loss and RPE damage result in retinal atrophy. The advanced stage is the so called geographic atrophy.

In OCT dry AMD can be characterized by the presence of drusen (all types), RPE mottling, atrophy and rarely structural cysts.

Diabetes



Diabetic macular edema (yellow arrow) note the microaneurysm (white arrow) corresponding to a leaking point on FA.

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Diabetic retinopathy is characterized by damages to the retinal vasculature resulting in a wide spectrum of retinal alterations ranging from microaneurysms and small intraretinal hemorrhages (early stages) to capillary ischemia, venous beadings and neovascularization in the advanced disease.

OCT allows to visualize alterations to the posterior pole including: intraretinal edema, microaneurysms, serous detachment of the neurosensory retina, hard exudates, cotton wools and intraretinal/pre-retinal hemorrhages. In advanced stages epiretinal membranes and neovascularizations can be also imaged.

Patterns of Diabetic Macular Edema 37



Pattern1: Diffuse retinal thickening which appears as increased retinal thickness with areas of reduce of intraretinal reflectivity especially in the outer retinal layers.

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Diabetic macular edema has been classified in 5 patterns according to fluid distribution within the retina.

Vitreoretinal Interface Pathologies 38



Posterior cortical vitreous (white arrow) is tightly adherent to the epiretinal membrane (yellow arrow) causing a distortion of the foveal surface and a disappearance of the physiological foveal depression.

Vitreoretinal interface alterations include several pathological conditions subdivided in different stages. For an updated classification and discussion we suggest the latest review by Duker et al. published on Ophthalmology in December 2013.³⁸ To summarize, we can consider any alteration of the posterior cortical vitreous, the inner limiting membrane or the spatial relationship between them and all the consequent retinal damage as a vitreoretinal interface pathology. The incomplete separation of the vitreous from the posterior pole can cause a vitreomacular adhesion, a vitreomacular traction or a disruption of the retina with tissue loss (ranging from a lamellar to a full thickness macular hole). The thickening of the posterior cortical vitreous, the inner limiting membrane or the formation of an epiretinal membrane due to an inflammatory or mechanical stimulus can lead to alterations and wrinkling of the inner retinal surface.According to the stages of the disease, loss of the physiological foveal pit, accumulation of intraretinal edema and macular hole formation can occur.

Retinoschisis 39



Inner retinoschisis (yellow arrow) and outer retinoschisis (white arrow) in a high myopic patient.

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The term Retinoschisis refers to a stretching of the retinal tissue that results in an increased distance between the different retinal layers. Typically the retina appears thicker and several vertical septa, corresponding to elongated muller's cells, can be visualized with the OCT. This condition (typical of the high myopic eye) can be extended to the whole retinal thickness or, more rarely, involve the inner layers or the outer layers alone.
Adult-onset Vitelliform Macular Dystrophy 40



A mid reflective material deposit beneath the fovea (yellow arrow) in a patient affected by vitelliform dystrophy. Note the intact Bruch's membrane beneath the material.

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Adult-onset Vitelliform Macular Dystrophy or Pattern dystrophy is a condition characterized by the presence of hyperfluorescent material deposits at the posterior pole (single or multifocal) usually appearing after the forth decade. The disease seems to be inherited in an autosomal dominant fashion with incomplete penetration. In OCT it appears as a deposit of mid-reflective material between the RPE and the outer retinal layers. Typically the integrity of Bruch's membrane is preserved. Since in fluorescein angiography the material can show some kind of staining this form is often misdiagnosed as a CNV. In the late stages of the disease the material can decrease in quantity and involve to atrophy of the overlaying retina.

Central Retinal Artery Occlusion (CRAO) 41



Acute phase of a central retinal artery occlusion. The retina appears thicker with inner layers mixed up and diffusely hyper-reflective.

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Central retinal artery occlusion is one of the few emergencies in ophthalmology. It's a condition characterized by the blockage of blood flow into the whole retinal circulation caused by the occlusion (mostly embolic) of the central artery of the retina. At presentation the vision is usually highly compromised and the outcome is frequently bad, even with an immediate treatment. In the acute phase, the intracellular edema secondary to hypoxia, causes an increase in thickness and reflectivity of the inner retinal layers. NFL-IPL-GCC usually can appears as merged together which appear as merged together. The outer retinal layers are poorly visualizable due to a backshadowing effect. In the late stages of the disease the ischemic retinal layers decrease in thickness, evolving to atrophy and the whole retina becomes thinner than normal.

Branch Retinal Artery Occlusion (BRAO) 42



BRAO of the half superior retina. The affected hemiretina (yellow arrow) appears thicker (especially the inner layers) as compared to the healthy hemiretina (white arrow).

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Branch retinal artery occlusion consists in a blockage of the blood flow in a retinal artery branch. The cause can be embolic or inflammatory. The result is ischemia of the retinal area deprived of blood support.

BRAO shows the same appearance of CRAO in OCT, but with alterations confined to the area of the retina originally perfused from the occluded artery brach. Intracellular edema secondary to hypoxia, causes an increase in thickness and reflectivity of the inner layers (NFL-IPL-GCC) which appear merged together. The outer retinal layers are poorly visualizable due to a backshadowing effect. In the late stages of the disease the ischemic retinal layers decrease in thickness, evolving to atrophy.

Central Retinal Vein Occlusion (CRVO) 43



Diffuse intraretinal edema accompanied by a subfoveal SRD in a patient affected by CRVO.

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Central retinal vein occlusion occurs when the blood flow leaving the eye through the central retinal vein is blocked. This results in an increased intravenous pressure causing vessels tortuosity, intraretinal hemorrhages, intraretinal edema and capillary ischemia. In OCT several signs can be visualized: intraretinal edema, hard exudates, cotton wools, intraretinal hemorrhages and, in case of extended ischemia, hyper-reflectivity of the inner retina due to intracellular edema (similarly to what seen in artery occlusions).

Branch Retinal Vein Occlusion (BRVO)⁴⁴



Branch retinal vein occlusion of the superior hemiretina. Intraretinal edema (white arrow) is clearly limited to the affected hemiretina. The fovea is half spared.

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Branch retinal vein occlusion is the result of blood flow blockage in a second order retinal vein. Although several etiologies can cause BRVO, this condition usually occurs as a consequence to vein walls compression in correspondence with an arteriovenous crossing. Clinically it resembles CRVO but with alterations confined to the area of the retina originally drained by the occluded vein brach.

In OCT the same signs found in CRVO can be visualized: intraretinal edema, hard exudates, cotton wools, intraretinal hemorrhages and, in case of ischemia, hyper-reflectivity of the inner retina due to intracellular edema (similarly to what seen in artery occlusions).

Focal Choroidal Excavation⁴⁵



Focal choroidal Excavation (yellow arrow) with no complications.

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Focal Choroidal Excavation (FCE) is a recently described abnormality represented by a limited area of excavation of the choroid not associated with a scleral alteration. The overlaying retina can remain unaltered or show RPE mottling. Association with CSCR or CNVs have been reported. In OCT FCE appears as a thinning of the choroid altering the RPE profile not associated with scleral lesions.

Choroidal Nevus 46



A choroidal nevus (yellow arrow) along the inferior temporal arcade

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Choroidal nevus is a clumping of choroidal melanocytes. It is a benign lesion but in some cases it can evolve to a choroidal melanoma. In OCT it appears as an area of increased reflectivity just beneath the RPE, generating backshadowing on the posterior structures. OCT also allows to visualize some signs that can be useful in distinguishing a nevus from a malignant lesion. A SRD overlaying the nevus is considered as a risk factor whereas the presence of drusen usually characterize benign lesions.

Macular Telangiectasia 47



A small hypo-reflective cavity of the inner neurosensory retina (yellow arrow) temporal to the fovea not corresponding to fluorescein leakage

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Macular Telangiectasia (Mac Tel) is a an idiopathic condition characterized by capillary network alteration in the macula region associated with loss of neurosensory retinal tissue. Mac Tel is usually divided into 2 main groups: Type 1: unilateral and congenital. Type 2: bilateral and acquired. Due to the presence of tissue loss usually presenting as structural cysts in the fovea region Mac Tel are frequently misdiagnosed as lamellar/macular holes. Differently from edematous intraretinal cysts empty cavities visible in Mac Tel are not associated with dye leakage on FA. Late stages of the disease can be complicated by CNVs or atrophy.

CHAPTER 6

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CHAPTER 7

Assessment

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Frage 1 von 30

Check the best fitting description for the B-scan





Frage 1 von 10

Check the best fitting description for the B-scan



🧭 A. Myopic retina with ERM and intraretinal tractional edema

- **B.** Myopic patient with CNV
- **C.** Myopic patient with scar
- **D.** Myopic retina with increased choroidal thickness and retino-schisis



Antwort prüfen

Frage 1 von 10

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Check the best fitting description for the B-scan





- **B.** Structural cysts associated with SRD
- **C.** Cystoid macular edema associated with VMT
 - **D.** Structural cysts associated with VMT



