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The choroid is situated between the sclera and Bruch's membrane, and most of its substance is occupied by blood vessels; more than 70% of all of the blood flow to the eye goes to the choroid [1]. The photoreceptors have the highest rate of oxygen use per unit weight of tissue in the body [2], and nearly all of that is accounted for by the mitochondria of the inner segments. The retinal circulation, which is about 5% of the blood flow to the eye, supplies the inner retina, but the choroid supplies the oxygen used by the outer retina, including the inner segments. The choroid is the only source for the avascular fovea. The choroid has additional functions including acting as a heat sink [3] and absorbing stray light, participating in immune response, and host defense [4] and is an integral part in the process of emmetropization [5]. Although the ocular manifestations of high myopia have become apparent over the past centuries, appreciation of the abnormalities within the choroid has occurred only recently. High myopia is associated with profound changes in the choroid that are important in the pathogenesis of many important visually significant abnormalities. Advances in imaging have greatly increased our ability to visualize the choroid, providing an opportunity to better understand the choroid in health and disease.

## 10.1 The Embryology and Anatomy of the Choroid

### 10.1.1 Embryology

Each optic vesicle forms as outpouching of the forebrain. This vesicle invaginates to form a double-walled optic cup. The inner layer of the cup is destined to form the retina and the outer layer the retinal pigment epithelium (RPE). The inferior portion of the cup initially has a gap that forms the

choroidal fissure, which allows access for the hyaloid artery to enter the eye. Eventually the gap closes. The uvea develops from the mesoderm and migrating neuroectoderm that surround the optic cup. Mesodermal cells start to differentiate into vessels around the same time that the RPE appears. The choriocapillaris starts to form at about the fifth to sixth week. The basal lamina of the RPE and of the choriocapillaris define the boundaries of the developing Bruch's membrane by week 6 [6]. The choriocapillaris becomes organized with luminal networks well before the rest of the choroidal vasculature develops. The posterior ciliary arteries enter the choroid during the eighth week of gestation, but it takes until week 22 before arteries and the veins become mature. Melanocytes precursors migrate into the uveal primordia from the neural crest at the end of the first month but start differentiating at the seventh month. The pigmentation of the choroid begins at the optic nerve and extends anteriorly to the ora serrata. This process is complete by about 9 months [7]. The sclera is derived from mesenchymal condensation starting anteriorly and completing posteriorly by week 12.

### 10.1.2 Choroidal Anatomy

The choroid is an unusual structure primarily composed of blood vessels but also has connective tissue, melanocytes, and intrinsic choroidal neurons. Birds have fluid-filled lacunae identified as true functional lymphatic system in their choroid [8]. Although humans don't have a lymphatic system in the eye, Schroedl and associates found human choroids have macrophage-like cells that stain positively for a lymphatic endothelium-specific marker, lymphatic vessel endothelial hyaluronic acid receptor [9]. Humans also have cells with nonvascular smooth muscle-like elements in the choroid [10, 11]. These cells are located around the entry of posterior ciliary vessels and nerves, along the vessels in the posterior segment, and under the foveal region. It has been proposed that the arrangement suggests the cells, which have actin contractile elements, may help stabilize the position of

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the fovea during accommodation [12]. The human choroid has intrinsic choroidal neurons, the functions of which are not known with certainty [13]. The choroid is attached to the sclera by strands of connective tissue which are easily separated anteriorly creating a potential space between them, the suprachoroidal space.

The blood from the short PCAs enters the eye and travels through successively smaller branches of arterioles within the choroid. The choroid is traditionally thought to be arranged in layers of vessels from the outer to inner part of the choroid labeled as Haller's layer, Sattler's layer, and the choriocapillaris. Haller's layer contains larger choroidal veins, while Sattler's layer has medium-sized vessels that branch inward to supply the choriocapillaris. There is no distinct border between Haller's and Sattler's layers or even an established definition of what is meant by large or medium. The pressure of the blood is reduced from about 75% of the systemic blood pressure at the short PCAs to that in the choriocapillaris, which has been measured in rabbits to be a few mm Hg greater than the intraocular pressure [14]. Increases in the intraocular pressure cause a proportional increase in the blood pressure in the choriocapillaris [14]. There does not appear to be effective autoregulation in the choroid, although myogenic mechanisms may be present. There is a sophisticated neural innervation that provides partial control. Like the brain, the eye has a high pulsatile blood flow rate and is encased in a noncompliant casing. As part of modulating pulsatile pressure in the cranium, the brain uses venous storage and a Starling resistor effect, to modulate venous outflow. An analogous function in the eye could be provided by the choroid, which contains fascicles of large veins that converge in vortices to drain out of the eye. This vortex area appears to be where the Starling resistor effect is possible.

The choriocapillaris is a planar plexus of small vessels with a lumen slightly larger than a typical capillary. The network of vessels in the choriocapillaris is tightly packed in the posterior portion of the eye, but the structure becomes looser in the periphery. The efferent and afferent vessels set up pressure gradients within the choriocapillaris to create a lobular flow. The flow characteristics are thought to be more dependent on complex gradients rather than anatomic patterns strictly dictated by choriocapillaris anatomy [15].

The vitality of the choriocapillaris is maintained in part by constitutive secretion of vascular endothelial growth factor (VEGF) by the RPE [16]. The choriocapillaris is highly polarized [17] with the internal surface having localized multiple localized areas of thinning of the capillary wall known as fenestrations. These thinner areas appear to facilitate the passage of material out of the capillaries and direct the flow toward the RPE. The number of fenestrations is more prominent in the submacular area as compared with the mid- or far periphery [18]. Similarly sized vessels in the retina do not have fenestrations. Soluble VEGF isoforms are required for fenestrations to occur in the choriocapillaris

[14], and these fenestrations disappear with VEGF withdrawal [19]. In experimental myopia, the choriocapillaris becomes less dense (Fig. 10.1), with decreased capillary lumens and a loss of fenestrations [20]. Also in myopes, as will be seen, the choroid is thinner than in emmetropes, and the vascular diameter of larger choroidal blood vessels is less as well.

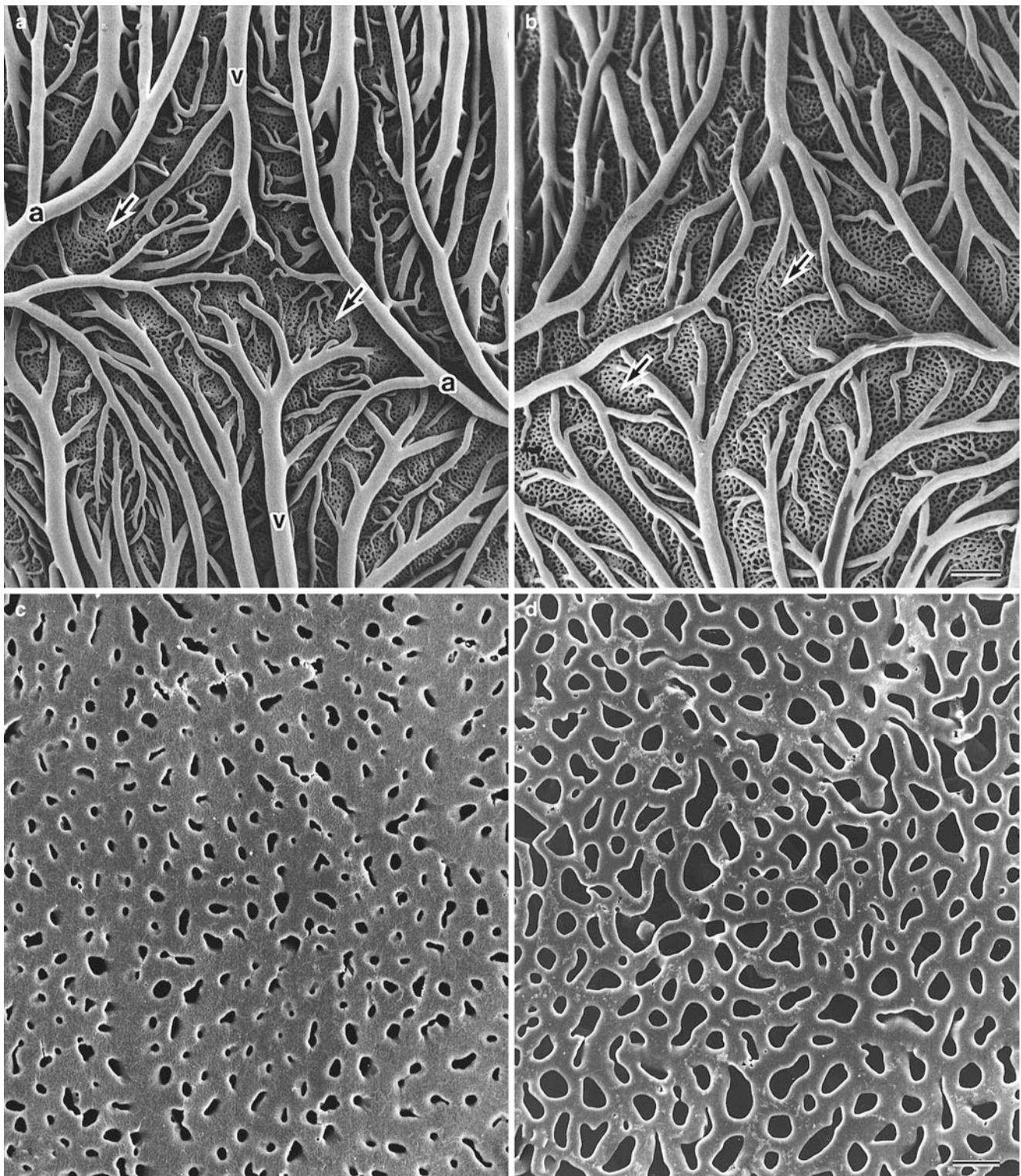
Blood from the choriocapillaris collects into venules that lead into larger venules that course in the outer choroid toward the ampulla of the vortex veins. The typical vortex vein passes obliquely through the sclera for a distance of about 4.5 mm as it exits the eye. Some drainage of the anterior choroid occurs through the anterior ciliary veins into the ciliary body. There are often four vortex veins per eye, with the ampulla of the vortex veins lying at the equator of the eye. The number can range from three to eight [21]; in high myopes, there is often more than four, and there may be posterior vortex veins known as ciliovaginal veins, which drain near or through the optic nerve foramen (Fig. 10.2). The number and configuration of vortex veins is different in myopia; since myopia develops over time, the implication is what appears to be additional vortex veins in myopia are acquired. The superior vortex veins drain into the superior and the inferior vortex veins into the inferior ophthalmic veins, although anastomoses occur between these two main drainage pathways in the orbit [14].

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## 10.2 Blood Flow Within the Choroid

Hayreh discovered many of the fascinating features of the choroidal blood flow from his observations of humans and monkeys [22, 23]. Although there are limited anastomotic connections, the arterial supply in the choroid is segmental as is the venous drainage; however, these segmental distributions do not correspond with each other. The choroid has high blood flow to deliver oxygen and metabolites to the retina and act as a heat sink. Blood is delivered to the choroid via the ophthalmic artery that branches to form (typically) two posterior ciliary arteries [23], which in turn branch to form many short posterior ciliary arteries and two long posterior ciliary arteries. There are no direct anastomoses between the PCAs or in arterial supply within the choroid. There is potential for local flow alterations to occur in the choriocapillaris based on pressure fluctuations. Once the blood leaves the choriocapillaris, it enters another segmented system, the venous outflow from the eye. The segmentation of the venous system is different from that of the arterial system, and the choroid is one of the few places in the body where this is true.

In the early phase of fluorescein angiography, it is common to see areas of the choroid that do not appear to fill with dye as quickly as adjacent regions. The designation of a watershed filling defect is made if the region of choroidal



**Fig. 10.1** Scanning electron micrographs of corrosion casts of the choroidal vasculature in control and myopic chick eyes at the fourth week. (a, b) The control eye (left) has a greater vascular density of larger vessels serving the choriocapillaris (arrows) than the myopic eye. The arterioles are designated by (a) and the venules (b). (c) The choriocapillaris

seen en face in a control eye has the expected high vascular density. (d) In a representative myopic eye, the individual vessels of the choriocapillaris have a lower packing density, and the vessels are smaller and more tubelike. (Derived from reference [20])



**Fig. 10.2** Otto Haab, a prominent Swiss ophthalmologist, described posterior venous drainage in high myopes and called the vessels posterior vortex veins, a name still used today. In this color drawing, taken from the third edition of Haab's atlas, a prominent vein is seen to exit the choroid superonasal to the nerve. Two smaller vessels are seen at the inferior border of the nerve. The drawing is an accurate reflection of the posterior venous drainage in high myopes. Unlike the typical vortex veins in the periphery, the posterior vortex veins do not have an ampulla or a spray of contributing vessels

filling is delayed past the laminar flow stage of the retinal veins [24]. A common appearance of a watershed zone is a stripe, one to several millimeters wide, running vertically at the temporal border of the optic disc in which the choroid is not as hyperfluorescent as surrounding areas [22]. This watershed zone is thought to be the boundary between areas of the choroid supplied by the medial and lateral PCAs. Eyes with more than two PCAs have more watershed zones, with a vertical stripe involving the optic nerve region and a number of radiating lines extending from the nerve seen dependent on the actual number of PCAs. Venous watershed zones exist for the venous circulation and form a cruciate pattern centered slightly temporal to the optic nerve [22]. In times of decreased perfusion, watershed zones may represent the regions with the poorest flow since they are at the shared boundaries of non-overlapping systems.

### 10.3 The Regulation of Choroidal Blood Flow

The retina has autoregulation of blood flow, but no autonomic nervous systems control within the eye. The retinal vessels are embedded in the retinal tissue and can respond to

metabolic demands and neurovascular coupling. The choroid is separated by several layers from the tissue it supplies, potentially limiting metabolic feedback mechanisms. The choroid has no autoregulation in the usual sense but is supplied by sympathetic, parasympathetic, and sensory nerve fibers [25]. These fibers are associated with the arteries and vein, but not the choriocapillaris. There are a variety of mediators that can be potentially released: the sympathetic nerve terminals release norepinephrine and neuropeptide Y [26, 27], the parasympathetic acetylcholine and also vasoactive intestinal polypeptide and neuronal nitric oxide synthase, and the sensory fibers substance P and calcitonin gene-related peptide [25]. Sympathetic stimulation causes a decrease in choroidal flow, which is potentially helpful in preventing overload in the choroid in "fight or flight" situations. Systemic increases in blood pressure would be countered by constriction of the choroidal arterioles. Stimulation of sympathetic innervation increases vascular resistance and decreases blood flow in the choroid. This is due to the release of norepinephrine and, possibly, neuropeptide Y release [28]. Parasympathetic stimulation causes choroidal vascular dilation [29]. The parasympathetic system is more dominant in "rest and digest" times and counterbalances the effects of sympathetic activation. The vascular tone in the choroid is modulated by acetylcholine, vasoactive intestinal polypeptide, and NO release from the parasympathetic nerve terminals.

The venous outflow from the choroid has an unusual anatomic arrangement. Blood from groups of choriocapillaris lobules are collected by draining venules, which consolidate to form larger veins. These larger veins do not continue to join other veins to form larger draining veins. Instead they course in a parallel fashion with minimal if any anastomosis with similarly sized veins until they converge on the ampulla of the vortex veins. Whereas blood vessel systems in the body form self-similar networks to form fractal-like arrangements, the choroidal veins do not follow allometric scaling laws. It has been proposed that this system can store venous blood to mitigate pulse pressure spikes during arterial inflow of blood during systole. A similar process occurs in the cranium, with the cerebral veins controlling blood flow into the superior sagittal sinus to help reduce pulse-related increases in intracranial pressure. The pressure in the vortex veins after they leave the eye is approximately 3 mm Hg, even though venous pressure in the choroid can be much higher than that. It has been proposed the venous outflow is controlled by a Starling resistor and is integrally related to intraocular pressure [14].

Perfusion in normal tissues in the body usually keeps the oxygen partial pressure at a relatively low level. The choroid is different – the oxygen partial pressure is very high, which from a teleologic standpoint is desirable so that the outer retina may receive as much oxygen as possible. The RPE

secretes vascular endothelial growth factor (VEGF) to help maintain the choriocapillaris. CD-36 is a scavenger receptor expressed in the basal RPE. Houssier and associates showed that CD-36-deficient mice fail to induce COX-2 and subsequent VEGF synthesis at the level of the RPE and develop progressive degeneration of the choriocapillaris [30]. Therefore, CD-36 binding by the RPE, such as what happens in the normal process of phagocytosis of the photoreceptor outer segments, seems to be one of the factors maintaining the vessels of the inner choroid.

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## 10.4 Other Choroidal Functions

There have been other reasons proposed for the large blood flow in the choroid. The amount of light energy delivered to the retina by incoming light is insufficient to cause a significant elevation in temperature and thus is an unlikely explanation [31]. It is possible that the high metabolism in the outer retina may produce enough heat to require mechanisms to reduce the local temperature. The high blood flow may help conduct heat away from the outer retina/RPE complex. The choroid contains melanocytes which improve optical function by absorbing scattered light and may also indirectly protect against oxidative stress. These melanocytes exist in an environment of high O<sub>2</sub> partial pressure, which, along with the light exposure, may be a risk factor for malignant transformation to melanoma. Melanocytes in human RPE are particularly rich in zinc and may serve as a reservoir for this metal ion [32–34].

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## 10.5 Imaging the Choroid

Because of its localization between the overlying pigmented RPE and the underlying opaque and rigid fibrous sclera, the choroid is difficult to visualize with conventional imaging. Methods employing light reflection or fluorescence generation are impeded by the pigment in the RPE and choroid. Conventional OCT is affected by the effects of melanin and also the scattering properties of the blood and blood vessels. The choroid is a deeper structure and the depth, which affects the detection sensitivity.

### 10.5.1 Angiography

Fluorescein is stimulated by blue light with a wavelength between 465 and 490 nm and emits at a green light with the peak of the emission spectral curve ranging between 520 and 530 nm and a curve extending to approximately 600 nm. Both the excitation and emission spectra from fluorescein are blocked in part by melanin pigment, which acts to decrease

visualization of the choroid. Fluorescein extravasates rapidly from the choriocapillaris and fluoresces in the extravascular space, and this also prevents delineation of the choroidal anatomy. The analysis of the choroid using fluorescein angiography is also limited by light absorption and scattering by the pigment in the RPE and choroid and by the blood in the choroid. Gross filling of the choroid can be seen, as can the converse, choroidal filling defects. Diseases causing arteritis, such as giant cell arteritis or Wegener's granulomatosis can cause regions of decreased perfusion of the choroid, but actual vessels are not visualized. Therefore, estimations of vascular density of the choroid are not easily done with fluorescein angiography. On the other hand, fluorescein angiography is good for visualizing retinal vascular abnormalities and many forms of choroidal neovascularization (CNV), particularly Type 2 CNV.

Indocyanine green (ICG) absorption peak is between 790 and 805 nm, and it fluoresces in a somewhat longer wavelength range, depending on the protein content and pH of the local environment. The longer wavelengths used have the attribute of penetrating the pigmentation of the eye better than the wavelengths used with fluorescein angiography. The retinal pigment epithelium and the choroid absorbs up to 75% of blue-green light used for fluorescein angiography but only up to 38% of the near infrared light used for ICG angiography [35]. ICG is 98% protein bound, with 80% binding to larger proteins such as globulins and alpha-1-lipoproteins [36, 37]. The amount of fluorescence derived from ICG during typical angiographic examination is much less than that obtained from fluorescein, and the resultant light is in the near infrared wavelengths. Because of the poor sensitivity to near infrared light by photographic film, the first practical imaging of ICG fluorescence in the clinic awaited commercial availability of digital charged couple devices (CCDs). Optical resolution is related to wavelength, and so, the resolution of ICG angiography is lower than fluorescein angiography.

ICG is highly protein bound, so there is less opportunity for the dye to leak from the normal choroidal vessels. During the earlier phases of ICG angiography, the choroidal vessels are visible. The vertical summation of the choroid is seen, making it difficult to delineate individual layers of vessels. Over the course of the angiogram, some staining of the extravascular tissue particularly Bruch's membrane occurs, obscuring visualization of deeper structures. This means flow can be estimated by looking at the early frames of the ICG angiogram, but later phases cannot be used for the same purpose.

Early after the availability of ICG angiography, many diseases were investigated, and new information that was not obtainable by fluorescein angiography was generated. Much of this information was interesting from a research standpoint but did not have practical clinical utility. For real-world

use, ICG is most helpful in diagnosing and evaluating polypoidal choroidal vasculopathy and central serous chorioretinopathy. Secondary uses include evaluation of choroidal inflammatory diseases, angioid streaks, and choroidal tumors and in providing rough estimates of choroidal blood flow. The advent of widespread use of autofluorescence imaging and optical coherence tomography (OCT) methods to evaluate the choroid has largely supplanted ICG angiography for these secondary uses.

## 10.5.2 Ultrasonography

Contact B-scan ultrasonography typically uses a 10–12 megahertz probe placed on the eyelid. The probe used contains a piezoelectric crystal that is stimulated to vibrate by a short duration of an electrical driving current. Reflected sound waves cause the crystal to vibrate, which through the piezoelectric effect causes an electrical current. Sound decreases in intensity with increasing distance because of divergence of the sound beam and attenuation of the sound by the intervening tissue. Thus, reflected sound waves vary in strength with the depth of the reflecting structure in the eye. To compensate for the decrease in signal strength with time of flight, the gain of the amplifier is increased over the detection interval. Depth information is derived directly from time of flight information and the speed of sound through the medium involved. The direction of the crystal then is rotated slightly by a motor within the probe to successively build a two-dimensional image, a B-scan.

Although each A-scan is shown as a needle thin line within the B-scan image, the actual situation is far different. The piezoelectric crystal has some focusing ability, but in reality the sound beam produced by a piezoelectric crystal in a conventional B-scan probe has a main lobe and several side lobes [38]. Even the main lobe can be 1 mm in diameter at the surface of the retina. The side lobes add to the ambiguity of the reflection as does scattering within the eye. Given the eye is a curved structure, the wide probing beam produces a returning echo from any given region in the posterior portion of the eye that is smeared over an interval of time. The wavelengths used in ultrasonography dictate a theoretical axial resolution of about 150 microns, but the actual resolution in clinical use is much lower. For example, a typical B-scan of the optic nerve will not show the cup unless there is a high cup-to-disc ratio because of the broad diameter of the curved target that is imaged. Another significant problem with ultrasonography is that the exact location of the image obtained is not known. The general region can be estimated by evaluating relationships with neighboring structures and by trying to imagine where the probe is aimed.

In non-pathologic conditions, the reflectivity of the choroid is difficult to distinguish from the overlying retina and

the underlying sclera. In high myopes, the thickness of the choroid can easily be less than the resolution of contact B-scan ultrasonography making any meaningful imaging of the choroid in populations of high myopes impossible. Contact B-scan ultrasonography is useful to examine the general contour of the eyewall and the visualize staphylomata.

## 10.5.3 Optical Coherence Tomography

### 10.5.3.1 Interferometry

In dry air, the speed of sound is 343.2 meters per second. The sound velocity in an average phakic eye is 1555 meters per second [39]. This means that the time it takes sound to travel the length of a phakic eye with an axial length of 24 mm is approximately 15.4 microseconds, which is easy to measure. Because light travels very rapidly ( $3 \times 10^8$  m/sec), it is not possible to measure the time-of-flight delay on a micron-scale level of resolution using an external system of time measurement. The time it takes light to travel a micron is the same or less than it would take an electron to travel the same distance in an electronic circuit. Measurement of multiple reflections with a detector and the subsequent required electronic circuitry requires conduction paths for electrons that are much longer than the variations in path length of the light rays. However, light rays have a repeating characteristic inherent in their own wave properties. A clever way to time how long light takes to travel a given distance is to use the wave-like character of the light itself as its own internal clock. Phase differences in waveforms can be detected and reveal very small changes in time of flight. That is what a Michelson interferometer does; the wavelength of the light is used as its own timing standard. The micron-scale resolution is achieved by comparing the time of flight of the sample reflection with the known delay of a reference reflection by using interference to find phase differences in the light waves.

Coherency of light is a measure of how correlated one wave of light is with another. Temporal coherency is a measure of how correlated one wave of light is with another generated at a different time. Coherence length is the distance light would travel during the coherence time. Light produced by a conventional laser has a long coherence time because one wave of light is similar to other waves of light produced at times before or after. It is possible to produce light with a short coherence length. In this situation, the waveform of light produced is the same for all of the light rays produced at any one instance, but this waveform is different from other waveforms produced at other times. This approach essentially puts a time stamp on the waveform. Low coherence light split into a reference arm can only interfere with light from the sample arm if the path lengths are the same or are nearly the same.

In time domain OCT, each point in the tissue is sampled one at a time. The probing beam illuminates the tissue, but information is obtained from a small portion of the tissue at any given instant. This means time domain OCT is less efficient at extracting information from tissue at any given total light exposure. The total amount of light that can be delivered to tissue is limited by safety standards. Spectral domain (SD) OCT takes the light from the interferometer and passes it through a grating to separate out the component wavelengths. Using a Fourier transform, it is possible to determine where, and how strongly, different reflections in the sample arm originated from simultaneously. In effect, all layers produce signal during each A-scan. Because of this feature, SD-OCT devices are much more efficient at extracting information from tissue at any given light exposure. This increase in efficiency is often translated to increased scanning speeds such that SD-OCT instruments typically scan the eye with speeds up to 100 times faster than time-domain OCT instruments. There are some problems inherent in SD technology. The deeper tissues produce higher-frequency signals, but the way the grating and detector sample this frequency is not linear. The higher frequencies are bunched together to a greater extent than lower frequencies. In addition, the sensitivity of the detection decreases with increasing frequency. This causes SD-OCT to have decreasing sensitivity and resolution with increasing depth.

A consequence of the decreasing sensitivity is that the choroid cannot be imaged in many emmetropes with conventional SD-OCT. Eyes with high myopia have thinner choroids and a relative depigmentation, making it possible to visualize the full thickness of the choroid in many eyes with conventional SD-OCT. Because a Fourier transform is used, two conjugate images are developed from the interferometric signal. In practical use, only one of these two images are shown, typically with the retina facing toward the top of the screen. If the peak sensitivity is placed posteriorly typically at the inner sclera, deeper structures such as the choroid can be seen. This method of imaging the choroid is called enhanced depth imaging (EDI) OCT. [40] It is now simply performed with SD-OCT instruments, often by just selecting EDI in the software of the instrument. To improve the signal-to-noise ratio and therefore image appearance, many B-scans can be averaged together, typically using 50 to 100 images. Segmentation of OCT images allows visualization and measurement of various layers in the eye. In high myopes, the choroid can be extremely thin, making it difficult to segment volume scans without attendant segmentation errors.

Swept-source OCT (SS OCT) uses a frequency-swept light source and detectors, which measure the interference output as a function of time [41, 42]. The sensitivity of SS-OCT varies with depth as well, but the roll-off in sensitivity is not as great as seen with SD-OCT. Current implementations of SS-OCT have light sources that use a longer center wavelength, which has improved ability to penetrate

through tissue. Therefore, both the vitreous and choroid can be imaged simultaneously; there is no need to pick one or the other. There are trade-offs with swept source OCT that have to be considered. Although longer wavelengths of light may penetrate tissue to a greater degree, the problem is water absorbs longer wavelengths of light. This restricts the range, or bandwidth of wavelengths that can be used in the eye, since the vitreous is mostly water. Increasing the center wavelength has the effect of decreasing the resolution for any given bandwidth. Water absorption of longer wavelengths is an important impediment to expanding the bandwidth of current 1 micron swept light sources, which limits the ability to overcome the decrease in resolution by increasing the bandwidth. Newer light sources operating at shorter wavelengths are being developed, and these light sources may avoid the problem of water absorption. For example, a SS-OCT using a large bandwidth light source with a center wavelength of 850 nm could provide very high-speed, high-resolution imaging with potentially less fall-off in sensitivity with depth as compared with SD-OCT implementations.

No matter what the imaging modality, high myopia represents special challenges for OCT. The extreme axial length of highly myopic eyes can represent difficulties in obtaining a usable image. The posterior portion of the highly myopic eye often has staphylomata, and curvatures of the eyewall appear exaggerated in OCT renderings. The depth in which images are obtained in most commercial OCT instruments is approximately 2–3 mm. Wide-angle scans image enough of the extent of a highly myopic eye that the vertical range of tissue can exceed the available depth range. Imaging of the areas outside of this 2 mm are seen as upside down conjugates. This produces artifactual image folding or mirroring. Imaging high myopes presents interesting opportunities, however. The choroid is thin and doesn't have much pigment, so with EDI-OCT or SS-OCT it is possible to visualize the full thickness of the sclera and even to see into the subarachnoid space around the optic nerve (Fig. 10.3) [43].



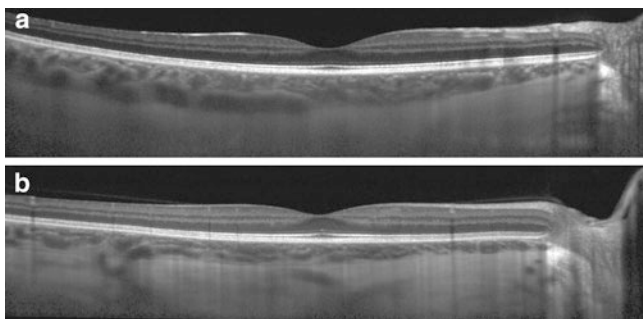
**Fig. 10.3** Swept source OCT is able to provide visualization of the subarachnoid space if there is peripapillary atrophy, which there usually is, particularly in the region of the conus. Note the beams of tissue visible (arrow)

## 10.6 Measurements and Reproducibility of Choroidal Thickness

There is a very good intersystem [44, 45], inter-observer, and inter-visit reproducibility [45] of manual choroidal thickness measurements. The inter-observer repeatability is good using EDI-OCT [45, 46], Cirrus HD OCT [44, 47], Optovue RTVue [45], and SS OCT. [45, 48] The intersystem reproducibility of choroidal thickness measurements has been assessed between EDI-OCT and SS OCT [45] and also between three different SD-OCT devices: Cirrus HD-OCT, Spectralis using EDI module, and RTVue [44]. Tan and associates found the intraclass correlation coefficient for inter-observer reproducibility of 0.994 but also the value of the mean difference between choroidal thickness measurements between graders that was 2.0  $\mu\text{m}$  for 24 normal eyes of 12 healthy subjects [46]. These levels of agreement are smaller than the diurnal variation in choroidal thickness in humans [46]. Automated segmentation methods are generally faster but substitute idiosyncrasies and biases of the coded algorithm for idiosyncrasies and biases of a human observer.

## 10.7 Normal Subfoveal Choroidal Thickness

Margolis and Spaide investigated 54 normal, non-myopic eyes with a mean age of 50.4 years using the EDI-OCT and reported a mean subfoveal choroidal thickness of 287 microns (Fig. 10.4) [49]. Normal was defined as patients without any significant retinal or choroidal pathologic features, uncontrolled diabetes or hypertension, and a refractive error less than 6 diopters of spherical equivalent. The choroidal-scleral interface has been identified in 100% of subjects in this study [49]. The authors showed that increasing age was correlated significantly with decreasing choroidal thickness at all points measured. The subfoveal choroidal thickness was found to decrease by 15.6 microns for each decade of age [49]. Ikuno and associates investigated 86 non-myopic eyes of healthy Japanese patients with SS-OCT with a mean age of 39.4 years and found a subfoveal choroidal thickness of 354 microns.



**Fig. 10.4** Choroidal thickness in (a) a 31-year-old emmetrope and (b) a 29-year-old  $-6$  myope. Note the subfoveal choroidal thickness is decreased in the myope as compared with the emmetrope despite their relatively young ages

Ikuno and associates found that the choroidal thickness decreased by 14 microns for each decade of age [50]. The mean subfoveal choroidal thickness has been found to vary among studies from 203.6 microns in 31 eyes with a mean age of 64.6 years [48] to 448.5 microns in 22 eyes with a mean age of 35.7 years [51]. The refractive error and age has to be taken into account, as does diurnal variation, making comparison of general mean values impossible for many studies. These comparisons are further hindered by some studies reporting choroidal thickness in patient groups using techniques that could not visualize the choroidal scleral junction in all eyes. The percentage of identification of the scleral choroidal interface was 74% of 34 eyes in one series using SD-OCT [47], for example. Some studies excluded patients with ocular disorders [47–49], some excluded patients with ocular and systemic disorders [50, 52], and some mentioned they excluded patients with systemic disorders that might affect choroidal thickness [48, 49]. Even though these studies propose to evaluate normal eyes, some of them included highly myopic eyes with a spherical equivalent error greater than  $-6$  diopters [48, 52, 53].

There are several possible reasons for the decrease in subfoveal choroidal thickness with age, such as loss of choriocapillaris, a decrease in the diameter of the choriocapillary vessels, decrease in luminal diameter of blood vessels, and, in some cases, a diminution of the middle layer of the choroid<sup>52</sup> [54, 55]. Histologic evaluation of eye bank and autopsy eyes found a yearly decrease in choroidal thickness of 1.1 microns per year, which was less than the amount measured *in vivo* [49]. The differences may be related to measurement technique as the histologic specimens were measured in autopsy eyes, which by default had no blood pressure and the choroid is an inflated structure [54–56].

The choroidal thickness has also been found to fluctuate with defocus in humans [46, 57]. Maintenance of emmetropia is now known to depend on active mechanisms that sense image blur and then take steps to improve the image to include moving retina to reduce the blur and permanently altering ocular dimensions. Among the first changes are an active increase or decrease in choroidal thickness that moves the retina, as shown in laboratory investigations in chickens [58, 59] and primates [60, 61]. Read and associates demonstrated that similar changes in choroidal thickness occur in humans in response to short-term unilateral image blur [57]. The choroid was found to thicken with the myopic defocus condition and to become thinner with the hyperopic defocus [62]. Humans have a diurnal variation in choroidal thickness [46, 63] that is related in magnitude to the baseline thickness of the choroid and systolic blood pressure [46].

## 10.8 Topography of Choroidal Thickness

In emmetropic eyes, the choroid thickness varies topographically within the posterior pole: the choroid was thickest under the fovea with a mean value, and the choroidal thickness



decreased rapidly in the nasal direction. The choroidal thickness appears to be thinner in the inferior macula as compared with the superior macula [47, 48, 50, 52]. The inferior peripapillary choroid is thinner than all other quadrants around the nerve [64] [65]. The reason for this finding is not known, but the optic fissure is located in the inferior aspect of the optic cup and is the last part to close during embryology of the eye. Another factor may be this area is in the typical watershed zone in the choroidal circulation. In their study, Ho and associates found that the choroidal thickness increases radially from the optic nerve in all directions in normal emmetropic patients and eventually approaches a plateau [64].

## 10.9 Imaging the Internal Structure of the Choroid

The basement membrane of the choriocapillaris is attached to the outer layer of the trilayer Bruch's membrane. The intercapillary pillars separate the vessels of the choriocapillaris. The outer band of reflectivity from the outer retina is ascribed to the RPE, but it is likely that Bruch's membrane, and therefore the choriocapillaris is incorporated in the summation of reflection attributed to the RPE obtained with commercially available OCTs. Fong and associates have hypothesized that hyperreflective foci visualized beneath the Bruch membrane line represent cross sections of feeding and draining arterioles and venules [66]. Larger choroidal vessels have hyporeflexive cores with surrounding hyperreflective walls. The luminal diameter of the images probably is proportional, but not necessarily exactly equal to the lumen diameter of the corresponding vessel. It is possible that some portion of the outer blood column could be imaged as being part of the wall.

## 10.10 Optical Coherence Tomography Angiography

In successive OCT images of the eye, provided the patient does not move, there is little change from one image to the next, except for blood flow. By obtaining several B-scans over a short time interval and computing the change over time, a flow signal can be detected [67]. Using many B-scans produces a 3-D block of flow information. In practical use, slabs of this block are condensed to produce en face representations of flow. The slabs selected typically are based on the anatomy of the retina or choroid. OCT angiography images of the choriocapillaris are noisy and in the past were analyzed based on areas of where flow signal was not detected. These are called flow deficits or signal deficits. Frame averaging of the choriocapillaris scans produces images of the choriocapillaris that can be binarized and then skeletonized. The capillary segments in the mesh can be quantitatively evaluated. Analyzing the choriocapillaris is done using slabs that are 10–20  $\mu\text{m}$  thick. As the total choroidal thickness of high myopes, particularly older subjects, may not be that much thicker, the choriocapillaris images also contain flow information from other layers in the choroid.

## 10.11 The Choroid in High Myopia

The thickness of the choroid has been found to vary inversely with the age of the subject and the amount of myopic refractive error (Tables 10.1 and 10.2). The choroidal thickness varies inversely with the axial length, with the regression models being nearly equivalent to those using refractive error. This is probably because high myopes seen in a retina

**Table 10.1** Determinants of Choroidal Thickness

Parameter estimates							
Parameter	B	Std. error	95% Wald confidence interval		Hypothesis test		
			Lower	Upper	Wald Chi-Square	df	Sig.
(Intercept)	310.693	27.3223	257.142	364.244	129.309	1	<0.001
Age	-1.550	0.4064	-2.347	-0.754	14.553	1	<0.001
Refraction	8.133	1.8408	4.525	11.741	19.520	1	<0.001

Dependent variable = subfoveal choroidal thickness

Predictors of subfoveal choroidal thickness of a group of 145 highly myopic eyes with no macular pathology. Each year of age is associated with a decrease of 1.55  $\mu\text{m}$  of choroidal thickness, while each diopter of myopic refractive error is associated with a decrease of 8.13  $\mu\text{m}$ . From reference [77]

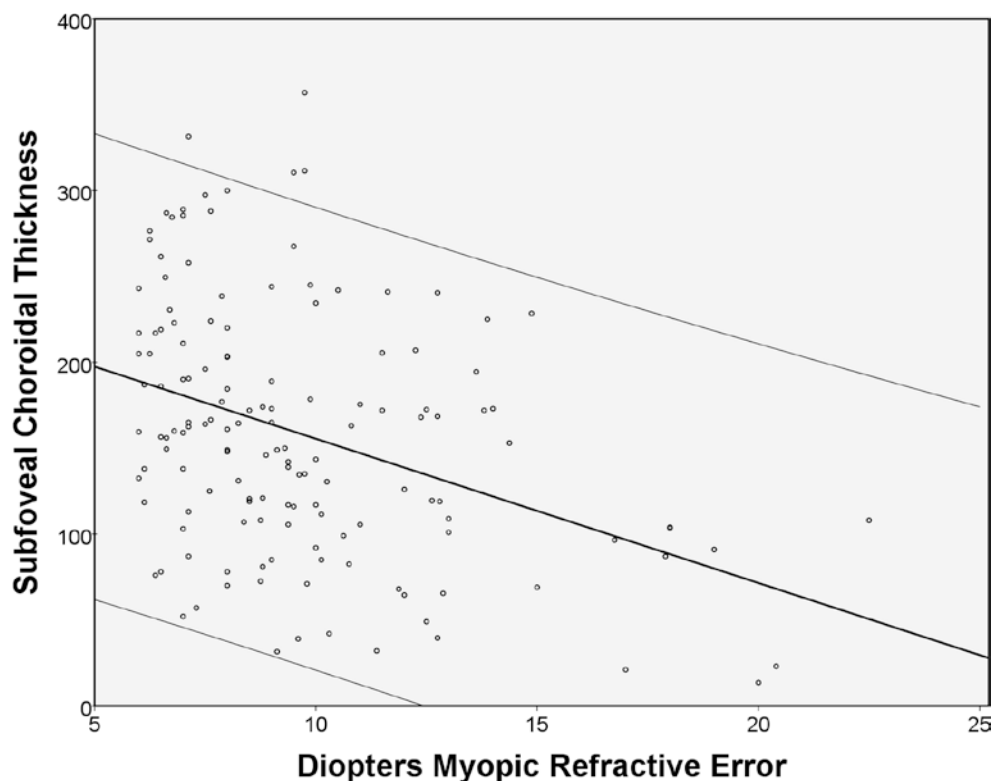
**Table 10.2** Visual Acuity and Choroidal Thickness

Parameter estimates							
Parameter	B	Std. error	95% Wald confidence interval		Hypothesis test		
			Lower	Upper	Wald Chi-Square	df	Sig.
(Intercept)	0.287	0.0630	0.163	0.410	20.689	1	<0.001
Subfoveal choroidal thickness	-0.0011	0.0003	-0.002	0.000	13.397	1	<0.001

Dependent variable: logarithm of minimal angle of resolution (logMAR)

Predictors of log MAR visual acuity in a group of 145 highly myopic eyes. Only the subfoveal choroidal thickness proved predictive. From reference [77]

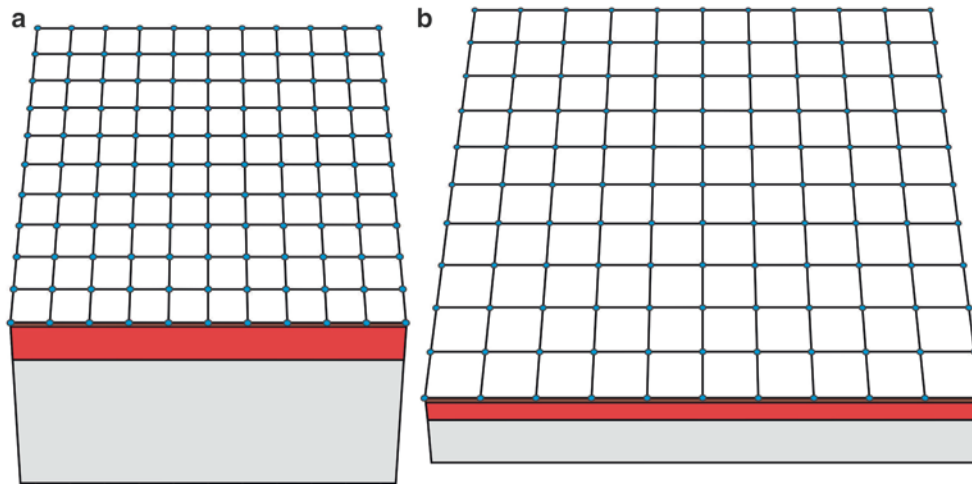
**Fig. 10.5** Subfoveal choroidal thickness versus myopic refractive error in a group of 145 highly myopic eyes with no macular pathology. The trendline demonstrates the decrease in thickness with increasing refractive error, and the thinner bordering lines show the 95% confidence interval of the trend line



clinic are almost always axial myopes; as such, this observation might not apply universally to the general pool of high myopes. In the process of becoming highly myopic, the eye appears to expand, but does not make additional tissue. For example, the collagen weight of the sclera does not increase with the development of experimental myopia; it actually decreases. The choroid may well be stretched to a certain degree by the development of myopia without the creation of additional vasculature. This determination has not been made yet and would be best modeled over the expanse of the eye and not just the limited area currently imaged with commercial OCT instruments. The decrease in thickness of the choroid in high myopes has, appropriately enough, been called myopic choroidal thinning (Fig. 10.5) [68]. The expansion of the eye seems to cause a decrease in the packing density of the photoreceptors [69], with retention of the same visual acuity because the extension of the axial length also causes a proportional enlargement of the projected image. Although the choroid is thinner, the oxygen requirements per unit area of outer retina may be decreased because of the reduced packing density (Fig. 10.6). However, the reduction in thickness of the choroid with age continues in non-myopes and myopes alike. Curiously the diminution in choroidal thickness with age is approximately the same in absolute amounts in high myopes as in eyes that do not have high myopia (Fig. 10.7) [68]. High myopes start out with attenuated thicknesses and progress to remarkably thin or

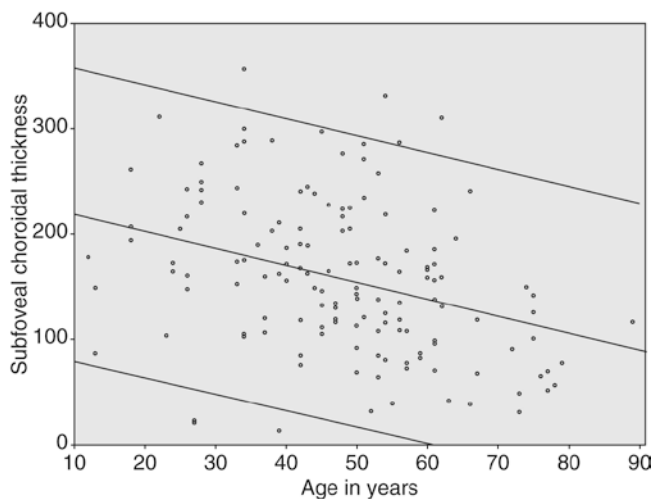
even absent areas of choroid. At some threshold, the choroid would have some difficulty in supplying enough oxygen and other metabolites. From that point, the term myopic choroidal atrophy is appropriate [68]. In elderly people without high myopia, the choroid may show reduced thickness in a process known as age-related choroidal atrophy (ARCA) [70]. These patients have normal axial lengths but show tessellation of the fundus, much the same as older high myopes, and beta-zone peripapillary atrophy. Eyes with decreased choroidal thickness as part of ARCA are more likely to have pseudodrusen, while highly myopic eyes almost never have pseudodrusen [71]. ARCA has been defined as a choroidal thickness of less than 125 microns based on population studies, while myopic choroidal atrophy has not had a thickness definition published.

Animal models of myopia were found to have decreased choriocapillaris density and diameter [20]. Angiographic studies of the choroid with ICG have also found that the choroidal vasculature was altered in highly myopic eyes [72, 73]. A color Doppler ultrasonographic study found that the choroidal circulation was decreased in highly myopic eyes [74]. The choroid of highly myopic patients is significantly thinner than the choroid of normal eyes [68, 75]. As the choroid supplies oxygen and nutrition to the retinal pigment epithelial cells and the outer retina, compromised choroidal circulation may account, in part, for the retinal dysfunction and vision loss that is seen in high myopia.



**Fig. 10.6** Hypothetical explanation for choroidal thinning and supply of oxygen and metabolites to the retina. (a) In an emmetropic eye, the photoreceptors (blue dots) have a certain packing density. These are arranged on the retinal pigment epithelium (brown layer), which in turn is on the choroid (orange-red layer). The sclera is depicted by the gray structure. In a high myope, (b) the posterior pole is stretched resulting in a lower packing density of the photoreceptors. The choroid is thinner

than an emmetrope. However, the ratio of the choroid's ability to supply oxygen and metabolites as compared with the packing density of the photoreceptors may not be adversely affected in high myopes, as evidenced by their good visual function, at least when young. With increasing age, the choroid thins, and later in life there is potential for decreased visual function as a consequence of choroidal atrophy



**Fig. 10.7** Subfoveal choroidal thickness versus age in a group of 145 highly myopic eyes with no macular pathology. The trendline demonstrates the decrease in thickness with age, and the thinner bordering lines show the 95% confidence interval. The Y-axis shows the thickness of the choroid in microns

## 10.12 Biometric Choroidal Changes and Their Clinical Significance

A group of 18 patients (31 eyes), with a mean age of 51.7 years and a mean refractive error of  $-15.5$  D, was evaluated with regular SD-OCT. The mean subfoveal choroidal thickness was only  $100.5$   $\mu\text{m}$  and was even thinner in older

patients and those with greater posterior staphyloma height [76]. The authors defined staphyloma height as the sum of four vertical measurements on SD-OCT foveal scans: the distance from the RPE line beneath the fovea to the nasal, temporal, superior, and inferior edges of the OCT image. This method does not mention how the presence, shape, and exact location of the posterior staphyloma were determined. By definition, a staphyloma is an outpouching of the eye and is a region where there is an exaggerated curvature of the wall of the eye. Any eye, whether it is myopic or not, is not a flat structure, and as such, it should have some "height" as it is defined by this SD-OCT method of measurement. Conventional SD-OCT allows a relatively good visualization of the choroidal-scleral interface in highly myopic eyes because of the dramatic choroidal thinning [75]. Ikuno and associates reported the scleral interface was undetectable in eyes with a choroidal thickness greater than  $300$   $\mu\text{m}$  with regular SD-OCT. [75] Visualization would be expected to be dependent on the amount of pigmentation of the RPE and choroid. Another group of 31 patients (55 eyes) with a mean age of 59.7 years and a mean refractive error of  $-11.9$  D was evaluated with EDI-OCT. The mean subfoveal choroidal thickness was  $93.2$   $\mu\text{m}$  and was negatively correlated with age ( $P = 0.006$ ) and refractive error ( $P < 0.001$ ) [68]. Eyes with a history of choroidal neovascularization also had a thinner choroid ( $P = 0.013$ ), but the patients in this study were treated with photodynamic therapy, which may have damaged the choroid [68]. In this EDI-OCT study, subfoveal choroidal thickness was found to decrease by  $12.7$   $\mu\text{m}$  for

each decade of life and by 8.7  $\mu\text{m}$  for each diopter of myopia. Nishida and associates evaluated 145 highly myopic eyes and found the choroidal thickness decreased by 15.5  $\mu\text{m}$  per decade of age and 8.13  $\mu\text{m}$  for each diopter of myopia [77].

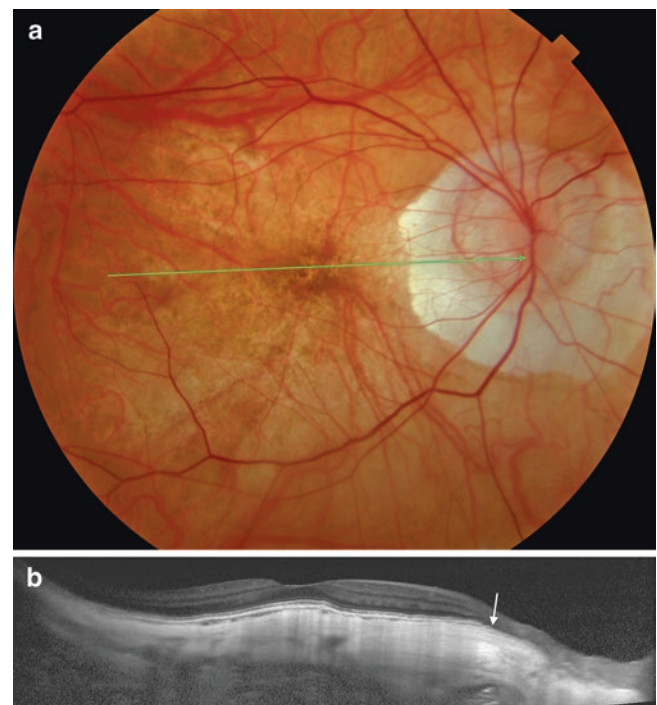
Given the knowledge that choroidal thickness decreases with both age and myopia, a study was done to look at factors related to visual acuity in highly myopic eyes with no other evident pathology. Two groups of patients, one from New York and the other Japan, were evaluated separately and as a pooled group [77]. Various features were measured in OCT scans by two masked readers. The only predictor of visual acuity, in each of the patient populations and in the pooled data, was the subfoveal choroidal thickness. The thinner the choroid, the less the acuity, although even patients with pronounced thinning of the choroid had what would seem like modest reductions in acuity. Of interest are measures of utility of vision, which show disproportionate loss with even mild changes in acuity. For example, the utility loss of an eye going from 20/20 to 20/40 is about the same as an eye going from 20/40 to 20/200. A study of 60 eyes of highly myopic patients without evidence of maculopathy found a negative correlation between visual acuity and macular choroidal thickness, subfoveal choroidal thickness, and photoreceptor/RPE aggregate thickness [78]. A study of 37 highly myopic eyes as compared with 86 normal eyes found an inverse correlation between choroidal thickness and visual acuity [79]. A case control study found axial length to be negatively correlated with visual acuity after adjusting for age. Addition of choroidal thickness did not cause a statistically significant change. In a study of 105 extremely high myopic subjects, choroidal thickness is inversely correlated with visual acuity, but following correction for spherical equivalent, among other things, the correlation was no longer significant [80]. Note the biggest predictors for choroidal thickness are age and refractive error (or axial length). That means if these variables are included in a regression equation, adding choroidal thickness on top of that as a variable would then only evaluate the shared variance in the variable choroidal thickness and acuity that is not accounted for by the shared variance between choroidal thickness and age and refractive error. Using the same logic, jumping off of the Empire State Building is no more risky than jumping off of a chair, corrected for height. It may be possible to include all of the variables if the sample size is large enough to overcome the effects of mutual confounding, as with the Beijing Eye Study, which evaluated 3233 subjects and found best corrected visual acuity was inversely correlated with subfoveal choroidal thickness even after including age and axial length [81].

In high myopia, we are often impressed by the minority of patients with retinal detachment or choroidal neovascularization, because they have sudden loss of large amounts of visual acuity. Many patients with high myopia have lesser

amounts of acuity loss that individually may not seem all that important. However, the number of eyes involved is immense. By analogy in some areas of the world, people have deficient intake of iodine. A small minority of people in those areas develop cretinism. A much larger proportion of people have a small decrease in mental function. The cretinism cases are vivid examples; these few people have lost a lot. From a societal standpoint, the many people losing a smaller amount is also important.

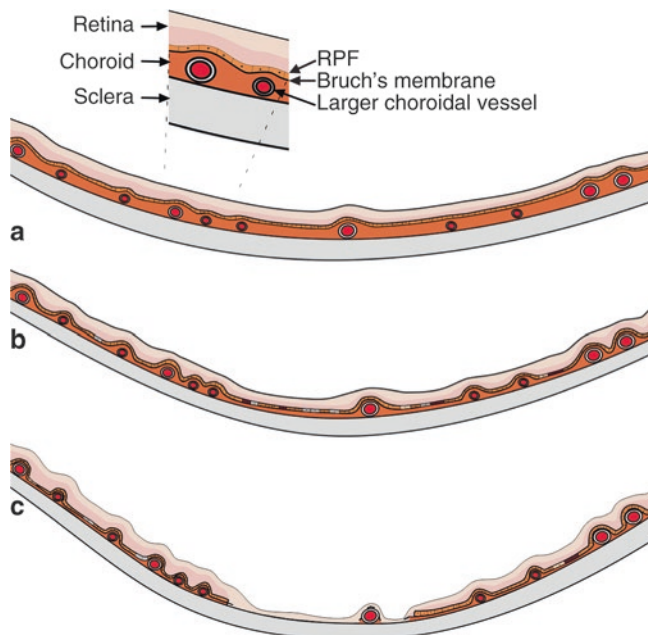
### 10.13 Chorioretinal Atrophy in High Myopia

Regression analysis of choroidal thickness shows a linear trendline descending in proportion to the amount of myopia or age (Fig. 10.8). In general, this is a true representation, but there is a lower limit to how thin the choroid theoretically could be and still be functional. Red blood cells have a finite size and the vessels carrying these cells by necessity have to be larger. In OCT images of high myopes, the choroid can be as thin as 15 microns or less. Eyes with choroids this thin have marked alterations of pigmentation to include clumping

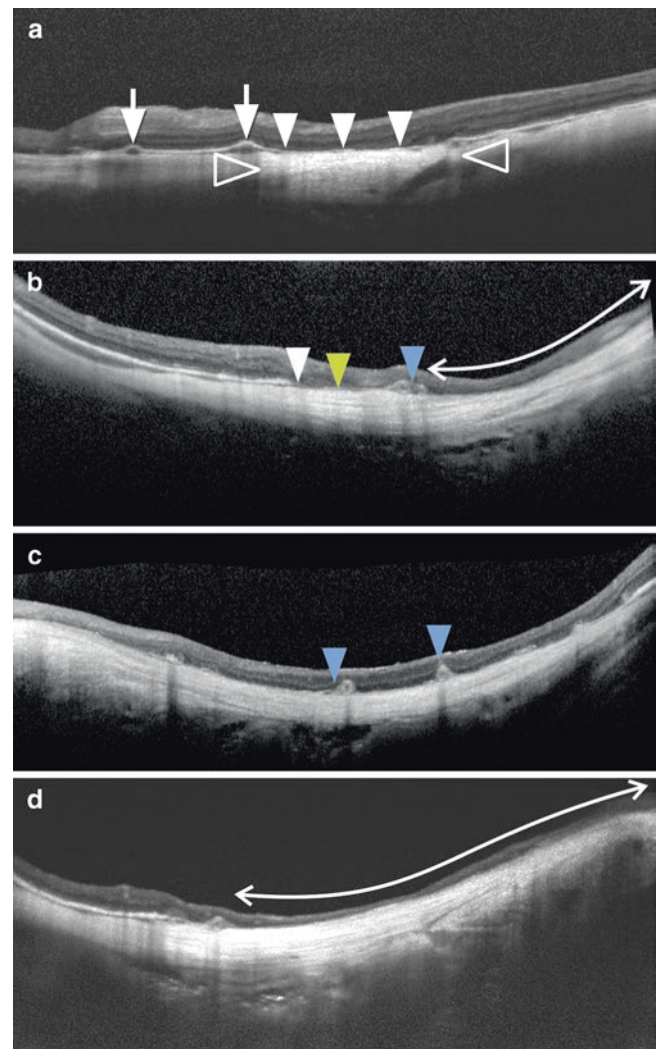


**Fig. 10.8** A 70-year-old woman with high myopia. (a) The fundus picture shows attenuation of the choroidal vessels. Note in the central macular region there is a relative paucity of vessels. She is lightly pigmented and therefore doesn't show a prominent tessellated fundus. There is peripapillary atrophy. (b) The enhanced depth imaging (EDI) optical coherence tomography (OCT) shows a choroid that is quite thin (arrowheads); the subfoveal choroidal thickness is 14  $\mu\text{m}$ . Note the choroid seems to come to an abrupt end at the border of the normal choroid and the peripapillary atrophy (arrow)

and rarefaction in adjacent areas. These areas of extreme attenuation of the choroid are seen adjacent to zones of what appears to be complete absence of the choroid. These areas are brilliantly white because there does not appear to be any extant RPE or choroid, and therefore the underlying sclera is readily visible (Figs. 10.9, 10.10, and 10.11). These areas have attenuation of the overlying retina and have been called patchy atrophy. (The term patchy atrophy is misleading in that in the surrounding areas the choroid is also atrophic.) At the border of the chorioretinal atrophy, the choroid does not necessarily gradually thin to non-existence, it often has a border where a very thin choroid abruptly terminates. This is probably secondary to the anatomic configuration of the remnants of choroid with vessels having either a quantum thickness or not being present at all. With loss of the choroid, there is a concomitant loss of the ability to supply oxygen and metabolites, so the remaining choroidal stroma and the overlying RPE and outer retina appears to wane. Another mechanism that can lead to complete loss is following lacquer crack formation. Each crack in Bruch's membrane causes a traumatic rupture of the choriocapillaris. The potential repair that takes place to the choriocapillaris is not known at present. However, repeated formation of lacquer cracks



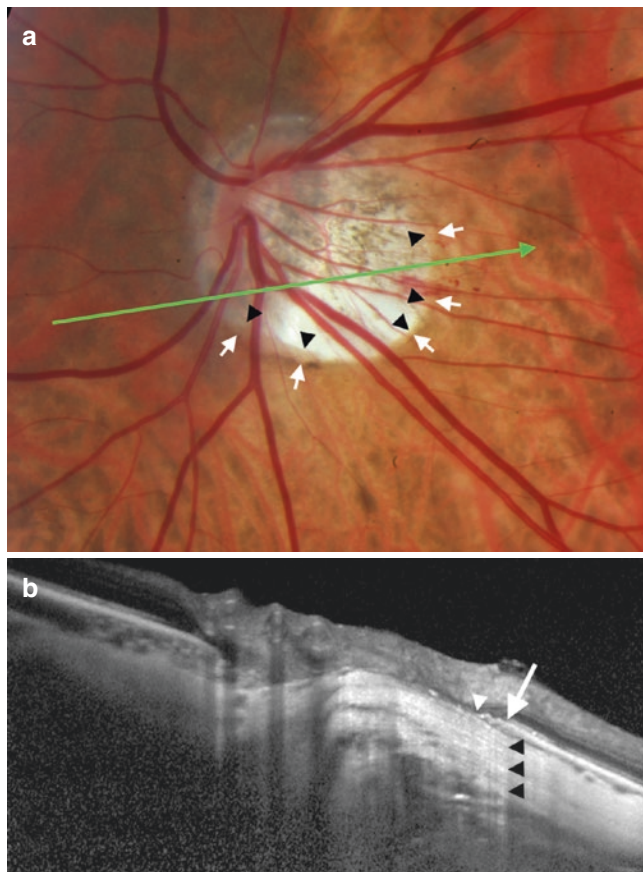
**Fig. 10.9** Schematic drawing of choroidal thinning and atrophy. (a) In high myopes, the choroid is thinner, with what appears to be attenuation of the middle choroid in particular. The larger choroidal vessels may fill much of the thickness of the choroid. (b) With increasing thinning of the choroid, the larger choroidal blood vessels indent the overlying RPE monolayer. (c) The choroid appears to become so attenuated in older highly myopic patients that it no longer maintains the vitality of the overlying retina and retinal pigment epithelium or itself for that matter. Areas of absence of the outer retina, RPE, and choroid appear. The remaining tissue is essentially the inner retina. Since this is transparent and the underlying tissue is the sclera, these areas appear white



**Fig. 10.10** OCT examples of advanced choroidal atrophy in high myopia. (a) The choroid is attenuated in this eye, and two larger choroidal vessels (arrows) are seen elevating the RPE. Some authors have called these elevations “choroidal microfolds,” which is clearly incorrect since the choroid is not folded. In areas of loss of the RPE, there is increased light transmission to deeper layers (open arrowheads). Within this zone, what appears to be Bruch's membrane is seen (arrowheads). (b) With more profound loss of the choroid, the RPE terminates leaving a vestige of Bruch's membrane (white arrowhead) and remnants of Bruch's membrane (yellow arrowhead). Around a larger choroidal vessel, there appears to be residual portions of associated choroidal stroma (blue arrowhead). The double-ended white arrow shows a stretch of the posterior pole without any visible vascularized choroid. Note the loss of substance and laminations in the overlying retina. (c) This eye shows a nearly complete loss of the choroid in the region of the OCT scan. There are two remaining larger choroidal vessels with small vestiges of choroidal tissue (blue arrowheads). (d) In an eye with more chronic loss of the choroid, as shown by the extent of the double-ended white arrow, the overlying retina is remarkably thinned

likely takes a toll and decreases the integrity of the choriocapillaris in an affected area.

Okabe and associates analyzed three eyes with chorioretinal atrophy and pathologic myopia enucleated for various



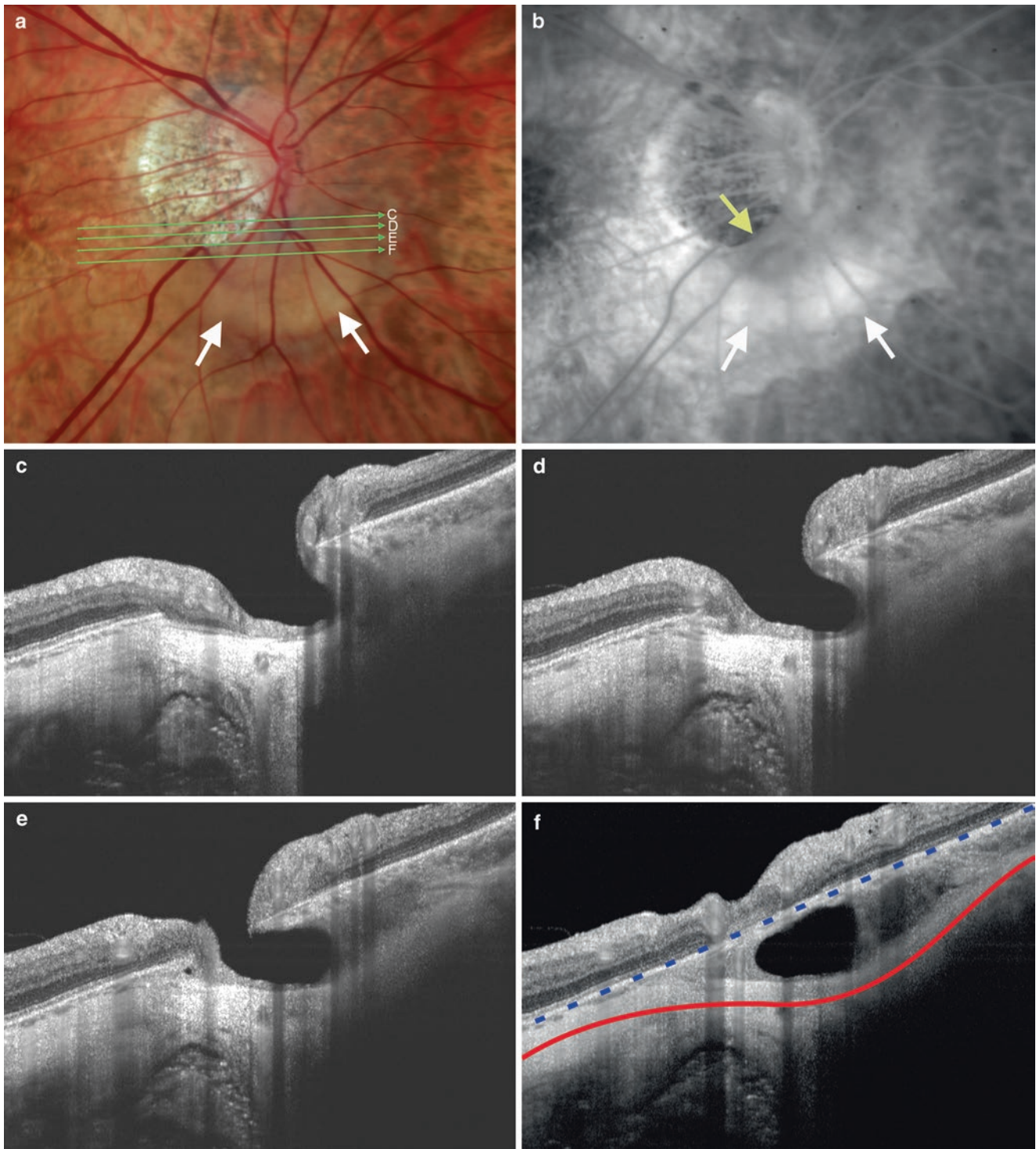
**Fig. 10.11** Tilted disc and conus in a high myope. The infrared scanning laser image was projected onto the color picture to be able to accurately locate the scan line shown as the green arrow. **(a)** This eye shows a tilted disc and profound atrophy within a conus inferotemporal to the disc. At the outer border of the conus are two concentric curves. The outer one (white arrows) is where the orange color terminates, and the second is the continuation of a more subtle zone of shading prior to the intensely reflective inner zone of the conus. This boundary is shown by the black arrowheads. **(b)** The termination of the orange color corresponds to the white arrow. Note the increased penetration of light posterior to this zone, as demarcated by the black arrowheads. These signs are taken to mean the RPE stops, or at least becomes attenuated, at this juncture. There is a thinner curved structure that stops nasally (white arrowhead), and this structure appears to be the termination of Bruch's membrane. The termination of this layer corresponds to the line demarcated by the black arrowheads in the color photograph

reasons: herpetic keratitis and secondary glaucoma, intraocular hemorrhage, and painful filamentous keratitis [82]. One eye had -20D of myopia, and the amount of myopia was not defined for the two other eyes included. Histopathological observations have provided valuable information in high myopia: the choroid was thin with vessels present in some areas but completely absent in others [82]. The authors hypothesized that the choriocapillaris was obstructed and disappeared earlier than the other choroidal vessels under the conditions of excessive myopia and that the choriocapillaris obstruction occurs in a lobulated fashion. The associated conditions in these eyes probably influenced the ultrastructure of the analyzed tissue.

## 10.14 Intrachoroidal Cavitation

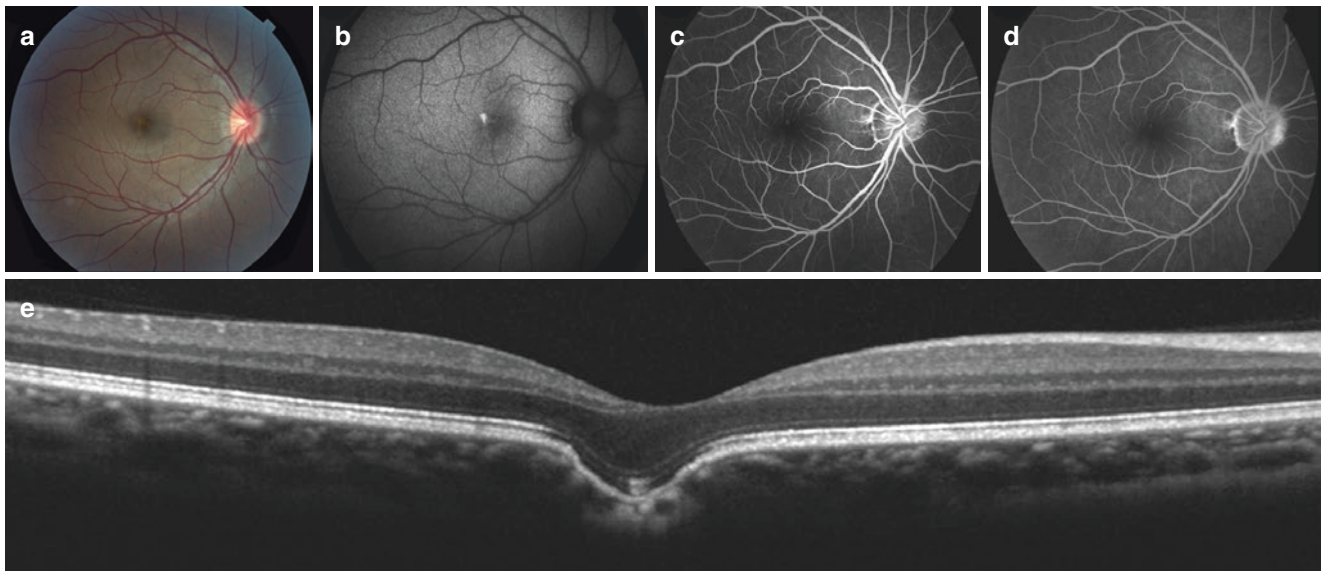
A yellowish-orange lesion typically located immediately inferior to optic nerve occurs in eyes with high myopia [83–89]. This lesion was originally termed peripapillary detachment in pathologic myopia because the defect was thought to represent an elevation of the retina and the retinal pigment epithelium (RPE). Peripapillary detachment in pathologic myopia was found in 4.9% of highly myopic eyes in a series reported by Shimada and coworkers [84]. A steep excavation of the inferior myopic conus was detected adjacent to the peripapillary detachment [85]. Revision of the concepts involving the lesion highlighted some aspects that were inconsistent with the known pathoanatomy of RPE detachments – the lesion appeared to be a cavity but appeared to be located in the choroid [86, 87]. Tateno and colleagues thought the RPE was not separated from the choroid; instead, there was a schisis within the choroid [86]. In their case description, Toranzo and colleagues stated “deep hyporeflectivity was present in the underlying choroid, resembling an intrachoroidal cavitation separating the retinal pigment epithelium from the sclera” [87]. As a consequence, they changed the name of the defect to peripapillary intrachoroidal cavitation (ICC) [87]. Wei and associates expanded on the concept of peripapillary ICC and proposed a complex of forces composed of “posterior expansion force, the vitreous traction force, and the vitreous fluid dynamics determine the size and shape of the lesion” [88]. Investigation of a series of 16 eyes with peripapillary ICC using EDI-OCT and SS-OCT showed an interesting anatomic configuration [89]. The sclera in the region of the conus was displaced posteriorly, and the backward deflection of the sclera continued into the region of the ICC. The overall curvature of the retina, RPE, and Bruch's membrane complex was seen to be relatively unaffected over the region of the ICC. The cavitation was created by the expansion of the distance between the inner wall of the sclera and the posterior surface of Bruch's membrane. There also appeared to be alterations of the anatomy around the optic nerve caused by the posterior displacement of the sclera (Fig. 10.12). A full-thickness defect in the retina was found in one quarter of the eyes at the border of the conus.

The eye ordinarily is inflated by its intraocular pressure with the wall of the eye acting as the outer barrier, resisting outward expansion. The ability of the wall of the eye to resist deformation is related to its inherent elasticity and its thickness. Over normal expanses, the wall of the eye is composed of the retina, RPE, Bruch's membrane, the choroid, and sclera. In the region of the conus, there is no choroid, RPE, Bruch's membrane, or outer retina. The inner retina can be very attenuated. The underlying sclera is thinned in eyes with high myopia, particularly in the region of the conus. The comparatively thin eye wall in the area of the conus is exposed to the same force per unit area from intraocular pressure as other areas in the eye and therefore is more likely



**Fig. 10.12** (a) This color photograph shows the yellow orange region of the intrachoroidal cavitation (white arrows). The green arrows show the locations of subsequent optical coherence tomography (OCT) sections. (b) A fluorescein angiogram shows a modest late collection of dye within the cavity. Note the edge of the retinal defect is more clearly evident than in the color photograph. (c–f) Successive serial sections using swept source OCT showing the inner retinal defect and the exten-

sion of the cavitation into the choroid. There is a veil of tissue extending through the thickness of the choroid at the border of the cavitation. In (f), note that the hyperreflective band corresponding to the retinal pigment epithelium is nearly straight, as illustrated by the blue dashed line overlay. The sclera shows an outbowing posteriorly with the red line at the center point thickness



**Fig. 10.13** A 33-year-old man with a conforming focal choroidal excavation. (a) Color photograph of the right eye reveals a perifoveal yellowish spot consistent with a small vitelliform lesion. (b) Fundus autofluorescent image of the right eye reveals a focal area of hyperautofluorescence corresponding to the vitelliform material. Late venous phase (c) and recirculation phase (d) fluorescein angiographic images

reveal a focal hyperfluorescent spot supratemporal to the fovea. (e) Spectral-domain optical coherence tomographic scan through the fovea reveals a conforming focal choroidal excavation with a small area of outer retinal hyperreflectivity corresponding to the vitelliform lesion (a). (From Reference [97])

to experience deformation as compared with regions of the eye having all layers intact. Since the sclera has some stiffness, the posterior deformation continues into surrounding normal areas, thus causing the separation or cavitation in the choroid. There appears to be more staphylomatous expansion of these eyes at the inferotemporal portion of the disc, possibly explaining the frequent inferior location of peripapillary ICC [89].

This same mechanical defect potentially can exist in other regions and may offer explanation for similar cavitations in the macular region of high myopes. These cavitations occurred in the posterior pole of eyes with neighboring areas of loss of the choroid and overlying RPE [90]. The posterior displacement of the sclera continued into relatively normal surrounding areas which appears to be the cause of macular ICC. Almost one-fourth of eyes with ICC have a retinal defect located near the border between the attenuated retina and the surrounding normal retina. In some patient, fluid dissecting under the retina has resulted in a localized retinal detachment.

### 10.15 Focal Choroidal Excavation

Eyes with myopia generally have decreasing choroidal thickness in proportion with their amount of myopic refractive error. An unusual group of patients have what is termed focal choroidal cavitation and entity in which there is a localized

loss of choroidal thickness within the macula [91–93]. These patients are generally myopic with some being highly myopic. Affected eyes have solitary localized areas that usually show pigmentary alterations, but the cavitation itself is difficult to see by biomicroscopy. The cavitations are readily visible using OCT (Fig. 10.13). These areas show hypofluorescence during both fluorescein and indocyanine green angiography and localized hypoautofluorescence. In a group of ten eyes, EDI-OCT was performed in six, and these showed a choroid that appeared to be abnormally thick in the regions surrounding the excavation [93]. The choroid was thin at the excavation, and the choroidal-scleral junction showed no abnormalities. The excavation was thought to represent a localized hypoplastic region. The same thinning can be seen following resolution of focal inflammation.

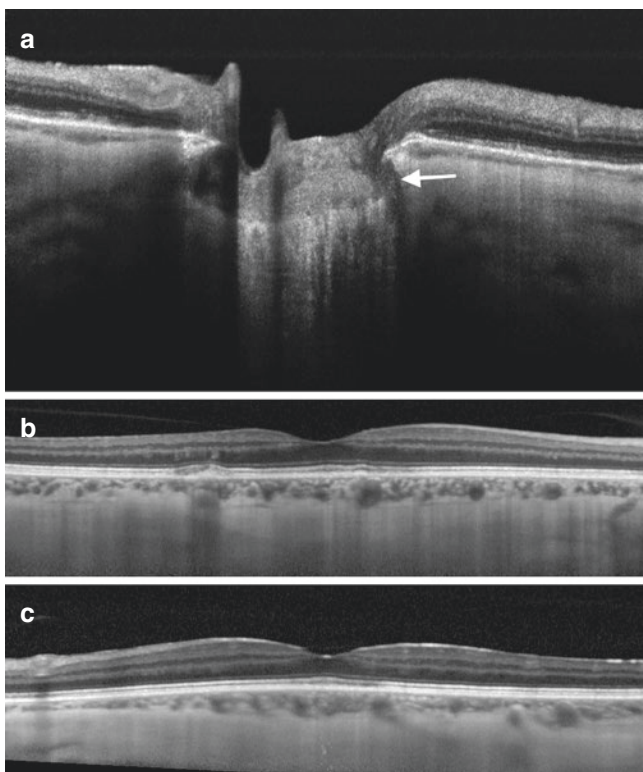
### 10.16 Future Trends for Research

There is much to be learned about the choroid in myopia. The process of emmetropization appears to be misdirected or abnormal in high myopes and is mediated in part by the choroid. Yet in high myopia, the choroid becomes increasingly abnormal. The influence these changes have on the progression of myopia is not known. The ability to image the thickness of the choroid using OCT is relatively recent, so there is an absence of any long-term data. Classification systems for the posterior pole changes in high myopia have relied on



ophthalmoscopy alone. Integrating choroidal thickness into the classification system would introduce a variable that has biologic plausibility to both influence visual function and preserve associated tissue. Decreased choroidal perfusion also may be related to secondary abnormalities seen in high myopia such as choroidal neovascularization as discussed in a separate chapter in this text.

There are many research efforts aiming to reduce the progression of myopia, but reduction of the choroidal effects related to myopia would obviate many of the common reasons for visual loss in the first place. Thickening of the choroid is seen in inflammatory diseases [94] and in central serous chorioretinopathy [95]. It is possible that pharmacologic manipulation can influence choroidal thickness. Oral sildenafil caused an increase in choroidal thickness in normal volunteers [96, 97]. Corticosteroids are associated with central serous chorioretinopathy and may have an associated effect of increasing choroidal thickness. One older high myope was imaged and found to have a thickened choroid. Interestingly, she had a kidney transplant in the past and had been treated with oral prednisone for many years (Fig. 10.14).



**Fig. 10.14** (a) This highly myopic, 66-year-old woman had typical features of a high myope, including a dehiscence in the lamina cribrosa as seen in this swept source OCT scan, but her choroid was unexpectedly thick. (b, c) Given her age and axial length, she would be expected to have a subfoveal choroidal thickness of about 50 microns. Instead her choroid was nearly 200 microns thick. She had a kidney transplantation and was using oral prednisone for many years to prevent rejection

### 10.16.1 Potential Use of Choroidal Thickness in Grading Myopic Fundus Changes

Epidemiologic studies use grading systems to classify and quantitate incidence and severity of myopic changes in populations. There are key attributes required of any grading system to be useful. The grading system should be exhaustive of all possibilities of disease expression, the stages in the grading system should be relevant to important stages of the disease process and be based on objective information, and the results should be accurate and reproducible. Current classification systems grade myopia based on attributes such as tessellation, diffuse atrophy, patchy atrophy, lacquer cracks, and Fuch's spots. This list does not represent an exhaustive tabulation of possibilities, grading of any of these attributes is quite subjective, and the presence of these findings is dependent on the population being graded. For example, tessellation is the presence of a striped pattern caused by visualization of larger choroidal blood vessels contrasted by intervening pigment in the outer choroid. Eyes with the tessellated fundus appearance have thinner choroids than eyes with a normal fundus appearance. Thinning of the choroid is associated with loss of the middle layer, allowing visualization of deeper layers. The contrast between the vessels and the pigmented portions depends in part on how much pigment is present. A person with a highly pigmented choroid would have tessellation only if the choroid was thinned from myopia. A person who is of Northern European extraction with less pigmentation could easily have tessellation with a normal thickness choroid and no myopia. Thus, the utility of tessellation may be dependent on pigmentation. Efforts have been made to quantify tessellation based on image analysis [98]. The degree of tessellation was highly associated with choroidal thickness. Fuch's spots are pigmented scars left by choroidal neovascularization. It is common for patients with blonde fundi to not develop a pigmented scar after choroidal neovascularization and for eyes treated with anti-VEGF agents to not develop scars in the first place. In the case of either tessellation or Fuch's spots, the grading of presence or absence is highly subjective and not a consistent sign among various groups of people.

### 10.16.2 Optical Coherence Tomography Angiography

OCT angiography is useful in evaluating myopic choroidal neovascularization, and this use is covered in a separate chapter. OCT angiography can be used to evaluate the choriocapillaris flow. Earlier application of the technology analyzed areas in which the flow could not be detected in the choriocapillaris layer, and these are called flow voids [99–101]. Frame averaging of choriocapillaris images



**Fig. 10.15** Choriocapillaris imaging. (a) Frame averaged OCT angiography demonstrates the choriocapillaris structure in an emmetrope. (b) Binarized image of (a). (c) Skeletonized image created from (b). This image can be analyzed for branch length and number of branches

per square millimeter. The choriocapillaris of a high myope. Although the choriocapillaris mesh is visible to a degree, the medium and large vessels of this subject are also visible in part

improves image quality by increasing the signal-to-noise ratio (Fig. 10.15) [102]. There are several problems with imaging the choriocapillaris in highly myopic eyes. The first area that can be imaged is somewhat limited because of the limited depth of imaging current commercial OCT instruments. Second, segmentation of highly myopic eyes can be error-prone, and so manual correction of the segmentation lines may be necessary. Third, the segmentation slab for the choriocapillaris can be 15 or 20  $\mu\text{m}$  in thickness. This may represent a significant portion of a highly myopic choroid, which have only 30  $\mu\text{m}$  in total thickness. Vessels below the level of the choriocapillaris are imaged as well. It can be difficult to subtract the deeper vessels from the more superficial in choroidal imaging. Without this removal, the vascular density and flow in the choroid may be overestimated. To gain an OCT angiographic image of the entirety of the choroid in high myopes, one interesting approach is to place the segmentation slab in the sclera and image the projection artifacts from the thickness of the choroid [103].

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