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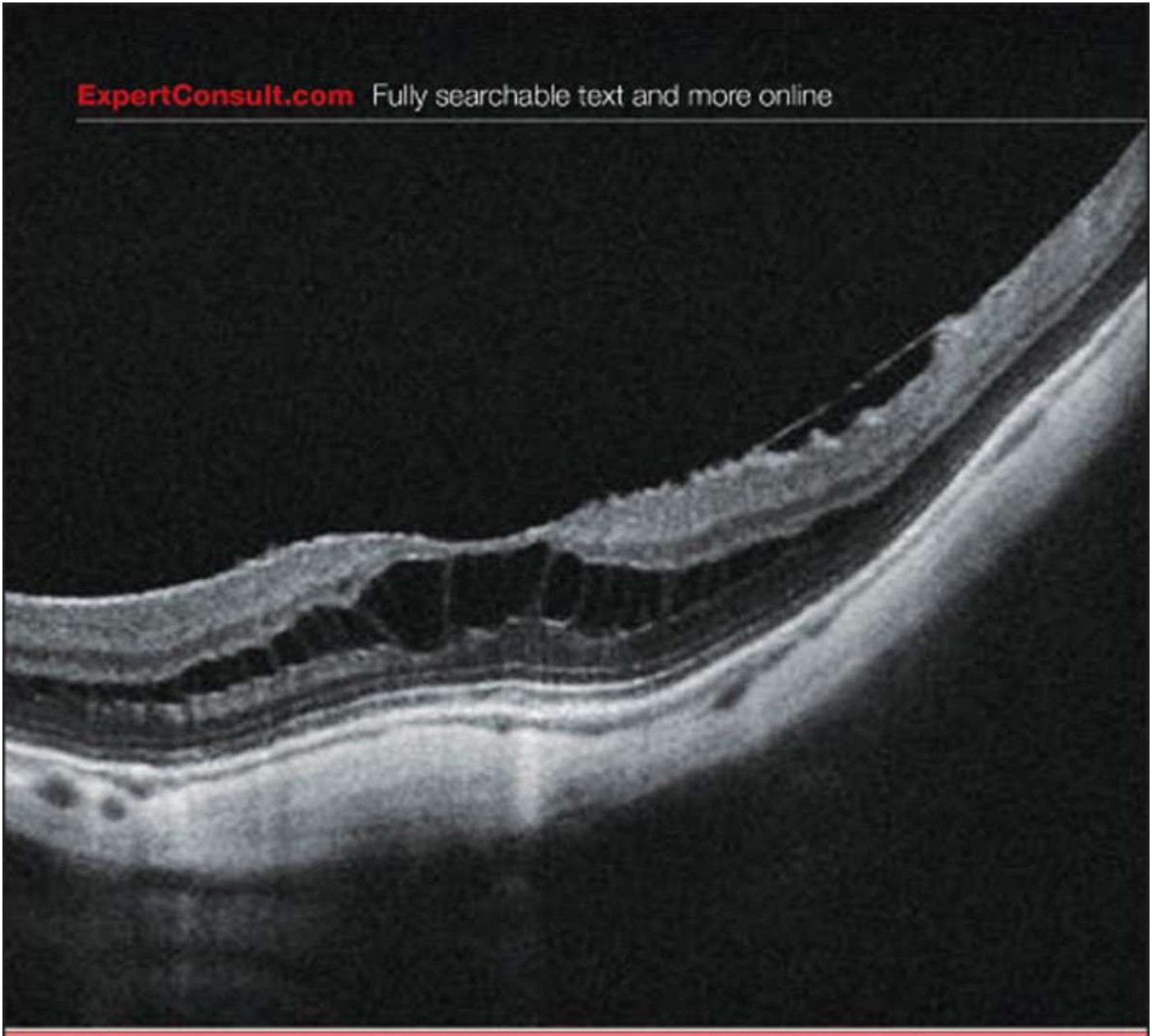

HANDBOOK *of* RETINAL **OCT**

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HANDBOOK *of* RETINAL **OCT**

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Preface

Optical coherence tomography (OCT) was 'discovered' in an optics lab at the Massachusetts Institute of Technology in the late 1980s by James Fujimoto and his collaborators: Carmen Puliafito, Joel Schuman, David Huang, Eric Swanson and Mike Hee. It began as an effort to experimentally measure excimer laser corneal ablation in real time. While it failed in that regard, the founders quickly identified the possibility that OCT could be employed to measure static ocular tissue thickness in real time. The first publication on OCT was in *Science* in 1991 and by 1996 the technology was transferred to a commercial company and soon thereafter commercial devices began to be sold.

In 2013, it is safe to say that OCT is one of the most important ancillary tests in ophthalmology and it is indisputably THE most important ancillary test in the subspecialty of the retina. We set out to produce an easy-to-read, brief but complete handbook of OCT images that was disease-based. Given the importance of OCT in our practices, we concluded that the OCT images should be the major focus of the book. Consistency of chapter layout, excellent images, and well-documented pathologic features were all goals. This book has minimal clinical description of the pathologic entities. There are plenty of excellent textbooks that cover these entities in more depth. We hope you find this handbook useful in your clinical practice on a daily basis.

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Acknowledgements

The development of optical coherence tomography and its emergence as the most important ancillary test in ophthalmology is inextricably linked to the New England Eye Center at Tufts Medical Center and its physicians. The clinical experiences summarized in this book are based on the collective expertise gained at the Eye Center over the past two decades and we are very grateful to our colleagues Caroline Baumal, Elias Reichel, Chris Robinson, Adam Rogers and Andre Witkin, with whom we are privileged to share patients and who have been an inexhaustible resource for this endeavor. We would also like to acknowledge the unparalleled ophthalmic imaging department at the New England Eye Center whose members acquired most of the images included in this book. Thanks also go out to the contributing authors and to our production team at Elsevier who worked on a very tight schedule to get the book published in just over six months. Our fellows and residents, whose questions provide constant intellectual challenge, also deserve acknowledgement. And last but perhaps most importantly, we would like to thank our families for their patience and support.

Dedications

To my wife Julie and my children, Jake, Bear, Sam and Elly whose support, love, patience and understanding allow me to pursue projects like this book. Also, to Carmen Puliafito, Joel Schuman and Jim Fujimoto – without them OCT would not exist and without their mentorship and collaboration I would never have been immersed in it.

Jay S. Duker

To Khadija and Ahmed, for their patience, generosity and encouragement. To my mother, the constant inspiration, without whom none of this would be possible. To my mentors past and present, and to my co-authors who made the process of writing this book such a phenomenally enjoyable and educational experience.

Nadia K. Waheed

To my wife Robin, whose constant love and encouragement allow me to pursue my passions, and to my parents Marisse and Tony and sister Candice, whose support I am forever grateful to have.

Darin Goldman

Glossary

AMD age-related macular degeneration
ARN acute retinal necrosis

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

CiRAO cilioretinal artery occlusion
CME cystoid macular edema
CNV choroidal neovascularization
CRAO central retinal artery occlusion
CRVO central retinal vein occlusion
CSCR central serous chorioretinopathy
CWS cotton wool spots

DME diabetic macular edema
DR diabetic retinopathy

EDI enhanced depth imaging
ELM external limiting membrane
ERM epiretinal membrane
ETDRS Early Treatment of Diabetic Retinopathy Study

FA fluorescein angiography
FAF fundus autofluorescence
FD Fourier domain
FTMH full-thickness macular hole

GA geographic atrophy
GCC ganglion cell complex

HE hard exudates
HRVO hemiretinal vein occlusion

ICGA indocyanine green angiography
ICP intracranial pressure
ILM internal limiting membrane
INL inner nuclear layer
IPL inner plexiform layer
IRF intraretinal fluid
IRMA intraretinal microvascular abnormalities
IS inner segment of photoreceptors
IS–OS inner segment – outer segment (of photoreceptors)

LE left eye
LMH lamellar macular hole

MacTel macular telangiectasia
MCP multifocal choroiditis with panuveitis

NFL nerve fiber layer
NPDR non-proliferative diabetic retinopathy
NVD neovascularization of the disc
NVE neovascularization elsewhere (retinal neovascularization)
NVI neovascularization of the iris

OCT optical coherence tomography
ONH optic nerve head
ONL outer nuclear layer
OPL outer plexiform layer
OS outer segment of photoreceptors

PCME postoperative cystoid macular edema
PCV polypoidal choroidal vasculopathy
PDR proliferative diabetic retinopathy
PED pigment epithelial detachment
PFC perfluorocarbon
PVD posterior vitreous detachment

RAP retinal angiomatous proliferation
RCH retinal capillary hemangioma
RD retinal detachment
RE right eye
RNFL retinal nerve fiber layer
RP retinitis pigmentosa
RPE retinal pigment epithelium

RRD rhegmatogenous retinal detachment
RS retinoschisis

SD spectral domain
SD-OCT spectral domain optical coherence tomography
SRF subretinal fluid
SS swept source
SVP summed voxel projection

TD time domain
TD-OCT time domain optical coherence tomography
TRD tractional retinal detachment
TSINT temporal, superior, inferior, nasal temporal scan pattern

VEGF vascular endothelial growth factor
VKH Vogt–Koyanagi–Harada
VMA vitreomacular adhesion
VMT vitreomacular traction
VRL vitreoretinal lymphoma

XLRS X-linked juvenile retinoschisis

PART 1: Introduction to OCT

1.1 Scanning Principles

Optical coherence tomography (OCT) is a medical diagnostic imaging technology that captures micron resolution three-dimensional images. It is based on the principle of optical reflectometry, which involves the measurement of light back-scattering through transparent or semi-transparent media such as biological tissues. It achieves this by measuring the intensity and the echo time delay of light that is scattered from the tissues of interest. Light from a broadband light source is broken into two arms, a reference arm and a sample arm that is reflected back from structures at various depths within the posterior pole of the eye.

There are two main ways in which the backscattered light can be detected:

- Time domain (TD) detection
- Fourier domain (FD) detection – which is further broken down into:
  - Spectral domain (SD)
  - Swept source (SS)

Time Domain OCT

In time domain OCT scanning, light from the reference arm and light reflected back from the sample undergo interference, and the interference over time is used to generate an 'A-scan' depth resolved image of the retina at a single point. Moving the sample and the light source with respect to each other generates multiple A-scans that are combined into a cross-sectional linear image called the B-scan or 'line scan'. Scanning speeds of TD-OCTs are typically around 400 A-scans/second. The primary commercially available TD-OCT device is the Stratus OCT™ made by Carl Zeiss Meditech.

Spectral Domain OCT

In this technology, the spectral interference pattern between the reference beam and the sample beam is dispersed by a spectrometer and collected simultaneously with an array detector. This simultaneous collection allows for much faster scanning speeds than the traditional time domain devices where a mechanically moving interferometer gathers the data over time. An A-scan is then generated using an inverse Fourier transform on the simultaneously gathered data. Commercially available SD-OCT devices have scanning rates of 18,000–70,000 A-scans/second.

Higher scan speeds in the SD-OCT faster acquisition time, which minimizes the chance of eye movements during acquisition, especially in patients with poor fixation. Both hardware and software enhancements permit precise image registration which allows for more reliable comparison between visits. Faster acquisition speeds also mean a higher sampling density of the macula, minimizing the chances of missing pathology. The higher speeds allow for the production of three-dimensional OCT scans. The broader light sources of SD-OCT devices achieve a higher axial resolution than TD-OCT, allowing better visualization of retinal anatomy. Commercially available SD-OCT devices include: the Cirrus OCT made by Carl Zeiss Meditech, the Spectralis OCT made by Heidelberg Engineering, 3D-OCT 1000 (Topcon), Bioptigen SD OCT (Bioptogen) and the RT-Vue (Optovue).

Swept Source OCT

In swept source (or optical frequency domain) OCT scanning, the light source is rapidly swept in wavelength and the spectral interference pattern is detected on a single or small number of receivers as a function of time. The spectral interference patterns obtained as a function of time then undergo a reverse Fourier transform to generate an A-scan image. Higher scanning speeds allow for denser sampling and better registration. The swept source OCT also has less sensitivity roll-off with depth, allowing better visualization of structures deep to the retina. At present, swept source OCT is not widely available commercially with the DRI-OCT 1 (Topcon) being the only commercially available device.

1.2 Basic Scan Patterns and OCT Output

Each commercially available OCT device has unique scan patterns that are programmed into the machine. There is considerable overlap between devices, however, with several general scan patterns available across all devices. The scan patterns for the major commercially available machines are summarized in Table 1.2.1. The two most commonly used scans in evaluating retinal disease are:

- Macular cube scan
- Line scan(s)

Depending on the particular machine, scan patterns may be programmable with respect to functions such as pixel density, B-scan density, speed, ability to oversample, and length of scanned image.

Macular Cube Scan

Cube scans are 'volume' or '3D' scans analogous to computed tomography or magnetic resonance scans that acquire volumetric cubes of data. SD-OCT machines acquire a rapid series of line scans (B-scans), generally in a 6 mm × 6 mm square area centered on the fovea. The scans are generally at relatively lower resolution, in order to minimize the time of scanning. As a result, when examining individual line scans from a cube scan, some detail is lost. As a default the cube scan is centered at the fovea, but other areas of interest can be captured by manually centering the scan elsewhere in the retina. Optic nerve topographic scans are cube scans centered on the nerve.

In the Zeiss Cirrus SD-OCT, there are two macular cube scans available, with no ability to customize. Both scans capture a 6 mm × 6 mm area centered at the macula. There is a faster 200 × 200 cube (200 B-scans each comprised of 200 A-scans) or the slightly slower 512 × 128 cube (128 B-scans each comprised of 512 A-scans) that has higher quality horizontal scans. The 'volume scan' on the Heidelberg Spectralis uses a similar raster scanning protocol with a 'fast' 25 B-scans each consisting of 512 sample points or A-scans, or with a 'dense' 1024 × 49 default scanning protocol. The Topcon 3D OCT uses a 256 × 256 or a 512 × 128 scanning protocol. The RT-Vue '3D macular scan' consists of a 4 mm × 4 mm macular cube scan with 101 B-scans consisting of 512 A-scans each, and the MM5 protocol uses a mix of vertical and horizontal B-scans to create a grid-like (not true raster) scanning pattern.

- **Raster Scans**: raster scanning is one method used to obtain cube scans of the macula. This involves a systematic pattern of image capture over a rectangular area using closely spaced parallel lines. It leads to a uniform sampling density over the entire area being scanned with the OCT.
- **Radial Scans**: these consist of six to 12 high resolution line scans taken at radial orientations, all passing through the fovea. The RT-Vue's MM6 is a radial line scanning pattern with 12 lines radially oriented to the fovea, each 6 mm long. The macular radial scanning pattern of the Spectralis and the 6-line radial scan of the Topcon 3D OCT 100 are similar. A disadvantage of the radial line scans is that the machine interpolates between the scans when generating macular thickness maps. This is reasonable for the fovea where the lines are close to each other, but can miss lesions further out in the macula where the lines are spaced further apart.

	Zeiss Cirrus	Heidelberg Spectralis	RT-Vue	Topcon 3-D	Canon HS-100	Nidek OCT RS-3000	Bioptogen SD-OCT
3D scans	Macular cube	Volume scan	3D macular MM5	Fast map Box scan	Macula 3D Multi-cross	Macula map	Rectangular volume Mixed volume
Line scans	5-line raster scan 1-line raster scan	7-line raster scan	Line scan HD Line Cross-line HD cross-Line	5- and 9- line raster Line scan Oversampled line scan	Cross	Macula multi Macula line	Linear scan
Radial scans	None	No presets, can be selected	Radial slicer MM6	12-line radial		Macula radial	Radial volume
Mesh scan	None		MM5			Macula multi	

Table 1.2.1 Scan patterns in commonly used OCT devices

- **Mesh Scans**: Some machines include a mesh scanning pattern that acquire vertical and horizontal B-scans over the area of interest. The MM5 protocol of the RT-Vue uses a less dense outer and a more dense inner grid. The outer grid has horizontal and vertical B-scans 0.5 mm apart and the inner grid has horizontal and vertical B-scans each 0.1 mm apart.

Line, Cross-Line and Raster Scans

SD-OCT line scans are a single B-scan composed of generally a higher number of A-scans than the cube scans. This higher sampling density allows higher resolution scans of the retinal tissue to be acquired. In addition, oversampling can be performed to increase signal-noise ratio (Fig. 1.2.1). The Cirrus 5-line raster consists of five horizontal 6 mm lines each scanned four times and averaged. The five lines in the raster can be collapsed to obtain a single line scan that consists of 20 averaged B-scans. The 'cross-line' scan of the RT-Vue consists of a horizontal and vertical line scan while the 7-line raster of the Heidelberg also spans a 6 mm × 6 mm area of the macula. Heidelberg can be programmed to oversample a line scan up to 100 times at each point.

Enhanced Depth Imaging

Enhanced depth imaging (EDI) protocols, now available in all major commercial OCT devices, use a combination of image averaging and of moving the zero delay line of the SD-OCT closer to the choroid, to obtain higher resolution images of the choroid. EDI is invaluable in diseases that involve the choroid where somewhat higher choroidal resolution is needed, as well as diseases with choroidal thickening where the sclerochoroidal border may not be visible on standard scanning protocols

Macular Maps

Macular maps are derived directly from either the cube scan data or radial scans, depending on the machine. They come in two forms:

- numeric displays showing the average retinal thickness in the zone of interest
- color-coded displays illustrating the difference between the examination and age-matched normative data base (Fig. 1.2.2).

C-Scans (*En Face* Images), OCT Fundus Image (Rendered Fundus Image, Summed Voxel Projection [SVP])

This image looks like a red-free image of the retina and is obtained by summation of data from all the B-scans. It is currently available in all SD-OCT machines except Heidelberg (Fig. 1.2.3).

Topographical maps

Retinal thickness data obtained from segmented 3D datasets are used to form a 2D topographical data set that can be displayed in false color (color-coded) displays, or as an overlay on the OCT rendered fundus image to obtain a quick topographic picture of the macula, internal limiting membrane or retinal pigment epithelium layer (Fig. 1.2.4).

Nerve Fiber Layer Map

Segmented 3D datasets over the optic nerve can be used to generate nerve fiber layer thickness measurements that can then be compared to age matched controls and displayed in a color-coded pattern (Fig. 1.2.5).

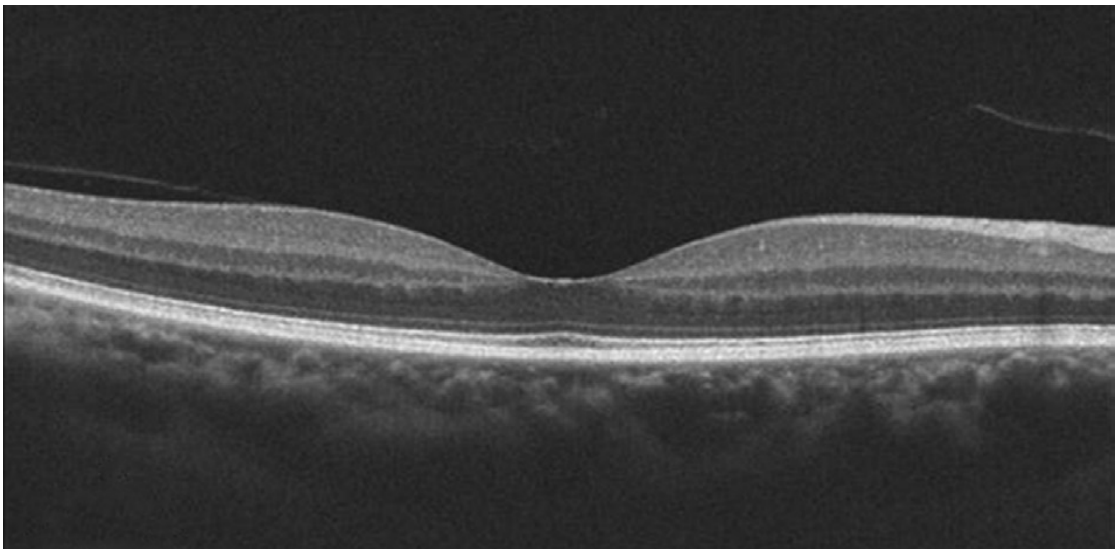


Figure 1.2.1 Line scan through the macula.

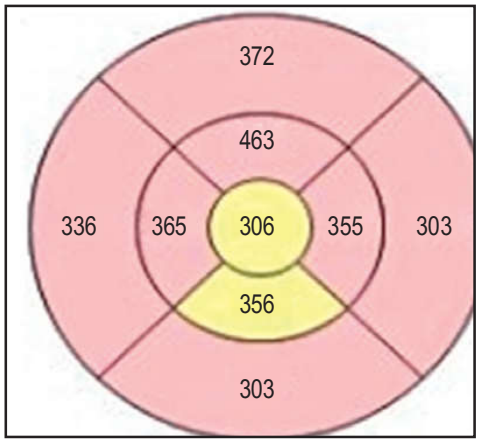


Figure 1.2.2 Macular map showing retinal thickness.

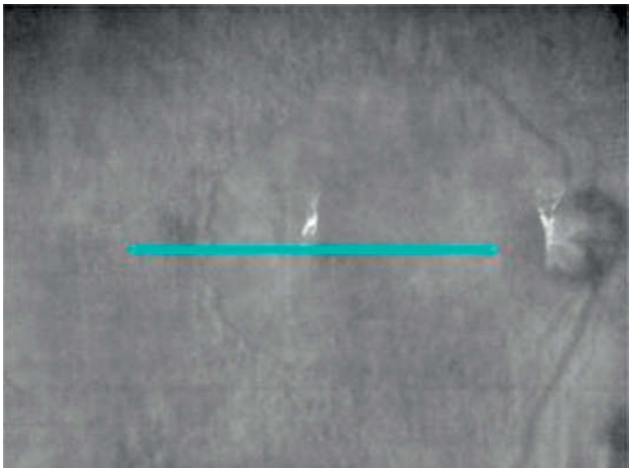


Figure 1.2.3 *En face* image or a summed voxel projection.

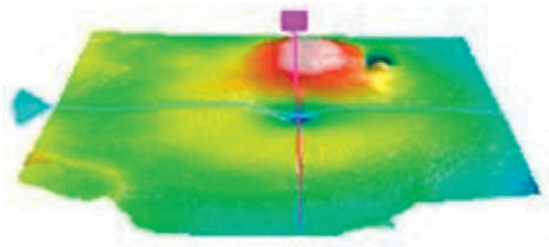


Figure 1.2.4 Topographical map.

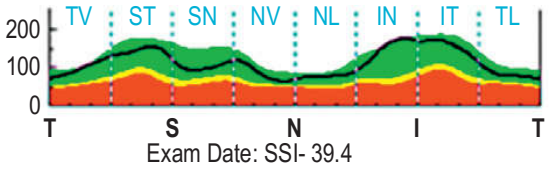


Figure 1.2.5 Retinal nerve fiber layer analysis.

2.1 OCT Interpretation

OCT interpretation can be both qualitative and quantitative. At present, in order to fully evaluate an OCT image, both are important.

Qualitative Interpretation

In qualitative interpretation, the clinician reviews individual line scans (B-scans) imaging the areas of interest in the retina and makes qualitative assessment of the presence or absence of pathology based on a knowledge of normal anatomy. B-scans can be rendered in a color-coded image or in a gray-scale image representing the reflectivity of the various layers. By comparing line scans performed over time, the course of the underlying disease and its response to treatment can be assessed.

When performing qualitative interpretation, it is important to be aware of the following issues:

- **Registration**: future line scans must be 'registered' to past scans. In other words, the examiner must be certain that the precise anatomic area of interest is scanned similarly in future tests. All SD-OCT machines have the capability of registering future line scans to past scans.
- **Sampling error**: if only one or several line scans are examined, the true pathology may be missed. It is important when doing qualitative interpretation that multiple line scans through the macula are examined.
- **Subjective evaluation**: by its nature, the lack of accurate quantitative numbers mean that line scan interpretation will be individualized. In addition, it is hard to gauge the effects of pathology that is improving in one area of the macula but getting worse in another.

Zones of line scans can be qualitatively described as hyper-reflective or hyporeflective, and demonstrate 'shadowing' or 'reverse shadowing.' **Hyper-reflective** areas reflect more light than normal for a given region. On the grey-scale image, they appear whiter than the surrounding areas. Examples include epiretinal membranes and hard exudates. **Hyporeflective** areas reflect less light than the surrounding areas. Areas with a higher fluid content, e.g. intraretinal cysts, are usually hyporeflective. **Shadowing** occurs when there is increased absorption of light compared to the surrounding tissue. This causes optical shadowing and decreased visualization of the outer tissues. Vitreous debris, larger retinal vessels, hard exudates and highly pigmented areas cause shadowing. **Reverse shadowing** occurs when there is loss/atrophy of pigmented tissue that allows excessive light to be transmitted through to the outer layers. The retinal pigment epithelium (RPE) is a major source of light absorption on OCT scanning, so atrophy of the RPE can cause reverse shadowing.

Quantitative Interpretation

Quantitative interpretation of OCT scans relies on the ability of the OCT software to distinguish the inner and outer margins of the retina or sub-layers (e.g. nerve fiber layer), referred to as segmentation, and accurately calculate retinal thickness and/or volume. Retinal thickness can then be compared to age-matched controls for assessment of normalcy, and monitored over time to judge the progression or regression of disease. Newer

generation OCT software features the ability to register subsequent OCT scans so that measurements of retinal thickness are compared over the same area of the macula every time. These are usually presented as Early Treatment of Diabetic Retinopathy Study grids or color-coded maps of retinal thickness.

When comparing quantitative OCT scans, it is important to compare scans obtained on the same machine, since different OCT machines draw the outer retinal boundary at different levels (inner segment–outer segment [IS-OS] photoreceptor junction, OS tips, RPE) and therefore may obtain different retinal thickness measurements on the same patient at the same visit.

The major drawback to quantitative assessment is that even in modern SD-OCT machines, quantitative scans are prone to artifacts. For example, the machine software may inaccurately identify the inner or outer retinal boundaries and the thickness measurement is therefore inaccurate. This is called software breakdown. Artifacts can induce errors in measurement making quantitative data inaccurate.

3.1 Artifacts on OCT

Artifacts can occur during image acquisition or analysis due to software, patient or operator factors. Artifacts may affect the qualitative or quantitative interpretation of images and are therefore important to identify.

- **Mirror artifact** (Fig 3.1.1): this artifact is unique to SD-OCT. It occurs when the area of interest to be imaged crosses the zero delay line and results in an inverted image. In practical terms, this happens when the OCT machine is pushed too close to the eye, or when the eye has pathology (e.g. retinoschisis or high myopia) in which a large axial range has to be imaged. The resulting image is inverted, partly inverted or may possibly have poor resolution.
- **Vignetting** (Fig. 3.1.2): this occurs when a part of the OCT beam is blocked by the iris and is characterized by a loss of signal over one side of the image.
- **Misalignment** (Fig. 3.1.3): this occurs when the fovea is not properly aligned during a volumetric scan. Typically it is due to the patient exhibiting poor or eccentic fixation or poor attention. When misalignment occurs, the normal foveal depression will not appear aligned with the center of the ETDRS map.
- **Software breakdown** (Fig. 3.1.4): software breakdown results from misidentification of the inner or outer retinal boundaries causing incorrectly drawn OCT segmentation lines, resulting in inaccurate mapping and quantitative measurements in a volumetric scan. These errors are more common in TD-OCT than in SD-OCT.

  Inner line breakdown typically happens in vitreomacular surface disorders such as vitreomacular traction or epiretinal membrane formation, while outer line breakdown happens in conditions involving the outer retina/retinal pigment epithelium such as central serous chorioretinopathy (CSCR), age-related macular dystrophy, cystoid macular edema and retinal atrophy. In pathologies such as CSCR where retinal thickness maps drive therapeutic decisions, these errors may be critically important.
- **Blink artifact** (Fig. 3.1.5): blink artifacts result in partial loss of data due to the momentary blockage of OCT image acquisition during the blink. Blink artifacts are easily recognized as black horizontal bars across the OCT image and macular map. Lubrication with artificial tears and/or protocols using shorter acquisition times may help to avoid these.
- **Motion artifact** (Fig. 3.1.5): this occurs when there is movement of the eye during OCT scanning leading to distortion or double scanning of the same area. It is seen as a sharp change in contour on the B-scan and as misalignment of blood vessels and blurring on the en face scans. Motion artifacts can occur because of poor fixation, tracking of the light source, heartbeat, respiration, drifts or saccades. It can cause errors especially in quantitative measurements. Mechanical tracking or software innovations can minimize motion artifact.
- **Out of range error** (Fig. 3.1.6): this error occurs because the B-scan is vertically shifted out of the scanning range (e.g. by the scanner being too close or too far away from the eye of the subject), causing a section of the OCT scan to be cut off.

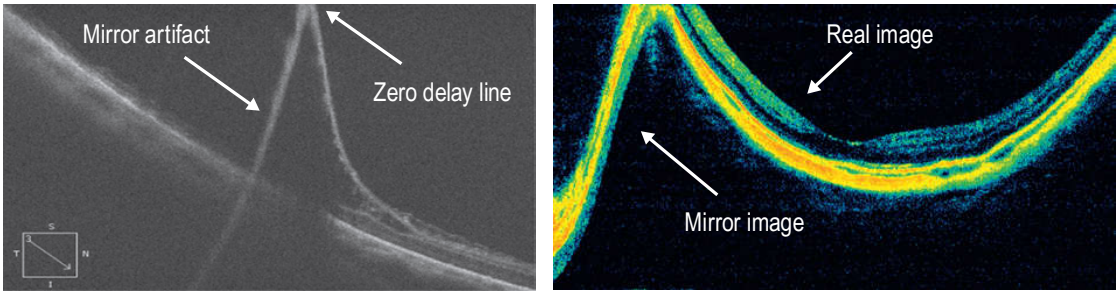


Figure 3.1.1 Mirror artifact occurring in a case of retinoschisis (above) and a high myopic eye with a long axial length. The inverted image can be seen adjacent to the regular image.

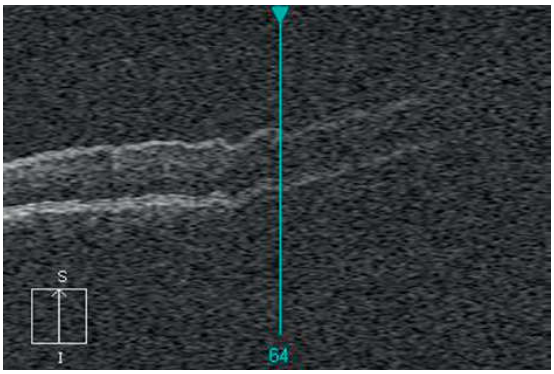


Figure 3.1.2 Vignetting is seen with loss of signal over the right side of the image.

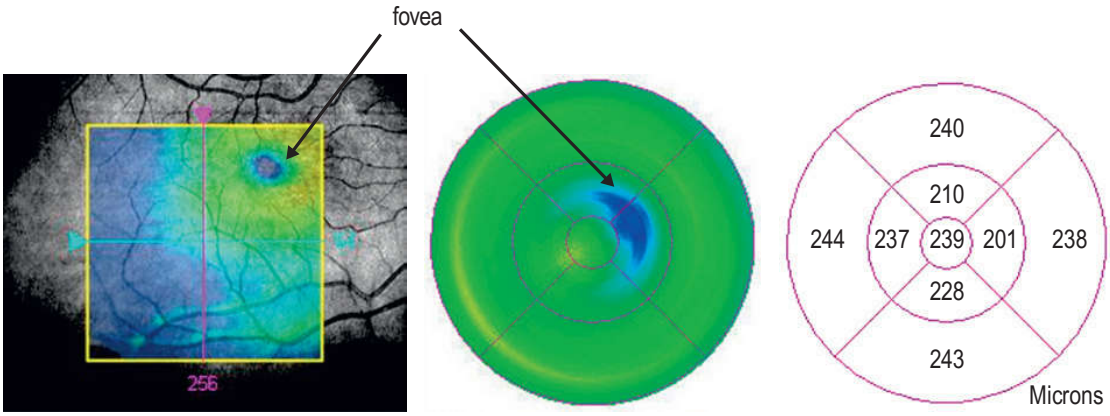


Figure 3.1.3 Misalignment error. Note that the fovea is not centered on the Early Treatment of Diabetic Retinopathy Study grid. On the macular thickness map, the thinnest point of the macula is decentered off the center of the map.

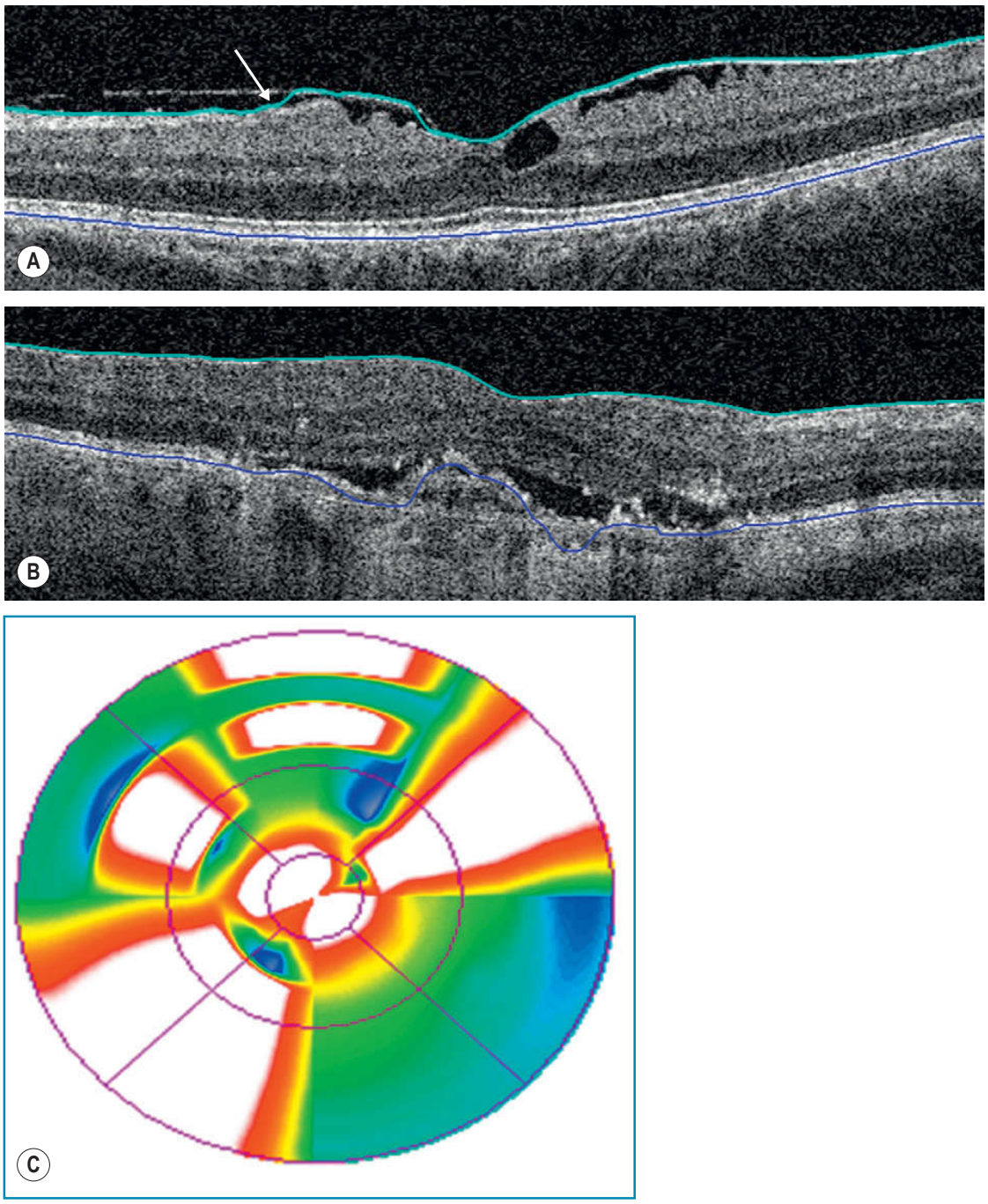


Figure 3.1.4 Software breakdown. Note the inaccuracy of tracing of the (A) inner retinal line (green) in a patient with epiretinal membrane, and (B) of the outer retinal/retinal pigment epithelium line (blue). (C) Software breakdown should be suspected when the macular thickness map shows a bowtie configuration or isolated islands of thinning and thickening.

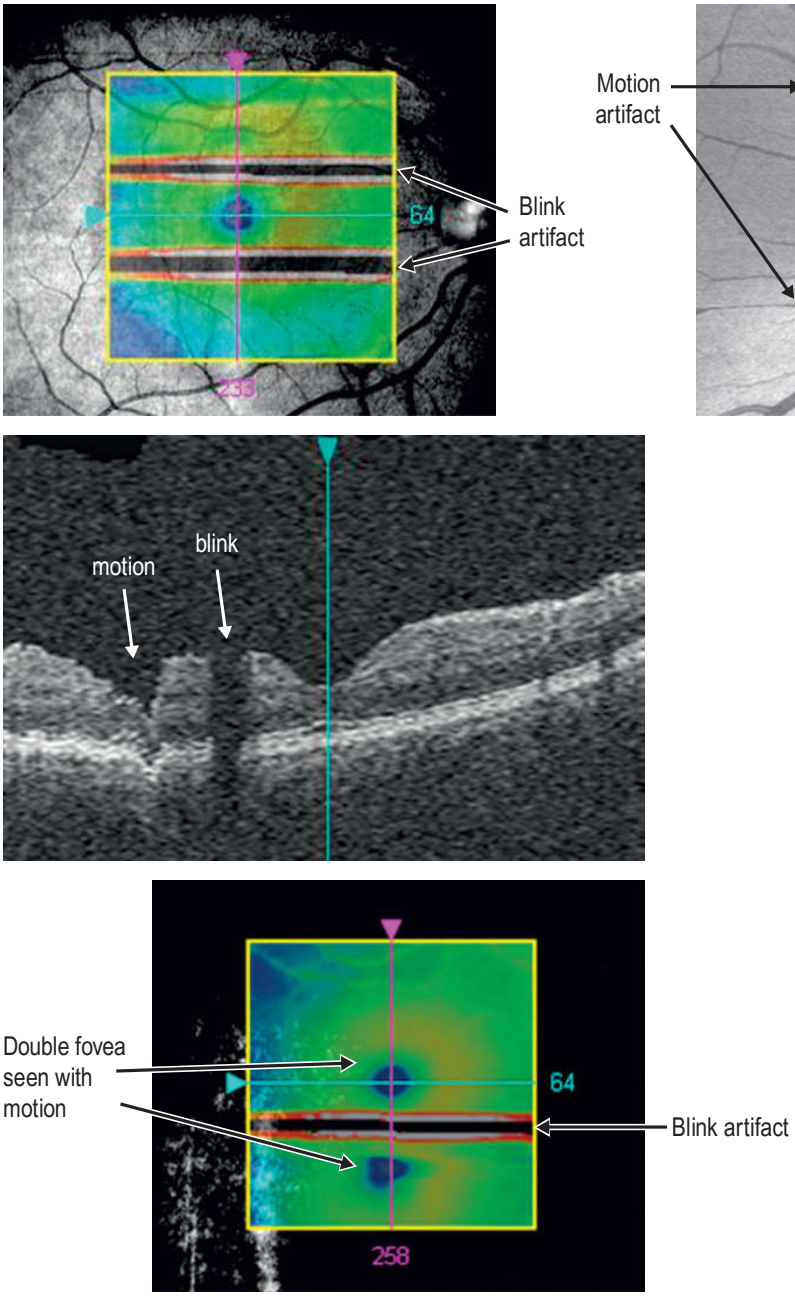


Figure 3.1.5 Blink and motion artifacts.

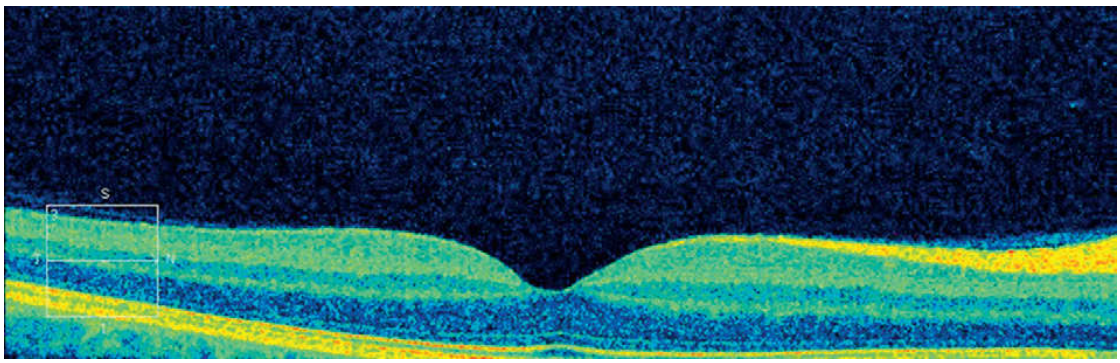


Figure 3.1.6 Out of range error. Notice that the outer retina/choroidal image is cut off because of improper positioning of the machine during image acquisition.

4.1 Normal Retinal Anatomy and Basic Pathologic Appearances

Normal Retinal Anatomy

Commercially available SD-OCT scanners have an axial resolution of between 4 μm and 7 μm and a transverse resolution of approximately 15 μm. This high resolution allows for exquisite viewing of the retinal detail. Due to the limited penetration of light beyond the pigmented RPE and the drop-off of the OCT signal with depth, the image at the level of the choroid has lower resolution. The layers of the normal retina are labeled in Figure 4.1.1.

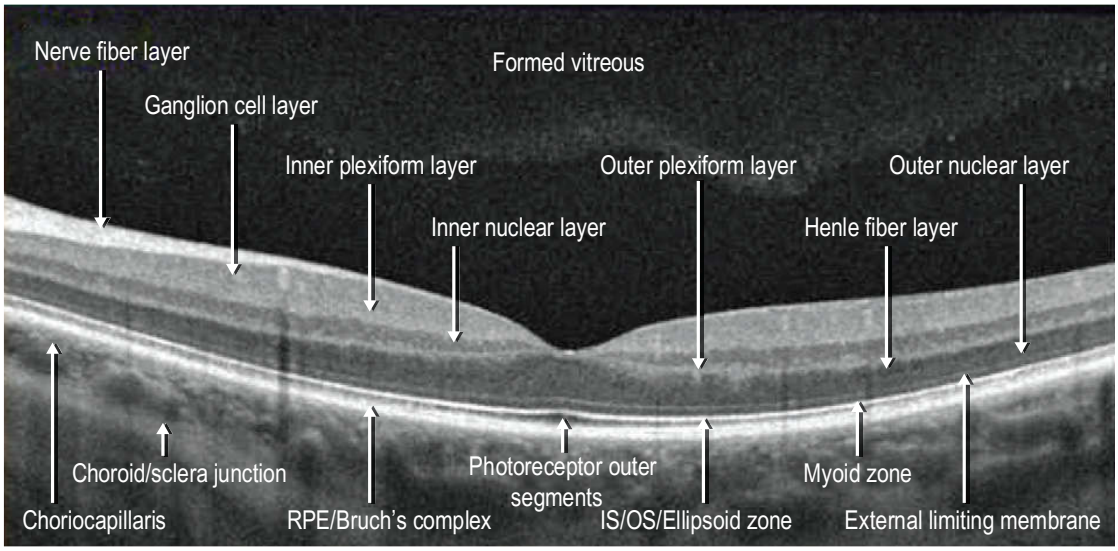
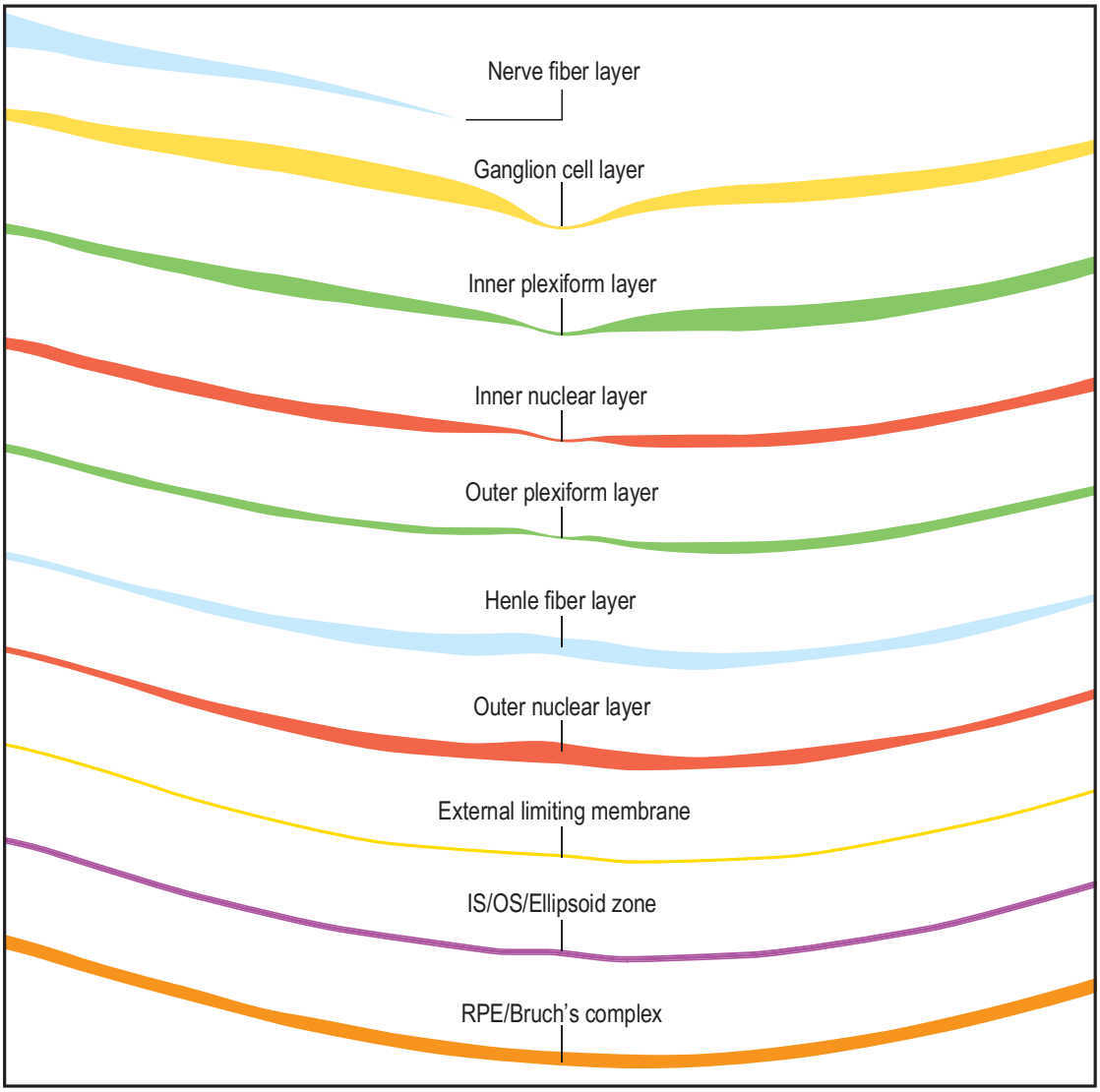


Figure 4.1.1 Normal retinal anatomy.



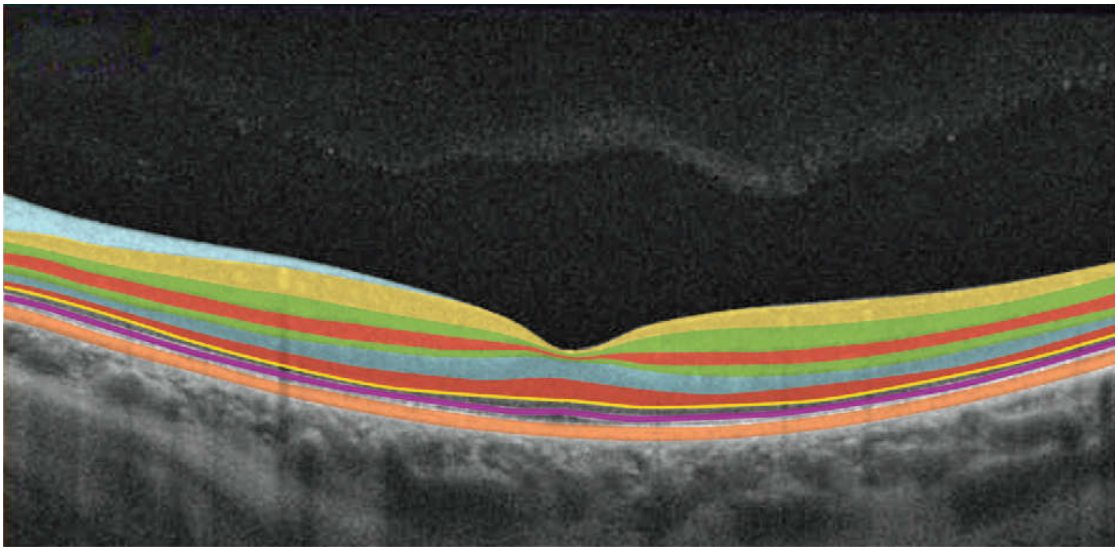


Figure 4.1.1 *Continued*.