Imaging the Choroid: Pearls From the Experts

Three clinician-researchers talk about the uses of choroidal imaging.

The Body of Knowledge Is Growing Monthly

By Richard F. Spaide, MD

The choroid is the main source of blood for the eye and as such plays at least some role in almost every area of ophthalmic disease. Our understanding of the choroid has been vastly augmented in recent years since the introduction of 2 modes of imaging the choroid: enhanced-depth imaging optical coherence tomography (EDI-OCT) and swept-source OCT (SS-OCT).

My colleague Sarah Mrejen, MD, and I recently performed a major review of the published literature on choroidal imaging.1 Although there is not the space (or necessity) to recap here all that we gleaned from the 240 works cited in that review, this article presents some highlights of this relatively new but rapidly burgeoning area of research.

Image Innovation

Because it lies behind the pigmented retinal pigment epithelium (RPE) and within the shell of the opaque and rigid sclera, the choroid has historically been difficult to image thoroughly. Conventional OCT imaging of the choroid is impeded by the scattering effects of the blood and vasculature and by the presence of melanin. Fluorescein angiography of the choroid is also blocked by melanin. Indocyanine green (ICG) angiography allows anatomic and dynamic evaluation of choroidal circulation, but it is difficult to appreciate individual layers of tissue because of the effects of vertical summation. B-scan ultrasonography is helpful for visualizing some tumors and other features, but it provides insufficient resolution to assess changes in choroidal thickness.

In conventional OCT, the zero-delay line—the line of peak sensitivity—is placed at the posterior vitreous. This makes clinical sense because it allows evaluation of the vitreoretinal interface, which plays an important role in many diseases. As a result, however, the choroid is somewhat out of range and cannot be seen very well. Because of the way the interferometric signal is decoded by Fourier transforms in OCT, 2 conjugate images are created. If the zero-delay line is placed further posteriorly, usually at the inner sclera, the choroid can be better visualized. The technique now known as EDI-OCT was implemented by inverting the upside-down conjugate image to allow it to be read like a conventional OCT image.2 Although this imaging technique was initially achieved by moving the OCT device closer to the eye and inverting the resulting image, software updates introduced by multiple manufacturers now make it straightforward to obtain choroidal images in EDI mode.

Making Measurements

Currently, when EDI-OCT is used, the outer border of the RPE and the inner border of the sclera are generally determined by the user, and digital calipers are used to measure subfoveal choroidal thickness. A number of studies have evaluated the reproducibility of subfoveal choroidal thickness measurements performed using multiple commercially available devices, including EDI-OCT and SS-OCT. These studies have found good intersystem, interobserver, and intervisit reproducibility, even with-

Figure 1. Age-related choroidal atrophy. The top left photograph shows tessellation and slight optic nerve pallor. Top right is an autofluorescence image showing no autofluorescence abnormalities. The EDI-OCT image (bottom) shows a remarkably thin choroid.
out the availability of automated software. For example, Tan et al., in assessing the diurnal variation of choroidal thickness in normal individuals, found that the intraclass correlation coefficient for interobserver reliability was 0.994, and the mean difference in choroidal thickness measurements between graders was 2.0 µm. This difference was less than the amount of diurnal variation seen in choroidal thickness measurements.

Choroidal thickness characteristics of healthy eyes have been documented by Margolis and Spaide. In 54 normal eyes of nonmyopic individuals aged a mean 50.4 years, they reported mean subfoveal choroidal thickness of 287 µm, and a decrease in choroidal thickness by 15.6 µm for each decade of life. The authors also noted that choroidal thickness is asymmetric, with the thickest measurements under the fovea and thinning in all directions, particularly the nasal direction; average thickness at 3 mm nasal to the fovea was 145 µm.

The choroid-scleral interface was identified in 100% of eyes in the Margolis and Spaide study. It should be noted that there is a potential for bias in reported choroidal thickness measurements if the scleral-choroidal interface cannot be identified in a high percentage of subjects in the population sample. If reliable measurements cannot be made in those with thicker choroids because the choroid extends beyond the instrument’s limit of imaging, results could be biased toward thinner choroidal measurements.

Tan and colleagues reported significant diurnal variation in choroidal thickness in normal eyes, with the highest thickness measurements in the morning and thinnest measurements in the evening. This variability should be taken into consideration in clinical practice, as well as in the design and execution of clinical trials in which choroidal thickness is assessed over time.

**CHOROIDAL THICKNESS IN DISEASE**

The list of diseases in which choroidal thickness has been assessed in the 5 years since the description of EDI-OCT is long and growing longer by the month.

Spaide’s description of a new entity, age-related choroidal atrophy (ARCA) was made possible at least in part by the availability of EDI-OCT (Figure 1). Choroidal thickness decreases with age in normal eyes, but some individuals experience pronounced loss of choroidal thickness over time. Although patients with ARCA retain relatively good visual acuity, they describe visual complaints often relating to reading and demonstrate fundus changes similar to those seen in myopic patients. There appears to be a loss of choroidal vessels in these patients and a corresponding enlargement of the remaining vessels. These larger ves-
sels are clearly visible on EDI-OCT. ARCA is distinct from geographic atrophy in dry age-related macular degeneration (AMD); geographic atrophy is a well-defined area in which the absence of RPE pigmentation makes the choroidal vessels visible, while ARCA is a generalized thinning of the choroid. ARCA may previously have been referred to as nongeographic atrophy, although this entity has never been clearly defined.

Choroidal imaging has become an important diagnostic modality for assessment of central serous chorioretinopathy (CSC). Imamura and colleagues found that the choroid is thickened in eyes with CSC as compared with normal eyes, and that the normal decline of choroidal thickness with age is not seen in eyes with CSC (Figure 2). Maruko and colleagues showed that serous subretinal fluid resolved in patients with CSC after treatment with either laser photocoagulation or photodynamic therapy; mean subfoveal choroidal thickness decreased significantly in those treated with PDT by 4 weeks posttreatment, but not in those receiving laser. Reduction in subfoveal choroidal thickness remained stable at 1-year follow-up. This information has potential clinical utility: Laser may help to resolve any individual episode of CSC, but it has no effect on recurrences. Recurrences of CSC after PDT are uncommon. It appears that PDT addresses the underlying problem of choroidal vascular hyperpermeability in CSC, but laser photocoagulation does not (Figure 3).

FURTHER STUDY

Choroidal imaging may prove to be a valuable tool for evaluating and monitoring inflammatory conditions in the posterior segment, many of which involve the choroid. Numerous studies have been published using choroidal imaging techniques to assess posterior uveitic conditions including Vogt-Koyanagi-Harada syndrome, multifocal choroiditis and panuveitis, acute zonal occult outer retinopathy, birdshot chorioretinopathy (Figure 4), toxoplasmic retinochoroiditis, and sarkoidosis.

Choroidal imaging modalities facilitate structural analysis and biometric measurements of the choroid, as well as qualitative analysis. These imaging modalities will be of particular utility in the area of ophthalmic oncology, allowing clinicians to identify small tumors not detected by ultrasound, analyze the reflectivity of tumors, and assess normal and abnormal vasculature. To validate the usefulness of these technologies in choroidal tumors, the findings of EDI-OCT and SS-OCT must be correlated with histology.

These imaging modalities will also no doubt prove useful in glaucoma, allowing the study of anatomic structures deep in the optic nerve complex such as the lamina cribrosa (Figure 5), central retinal vein and central retinal artery, peripapillary choroid and sclera, and subarachnoid space around the optic nerve. Choroidal imaging will offer the opportunity to study these structures in vivo, providing a novel perspective on glaucomatous neurodegeneration.

As noted above, the literature on choroidal imaging in health and disease is growing monthly, and by the time you read these words our just-published review will already be out of date. Choroidal imaging can increase our understanding of many diseases of the eye and facilitate the recognition of new entities. It will be worthwhile for all clinicians to stay abreast of the important insights that these new choroidal imaging modalities will continue to bring to the body of ophthalmic knowledge.

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New Modality is Helpful in Narrowing the Differential Diagnosis

By Justis P. Ehlers, MD

Since the description of enhanced-depth imaging spectral-domain optical coherence tomography (EDI-OCT) in 2008,1 clinicians have been striving to learn how this new mode of choroidal imaging can enhance our understanding of retinal diseases. Choroidal imaging provides another element in the clinical picture that can be utilized alongside the results of clinical examination, standard-depth SD-OCT, angiography, and other tests. It is particularly helpful in assessing entities affecting or potentially affecting the choroid and/or the sub-retinal pigment epithelium (RPE) space. Because this is an emerging technology, normative data is limited regarding choroidal thickness, but, in general, “normal” choroidal thickness is thought to be similar to “normal” retinal thickness (Figure 1).

NARROWING THE DIFFERENTIAL

At present, for many diseases, the greatest clinical utility of EDI-OCT may lie not in providing a definitive diagnosis, but rather in guiding and narrowing our differential diagnosis. When used as part of a multimodality approach to a diagnostic workup, EDI-OCT can provide novel information that may be critical in guiding diagnosis, additional testing, and treatment.

Choroidal imaging may be used, for instance, to distinguish age-related macular degeneration (AMD) from other potential masquerade syndromes. For example, patients may present with reduced vision and macular pigmentary changes. EDI-OCT in these patients can be quite helpful in identifying the presence of drusen or revealing a thin, atrophic choroid, suggesting age-related choroidal atrophy. Recently described by Spaide, age-related choroidal atrophy should be considered in the differential for patients presenting with an AMD-like picture with minimal drusen, particularly those with predominately pigmented changes, minimal choroidal vessels, and vision loss (Figure 2). It remains unclear if this is a distinct entity or a condition on the spectrum of age-related macular degeneration.2 In addition, our group and others have examined the role of choroidal thickness in visual function in dry AMD. Preliminary research suggests that decreased choroidal thickness may be associated with vision loss in dry AMD independent of geographic atrophy and other factors.3

In neovascular AMD, choroidal imaging may be a useful diagnostic adjunct. Typically, with age, the choroid thins over time. Resistance to anti-VEGF therapy in neovascular AMD should prompt consideration of alternative diagnoses. EDI-OCT can be particularly useful for identifying choroidal abnormalities that may point to a different disease. Central serous chorioretinopathy (CSC) and polypoidal choroidal vasculopathy (PCV) are both common underlying offenders in tough-to-treat “wet AMD.” Choroidal imaging in CSC may reveal a grossly thickened choroid (Figure 3).4 In PCV, EDI-OCT may facilitate identification of polyps and sub-RPE pathology consistent with PCV.

Choroidal imaging may also offer additional information in the presence of inflammatory conditions. Choroidal infiltration may result in a thicker choroid that can be visualized with EDI-OCT. This modality is also helpful for assessing the characteristics of subretinal/choroidal lesions. For example, the region of origin may be able to be identified (eg, subretinal space, sub-RPE, choroid; Figure 4). In addition to location, OCT may help to differentiate the consistency of the lesion, including...
characteristics such as vascularity or density.

Retinal degenerations may also have associated choroidal pathology. Our group recently investigated the choroidal characteristics of patients with retinitis pigmentosa (RP) using EDI-OCT. We found that submacular choroidal thickness was significantly reduced in patients with RP compared with normal controls but interestingly did not correlate with visual acuity or retinal thickness.

Another recently identified characteristic of the choroid that can be helpful clinically is the association between high myopia and a thinner choroid (Figure 5). Where to draw the line between the spectrum of normal anatomic configuration in a high myope and pathologic myopia is still unclear. However, in a high myope with vision loss, it may be informative to look at the choroid and assess the status of the vascular supply to the macular region. In pseudophakic patients with an unknown refractive history, posterior bowing and choroidal thinning on OCT may alert the clinician of a possible history of high myopia.

These examples illustrate how choroidal imaging can help narrow the differential when considered as part of the patient’s whole clinical picture, guiding one’s thought process to decide on directions for treatment or further diagnostic investigations. Choroidal imaging may not necessarily provide a definitive diagnosis, but it does help facilitate diagnosis in many clinical scenarios. It provides another piece of information that was not available 5 years ago.

**STILL LEARNING**

Many papers have been published recently exploring the implications of choroidal imaging. Researchers are evaluating the characteristics of the choroid in ophthalmic as well as systemic diseases that may impact blood flow and choroidal perfusion. It is still a new imaging technique, and we do not yet know all the answers.

For these reasons, the role of choroidal imaging must be considered in this context. For example, CSC, which is associated with a thickened choroid, is frequently seen in young individuals. Young individuals also tend to have thicker choroids than older people. As yet, we do not have a normative database to tell us where the limit is between normal and abnormal, so caution should be exercised in interpreting choroidal imaging.

In the past 5 years, clinical use of EDI-OCT for choroidal imaging has become fairly straightforward and practical. Device and software upgrades have allowed the imaging modality to become a streamlined part of diagnostic work-up of appropriate patients. At the Cole Eye Institute, we use several of the SD-OCT systems that allow choroidal imaging. While they all include different features, from a clinical standpoint they all provide high quality images to guide our clinical judgment.

Choroidal imaging is currently a hot area of research, and as investigation continues we will develop a better idea of the role of choroidal imaging in clinical practice. At present, it is a helpful addition to our diagnostic armamentarium that can be useful in narrowing a challenging differential diagnosis and facilitating optimal disease detection.
Choroidal imaging is an area of rapidly expanding interest among researchers and clinicians. New imaging techniques such as enhanced depth imaging optical coherence tomography (EDI-OCT) and swept-source OCT (SS-OCT) allow clinicians to look more deeply into the vascular layers beneath the retina. The literature on choroidal imaging is growing explosively, as research centers around the country and the world explore the uses and implications of this new window into the back of the eye.

When an SD-OCT device takes an image of the retina, it also obtains a mirror image in which the strongest signal, or the “zero-delay line,” is deeper within the eye. EDI-OCT takes advantage of this mirror image to obtain details of the choroid. Since EDI-OCT was first described by Spaide,1 many centers have been exploring the characteristics of the choroid in sickness and in health, in an effort to define the norms of choroidal morphology as seen through choroidal imaging technologies.

One of the principal aims of this work has been to study choroidal characteristics in different disease states, and to determine whether differences in choroidal thickness might be a diagnostic or prognostic factor. A caveat to all these studies to date, however, is that there is wide variation in choroidal thickness among individuals. So while EDI-OCT may be useful in evaluating primary choroidal diseases and tumors, its practical use in following retinal diseases remains unclear.

Be Aware of Inter- and Intraindividual Variations In Choroidal Thickness

By Glenn Yiu, MD, PhD

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Figure 1. EDI-OCT image from a patient with a healthy thick choroid.

THICKER AND THINNER

A number of studies have used choroidal imaging to explore choroidal thickness in healthy eyes. In 54 eyes of 30 patients ranging in age from 19 to 85 years, Margolis and Spaide2 found that choroidal thickness varies topographically within the posterior pole, and there is a negative correlation of choroidal thickness with age. Using EDI-OCT, they found that the choroid is thickest beneath the fovea (mean 287 ±76 µm) and becomes thinner in all directions, especially nasally (mean 145 ±57 µm at 3 mm nasal to the fovea). Increasing age was associated with decreasing thickness, by approximately 15.6 µm for each decade of life, and thinning with age was seen at all points measured.

Usui and colleagues3 used a prototype SS-OCT, which uses a longer wavelength of light that penetrates more deeply into the eye, to measure diurnal variations in choroidal thickness. In 38 eyes of 19 healthy volunteers, they noted significant circadian variation in subfoveal choroidal thickness. The mean overall choroidal thickness was 280.3 µm, but there was a diurnal curve, with the choroid being thinnest at 6 PM (271.9 µm) and thickest at 3 AM (290.8 µm).

Looking at highly myopic patients, Fujiwara and colleagues4 found that the choroid was very thin in these eyes and that further thinning was associated with increasing age and degree of myopia. In 55 eyes of 31 patients ranging in age from 24 to 90 years, with mean refraction error of -11.9 D, mean choroidal thickness was 93.2 µm, and the researchers calculated that mean choroidal thickness decreased by 8.7 µm for each diopter of myopia (Figures 1 and 2).

Choroidal thickness has been associated with diseases as well. Spaide described an entity called age-related choroidal atrophy, characterized by global thinning of the choroid resulting in vision loss.5 On the other end of the spectrum, the choroid becomes very thick in some diseases, such as central serous choriorretinopathy (CSC). Imamura et al.6 found that subfoveal choroidal thickness in patients with CSC was significantly greater than in normal eyes, and that the normal trend of age-related choroidal thinning was not seen in eyes with CSC. Maruko and coworkers’7 subsequently showed that pho-
todynamic therapy (PDT) significantly reduced choroidal thickness in CSC, with onset of effect within days after treatment.

CLINICAL UTILITY

Some of the above findings can be clinically useful, as EDI-OCT can help to narrow the differential diagnosis and then aid in gauging the effectiveness of treatment. For example, some diseases may mimic CSC due to the presence of subretinal fluid and leakage on fluorescein angiography. However, because CSC is likely caused by choroidal perfusion abnormalities, the absence of a thickened choroid on EDI-OCT should prompt the clinician to investigate other possible etiologies.

EDI-OCT is also especially useful in the diagnosis and management of choroidal tumors. The default imaging technique for evaluation of posterior segment masses has been B-scan ultrasound, which is helpful to establish a diagnosis and to estimate tumor size and extension. Standard-depth OCT can provide information mostly about the overlying retina, but EDI-OCT lets the clinician see the choroidal lesions themselves.

EDI-OCT can be helpful, for example, in narrowing the differential diagnosis between a choroidal tumor and masquerade lesions, such as sclerochoroidal calcifications. In these cases, choroidal imaging demonstrates the choroid to be thin, with protrusion of the thickened sclera from below. By contrast, in the presence of a choroidal tumor, the choroid itself would appear thickened. EDI-OCT also provides better visualization of the outer retinal layers. Shields et al reported that characteristics such as shaggy photoreceptors and disruption of outer retinal layers, as seen on EDI-OCT, can help distinguish a small choroidal melanoma from a benign nevus. The same study also showed that EDI-OCT provides more accurate measurements of lesion thickness than traditional B-scan ultrasonography when used to follow subtle changes in lesion height.

BIG CAVEAT

The caveat to keep in mind regarding most choroidal imaging studies to date is that there is significant variation in choroidal thickness between individuals. Retinal thickness, as seen on standard OCT, is relatively uniform among individuals because the retina is composed of neural tissue, which does not normally vary or fluctuate in size. In contrast, the choroid is a vascular structure—essentially a network of blood vessels, which behaves very differently from the neurosensory retina. As noted above, the choroid is generally thinner in individuals who are elderly or highly myopic. There is still a wide standard deviation, however, in the distribution of choroidal thickness, not to mention diurnal variation. This poses a particular difficulty in studying retinal diseases in which the role of the choroid is unclear, especially if choroidal thickness changes are small. For example, in age-related macular degeneration (AMD), small changes in retinal thickness may be used to measure disease progression. But while some studies have postulated choroidal thinning or thickening in different stages of AMD, considerable variability limits our ability to definitively form a conclusion about the choroid’s role in AMD pathogenesis.

GETTING THE PICTURE

In recent years since EDI-OCT was described, device manufacturers have gotten on board with software and hardware changes to accommodate this new imaging modality. Some OCT machines now have an EDI mode that uses native software to adjust the zero-delay line and flip the inverted image. Given clear media and a skilled photographer, good quality images can usually be obtained readily.

Lin et al recently compared several currently available choroidal imaging modalities and found similar efficacy in visualizing the choroid-scleral junction (CSJ) and measuring choroidal thickness among the Spectralis (Heidelberg Instruments) in EDI mode, the Spectralis inverted image, the Cirrus HD-OCT (Carl Zeiss Meditec) in upright mode, and the Envisu SD-OCT (Bioptigen) inverted. However, the authors concluded that measurements could not be compared between the different machines because of differences in conversion factors, and they cautioned researchers against directly comparing choroidal thickness measurements made on different machines.

One challenge in EDI-OCT is in imaging individuals with very thick choroids. EDI mode penetrates deeper than conventional OCT. But if the choroid is very thick, the CSJ may be too deep to be adequately visualized. This is a problem not only clinically, but also as a potential source of bias regarding the “average” choroid in cohort studies. If complete images cannot be obtained in subjects with very thick choroids, those data tend to be dropped from analysis, thereby biasing the results toward thinner choroids.

It is hoped that, with the development of SS-OCT, the longer wavelength signal will penetrate deeper and pro-
vide better images in individuals with thicker choroids. These technologies are in the pipeline and may potentially surpass the performance of EDI-OCT when they become available.

CONCLUSION

Choroidal imaging is an exciting, novel approach to understanding the role of the choroid in the pathophysiology of various diseases. Clinically, choroidal imaging is most useful in evaluating primary choroidal diseases such as CSC and choroidal tumors. However, it is important to realize that choroidal thickness is highly variable between individuals. Subtle differences in choroidal thickness between patients, or small changes in choroidal thickness in the same person, may not be clinically significant.

Moreover, total choroidal thickness may not be as important as changes in the choriocapillaris, the thin layer of small choroidal vessels closest to the retina that is involved in outer retinal perfusion. Researchers are now working to measure the choriocapillaris independently, hoping to identify pathologic changes that may be overlooked when measuring total choroidal thickness. It should also be noted that there is no clear evidence to support a correlation between choroidal thickness and choroidal blood flow. Many recent papers have described choroidal thickness in different disease processes, but whether choroidal thickness correlates with changes in choroidal blood flow, or whether these changes are relevant to disease pathogenesis, remain unclear.

More studies in choroidal imaging, now on the horizon, will no doubt provide new insights into the role of the choroid in various retinal diseases.

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