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Proposed Lexicon for Anatomic Landmarks in Normal Posterior Segment Spectral-Domain Optical Coherence Tomography

The IN•OCT Consensus

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Purpose: To develop a consensus nomenclature for the classification of retinal and choroidal layers and bands visible on spectral-domain optical coherence tomography (SD-OCT) images of a normal eye.

Design: An international panel with expertise in retinal imaging (International Nomenclature for Optical Coherence Tomography [IN•OCT] Panel) was assembled to define a consensus for OCT imaging terminology.

Participants: A panel of retina specialists.

Methods: A set of 3 B-scan images from a normal eye was circulated to the panel before the meeting for independent assignment of nomenclature to anatomic landmarks in the vitreous, retina, and choroid. The outputs were scrutinized, tabulated, and used as the starting point for discussions at a roundtable panel meeting. The history of anatomic landmark designations over time was reviewed for the various cellular layers of the ocular structures that are visible by SD-OCT. A process of open discussion and negotiation was undertaken until a unanimous consensus name was adopted for each feature.

Main Outcome Measures: Definitions of normal eye features showed by SD-OCT.

Results: Definitions for various layers changed frequently in the literature and were often inconsistent with retinal anatomy and histology. The panel introduced the term "zone" for OCT features that seem to localize to a particular anatomic region that lacks definitely proven evidence for a specific reflective structure. Such zones include the myoid, ellipsoid, and the interdigitation zones.

Conclusions: A nomenclature system for normal anatomic landmarks seen on SD-OCT outputs has been proposed and adopted by the IN•OCT Panel. The panel recommends this standardized nomenclature for use in future publications. The proposed harmonizing of terminology serves as a basis for future OCT research studies. *Ophthalmology 2014;121:1572-1578 © 2014 by the American Academy of Ophthalmology.*

*Supplemental material is available at www.aaojournal.org.

The first report on the clinical application of optical coherence tomography (OCT) to image the fundus of the human eye in vitro was published in 1991. It described a time domain system that had a resolution of 17 μm in air and required 1.25 seconds to acquire an A-scan.[1] Widefield images with this system consisted of 150 A-scans, which took about 190 seconds to acquire, and therefore eye bank eyes were used as specimens. The authors stated that the nerve fiber layer could be visualized as a hyperreflective zone and the outer retina was hyporeflective. The retinal pigment epithelium (RPE) was visualized as a hyperreflective band distinct from the retina that had become detached. Two years later, Swanson et al[2] described a system that was compatible with scan acquisition in vivo without causing injury to living tissues. The authors reported that the retinal nerve fiber layer was highly reflective, and the photoreceptor layer had low reflectivity. Hee et al[3] described the clinical use of OCT in 1995 with a scanner capable of acquiring 100 A-scans in 2.5 seconds. This device had an axial resolution of 10 μm in the retina. Moving from within the vitreous toward the outer layers of the globe, they demonstrated that 2 regions had high reflectivity. The first layer was at the vitreoretinal interface and retinal nerve fiber layer. The second lay on the outer aspect and had an even stronger reflective signal than the first. The authors reported that this second region possibly represented "the retinal pigment epithelium and the choriocapillaris," although later in the article the authors stated the choriocapillaris alone was responsible for the second band.[3]

In an article published in 1997, Toth et al[4] compared the OCT and histologic findings of a *Macaca mulatta.* They used an OCT device with high sensitivity, 109 dB, and scanned the retina at a rate of 50 A-scans per second. The histologic images were acquired, warped to fit the OCT, and the margins of the anatomic layers were traced onto the OCT image. Areas of high relative reflectivity within the retina

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included the nerve fiber layer and the plexiform layers. The authors concluded that the outer nuclear layer and the inner and outer segments of the photoreceptors all consistently had low relative reflectivity. The RPE and the choroid together were thought to constitute a band of high relative reflectivity. Huang et al[5] in 1998 examined the characteristics of the OCT image in chickens. They saw a hyperreflective zone at the inner border of the retina and another deeper one that was similar in location to what Hee et al described. Huang et al called the second band the "outer retinal choroidal complex." The authors attributed the reflection to "multiple layers in the distal retina and proximal choroid," and specifically highlighted the possibility of the single band originating from the ellipsoid portion of the inner segments, the outer segments, the RPE, or the choroidal pigment, but discounted the possibility that the choriocapillaris contributed to the reflection.[5]

A significant advance occurred with the development of what was called "ultrahigh resolution OCT," a modality that allowed visualization of multiple bands in the outer retina. In this region, previous OCT instruments had insufficient resolution to detect and delineate the multiple layers of the outer retina and its junction with the RPE.[6] In the 2001 publication in *Nature Medicine*, Drexler et al[6] reported visualization of 3 reflective bands, which they labeled as the outer segments of the photoreceptors, the RPE, and the choriocapillaris. To further understand the relationships between ante-mortem tomographic representations of the eye and post mortem histology, Gloesman et al[7] and Anger et al[8] performed correlational studies using pigs and monkeys, respectively. In each case, the highly reflective structures in the region of the outer retina were determined to co-localize with the inner and outer segments of the photoreceptors and the RPE. The boundary between the inner and outer segments was seen to reflect little or no light.[7,8] The authors used a negative representation of the backscatter signal in which stronger reflections were viewed as darker images. Therefore, the inner segments were seen to be relatively dark, the outer segments were dark, and the RPE was dark. The junction between the inner and outer segments was bright, indicating a relative lack of backscatter. In 2003, a publication showed ultrahigh resolution OCT of the human macula.[9] In this report, the authors' annotations of the published images reveal a dark zone at the inner segments, a bright boundary between the inner and outer segments, and a dark zone for the outer segments. This kept the same dark-light-dark cadence assigned in the previous animal OCT and histology co-localization studies. Unfortunately, the OCT images were positive images, in which the stronger reflections produced brighter images. This resulted in the labeling of the boundary between the inner and outer segments as a bright band, when, in fact, previous histologic evaluations determined there was little significant reflection from this structure. Subsequent publications continued this practice of showing the boundary to be a highly reflective structure.[10]

In 2005, Zawadzki et al[11] published an article concerning what they called high-speed, high-resolution OCT imaging of the human macula. With this advance in imaging, 4 distinct bands were visible in the outer retina. The innermost was thought to be the external limiting membrane. The band below was termed the connecting cilium, which is a specific anatomic structure in the border region between the inner and outer segments of the photoreceptors. External to this structure, the authors identified a new band they thought corresponded to Verhoeff's membrane, which itself has been described as representing the dense structures of the tight junctions between the RPE cells. The outermost band was thought to be the RPE. The authors did not state how the tight junctions between the RPE cells could form a separate and distinct band with a centerline located 20 μm internal to the monolayer of cells. Thus the newly identified band could not have been Verhoeff's membrane.[12]

Internal to these bands, a relatively hyporeflective region was seen and identified as the outer nuclear layer, even in the earliest publications. The nuclei, of course, are those of the photoreceptors. The layer internal to the outer nuclear layer is the inner plexiform layer, which is a complex zone of interneuronal synapses. In histologic examination, the outer nuclear layer is about as thick as the outer plexiform region.[13] In OCT images, the outer nuclear layer is often 4 times thicker than the outer plexiform layer. One possibility for the disparity might have been incorrect assignment of a portion of the outer plexiform layer as the outer nuclear layer. Pircher et al[14] used phase resolved polarization sensitive OCT and found phase retardation at the inner aspect of the hyporeflective zone. This suggested that Henle's fiber layer was incorrectly attributed to what was called the outer nuclear layer. Unfortunately, many layers were mislabeled in the accompanying illustrations, which reduced confidence in the reported findings.

Advances in resolution, scan density, speed, and signal-to-noise ratio have now allowed discrimination of subtle layer differences in the retina. External to the highly reflective retinal nerve fiber layer is the ganglion cell layer,[15,16] which can be segmented and measured. Estimation of ganglion cell thickness has been proposed as an alternate method to test for glaucomatous damage in cases where the nerve fiber layer thickness cannot reliably be measured, such as in high myopes.[17]

The rapid development of OCT technology, particularly over the last decade, has led to the ability to resolve the multiple layers that constitute the vitreous face, retina, RPE, Bruch's membrane, and inner choroid. However the anatomic correlates that have been proposed are inconsistent and differ from known anatomy. Widespread adoption of spectral-domain (SD-)OCT devices has placed imaging technology previously reserved for a select group of research laboratories into clinical environments around the world. The nomenclature adopted by clinicians has been derived from contemporaneous designations used in some research centers when SD-OCT was first introduced. It has remained static since then, notwithstanding the variability in the names that were assigned for the various reflective layers before this time and subsequent improvements in technology.

Our understanding of disease processes, monitoring disease activity, and evaluating disease progression ultimately relies on accurate conceptualization of underlying principles of pathophysiology. Unlike many branches of medicine in which biopsy can be readily performed, the study and practice of vitreoretinal disease is uniquely dependent on

Table 1. Agreement Results from Premeeting Experts Responses

Column 1: Unanimous Agreement on Anatomic Layer and Consistency of Nomenclature	Column 2: Unanimous Agreement on Anatomic Layer But Inconsistency of Nomenclature	Column 3: Disagreement on Anatomic Layer and Inconsistency of Nomenclature
Zone 4: Ganglion cell layer	Zone 1: Posterior cortical vitreous	Zone 3: Nerve fiber layer
Zone 5: Inner plexiform layer	Zone 2: Pre-retinal space	Zone 8: Outer nuclear layer
Zone 6: Inner nuclear layer	Zone 9: External limiting membrane	Zone 10: Myoid zone of the photoreceptors
Zone 7: Outer plexiform layer	Zone 12: Outer segments of the photoreceptors	Zone 11: Ellipsoid zone of the photoreceptors
Zone 18: Choroidal-scleral juncture	Zone 14: Retinal pigment epithelium-Bruch's membrane complex	Zone 13: Cone interdigitation zone with retinal pigment epithelium
	Zone 16: Sattler's layer	Zone 15: Choriocapillaris
	Zone 17: Haller's layer	

imaging. Aristotle started our understanding of the correspondence between correctly representing objects, both in words, and now their images, as the foundation of truth. Questionable anatomic attributions interfere with the understanding of both anatomy and disease pathophysiology and thus are a hindrance to communication. With the foregoing in mind, an international panel with expertise in vitreoretinal diseases and imaging gathered to review the evidence and agree on the anatomic correlates of the zones and layers seen in OCT scans.

Methods

Selection of Participants

The planning committee for the International Nomenclature (IN) exercise consisted of 2 retinal imaging specialists (S.S., G.S.) who developed the format for the consensus proceedings. Nomenclature is the term applied to names that are given to specific features in a certain field, and this is often derived through consensus. In medical imaging, this may not necessarily correspond with anatomic terminology. The composition of the consensus panel was determined on the basis of previous notable scientific contributions to retinal imaging and disease phenotyping. Participants are listed in Appendix 1 (available at www.aaojournal.org).

Development of the Test Set of SD-OCT Images from Normal Eyes

A set of 3 individual, high-quality B-scan images from a normal eye that illustrated the various hyper- and hyporeflective bands and layers evident on OCT was assembled. Two B-scans were obtained on the Spectralis HRA+OCT (Heidelberg Engineering, Heidelberg, Germany) with an ART level of 100 frames, 1536 A-scans, and 30° wide. The third B-scan was obtained on the Cirrus HD-OCT (Zeiss Meditec Inc, Dublin, CA) using the HD Single Line Scan, composed of 1024 A-scans on a length of 9 mm, repeated 20 times, and merged with a selective pixel profiling algorithm.

On each image, selected features of the vitreous, retina, and choroid were delineated with arrows and numerically tagged. This set of tagged images was circulated electronically to all panelists 12 weeks before the planned roundtable meeting. Panelists were asked to provide a preferred name for each tagged band or feature on the OCT B-scans. Tagged images from eyes with disease were also circulated to the panelists, but are not the subject of this initial study. For each tagged structure the responses were tabulated to provide a preliminary overview of the level of consensus in nomenclature before the meeting. This process allowed the identification of those features that had the least consensus and thus were most likely to require the greatest extent of discussion. Some experts only provided a single preferred name, whereas others included a definition along with the single preferred name.

Roundtable International Nomenclature for Optical Coherence Tomography Meeting

The format of the meeting consisted of an initial presentation of the findings from the premeeting exercise. Next, a history of the naming conventions of the various structures in the fundus was presented, highlighting the variability of the names previously used for the various image features. These names were obtained by a comprehensive search of Medline. The increase in the number of layers visualized with advances in OCT and the subsequent expansion in the names attributed to the newly identified layers were reviewed. B-scan images exhibiting the tagged structures were sequentially reviewed with an ensuing discussion. The most frequently used preferred term from the premeeting survey was selected as the candidate label and served as a launching point for discussion. Dialogue was continued until consensus was achieved. In most instances, the most frequently used preferred term was selected as the consensus name. Occasionally, a less frequently used term was selected because the panelists felt that this best reflected the current level of knowledge after review of the evidence from OCT and histologic studies.

Results

Premeeting Survey Results

The expert responses in the identification of the multiple reflective layers of the posterior ocular structures on tomography showed broad consistency for some and considerable variation for others (Table 1). Column 1 shows the characteristics where there was unanimous agreement on what the OCT layer represented in anatomic terms, as well as consistency of nomenclature. Column 2 lists the layers where there was considerable agreement on what the OCT characteristic represented in anatomic terms but inconsistency of nomenclature. Column 3 lists the layers where there were both disagreements on what the OCT layer represented along with inconsistencies of nomenclature. In particular, disagreements related to descriptions of the boundaries between retinal subcompartments or where the separation between the tomographic layers was poor owing to poor resolution and merging of bands.

Table 2. List of Optical Coherence Tomography Layers as Agreed on by the International Nomenclature for Optical Coherence Tomography Panel

Layer No.	OCT Description	Consensus Nomenclature
1	Hyperreflective	Posterior cortical vitreous
2	Hyporeflective	Pre-retinal space
3	Hyperreflective	Nerve fiber layer
4	Hyporeflective	Ganglion cell layer
5	Hyperreflective	Inner plexiform layer
6	Hyporeflective	Inner nuclear layer
7	Hyperreflective	Outer plexiform layer
8	Hyporeflective band	Inner half: Henle's nerve fiber layer; outer half: outer nuclear layer
9	Hyperreflective	External limiting membrane
10	Hyporeflective	Myoid zone of the photoreceptors
11	Hyperreflective	Ellipsoid zone of the photoreceptors
12	Hyporeflective	Outer segments of the photoreceptors
13	Hyperreflective	Cone interdigitation with RPE
14	Hyperreflective band	RPE/Bruch's membrane complex. On occasion this can be separated into more than 1 band
15	Thin layer of moderate reflectivity in inner choroid	Choriocapillaris
16	Thick layer of round or oval-shaped hyperreflective profiles with hyporeflective cores in mid-choroid	Sattler's layer
17	Thick layer of oval-shaped hyperreflective profiles with hyporeflective cores in outer choroid	Haller's layer
18	Zone at the outer choroid with a marked change in texture in which large circular or ovoid profiles abut a homogenous region of variable reflectivity	Choroidal-scleral juncture

OCT = optical coherence tomography; RPE = retinal pigment epithelium.

Expert Discussions at the Roundtable International Nomenclature for Optical Coherence Tomography Panel Meeting

Having considered the variation in description and terminology that became apparent in the naming exercise, the group formulated certain rules that were adhered to during the discussion process.

- To number each of the reflective bands from the vitreous to the choroid.
- To provide a definition for each of the numbered reflective bands through attribution to the anatomic correlate.
- To avoid the use of the term "line," which is not relevant to anatomic correlates because a "line" is a 1-dimensional structure.
- To use terms such as "band" or "layer" to describe a discrete and defined lamina (eg, inner plexiform layer).
- To use the term "zone" as needed when it has better applicability to the description of tissue components. This helps to deal with regions of tissue that cannot be clearly delineated from each other with present technology. This can occur when an OCT feature is seen to be localized to a particular anatomic region, but the specific reflective structure has not been definitively proven or because the anatomic layers are inseparable owing to interdigitation of cellular structures and tissues (e.g., RPE/Bruch's complex).

The group considered each of the visualized features in turn, commencing with the innermost at the vitreoretinal interface and progressing toward the choroid–scleral interface. Table 2 lists 18 zones in numerical order, progressing from the innermost to the outermost OCT-determined layers of the retina as agreed by the experts (Figs 1 and 2).

Regions Eliciting Discussion

Zone 8: Outer nuclear layer and Henle's fiber layer. The hyporeflective zone between the external limiting membrane and the outer plexiform layer was previously attributed to the outer nuclear layer. However, the relative thickness of this zone in the SD-OCT outputs is exaggerated when compared with histologic preparations. By changing the angle of the SD-OCT illumination beam,[18,19] Henle's fiber layer, composed of the axons of photoreceptors, becomes visible, and can be seen to contribute to the inner region of this zone. Close examination of an untilted OCT scan shows a subtle demarcating transition at the same defining zone as the altered reflectivity caused by tilting. The portion internal to the demarcation was attributed to Henle's fiber layer and the outer portion to the actual outer nuclear layer. Henle's fiber layer is among the defining features of the macula; consequently, the relationship described herein would not be seen in the peripheral retina. In addition, the central bouquet of Rochon-Duvigneaud,[20] found in the fovea, is a special eruption of diverging cones and Muller cells that synapse with ganglion cells in the perifoveal region.

The hyperreflective layer attributed to the outer plexiform layer corresponds with the synapses between cone pedicles and rods spherules with dendrites of horizontal and bipolar cells. For the reasons cited, it seems reasonable to refer to this layer as the dendritic outer plexiform layer.

Zone 10: Myoid zone. The hyporeflective region between zone 9 (external limiting membrane) and zone 11 (ellipsoid zone) has not been recognized as a distinct layer in the OCT literature. The anatomic correlate for this region has been proposed,[10,21] and current evidence supports the attribution of this OCT feature to the myoid portion of the inner segments. Given that it is difficult to attribute the lack of a reflection to a particular structure, the term "myoid zone" was selected. The reduced reflectivity of this zone is thought to be owing to the lower packing density of mitochondria in the myoid as opposed to the ellipsoid region of the photoreceptor.

Zone 11: Ellipsoid zone. The hyperreflective region (number 11) has been termed, among other names, as the interface between inner and outer photoreceptor segments. This view has been disputed because it would be in the incorrect position between the external limiting membrane and the RPE, the reflectivity is high, and thickness of the zone in SD-OCT is inconsistent with the reflection originating from a boundary. Another suggestion for this layer was that the reflection originated from the connecting cilium. This seems even less likely because the cilium is a loose collection of microtubules that has an aggregate diameter of 0.25 μm. Recent data with anatomic reconstruction show better correlation with the ellipsoid component of the photoreceptors,[21] which are packed with mitochondria and have the potential for high reflectivity. The group proposed that this hyperreflective zone should be

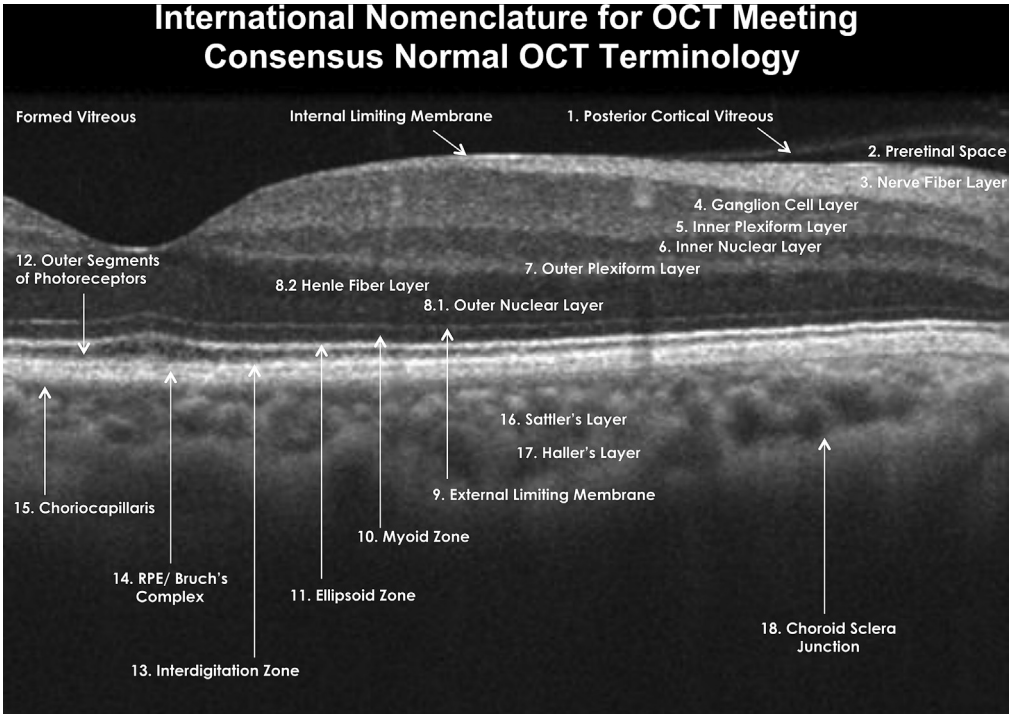

Figure 1. Nomenclature for normal anatomic landmarks seen on spectral domain optical coherence tomography (OCT) images proposed and adopted by the International Nomenclature for Optical Coherence Tomography Panel. Healthy retina imaged using Heidelberg Spectralis. RPE = retinal pigment epithelium.

designated the "ellipsoid zone." This name avoids attribution of the OCT feature specifically to 1 anatomic structure until more definitive evidence becomes available, but it retains the information content of currently available evidence.

Zone 13: Interdigitation zone. The outer hyperreflective band has been attributed to Verhoeff's membrane.[11,22] Verhoeff's membrane has been described as the tight junctional complexes between RPE cells that are visible as a band on electron microscopy. However, hyperreflective zone 13 lies anterior to the RPE complex and thus has been proposed to represent photoreceptor outer segment tips as its anatomic correlate.[23] However, the zone has a thickness greater than would be suggested by just the outer

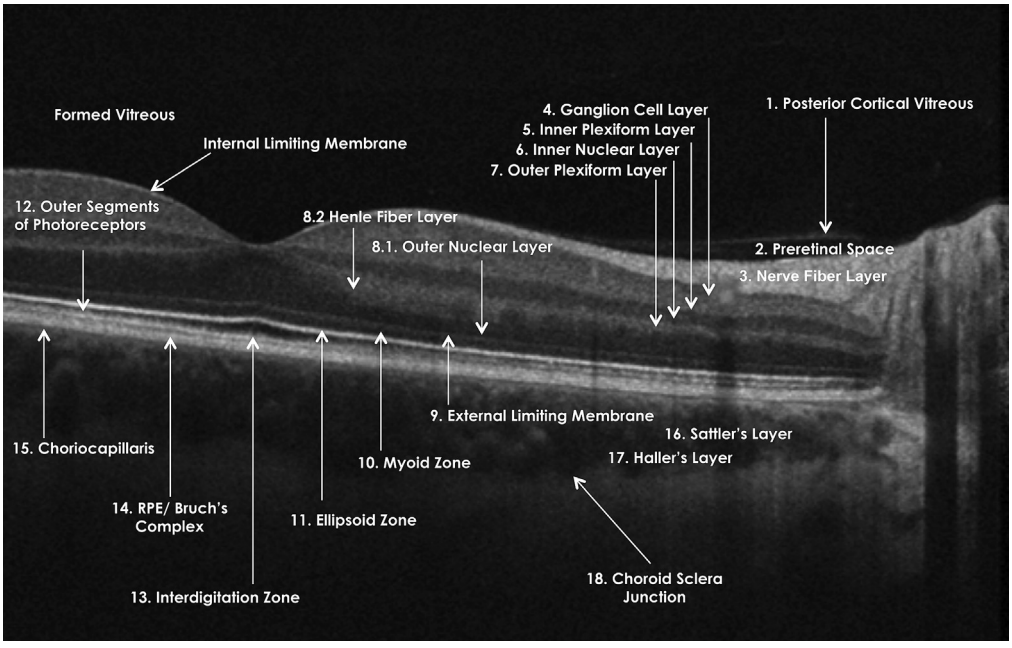

Figure 2. Nomenclature for normal anatomic landmarks seen on spectral-domain optical coherence tomography (OCT) images proposed and adopted by the International Nomenclature for Optical Coherence Tomography Panel. Healthy retina imaged using Zeiss Cirrus. RPE = retinal pigment epithelium.

segment tips and may represent the interdigitation of the apical processes of the RPE with the cone outer segments. As such, stating the reflection is solely from the cone tips seems to be an overspecification without sufficient supporting evidence for such a restrictive interpretation of the feature. Because the band is in the region where the interdigitation should occur, the group therefore agreed that this band should be termed the "interdigitation zone."[13]

Zone 14: RPE/Bruch's complex. With the higher resolution of SD-OCT, the single band previously attributed to the RPE can now occasionally be seen as 2 distinctive hyperreflective bands separated by a hyporeflective zone, particularly when pathology is present. The group agreed that these 2 hyperreflective bands correspond with the RPE and Bruch's membrane and that they are often not separable under normal conditions. Therefore, this zone should be defined as "RPE/Bruch's complex."

Zones 15 to 17: Choriocapillaris, inner and outer choroid. With enhanced depth imaging of the choroid, distinct layers of varying reflectivity can be observed. The innermost portion of the choroid is relatively hyporeflective. Current limitations in optical penetrance and resolution prevent definitive identification of the choriocapillaris in normal eyes. Immediately posterior to where the choriocapillaris is located, small hyperreflective structures can be seen and have been attributed to feeding arterioles to and draining venules from the choriocapillaris. The precise distinction between the medium and large choroidal vessels that comprise Sattler's and Haller's layers respectively was defined clearly before OCT, and no clear differentiation is visible by OCT. This is understandable because Sattler's original description concerned a reputed elastic layer in the middle of the choroid and not the vessels. Therefore, it seems more appropriate to assign the small oval vascular profiles to the Sattler's layer and the larger outer oval vascular profiles to the Haller's layer in keeping with the ambiguous histologic definitions currently in place.

Discussion

In this report, we have described the consensus nomenclature for OCT findings in normal eyes based on the deliberations of retinal and imaging experts comprising the International Nomenclature for Optical Coherence Tomography (IN•OCT) Panel. The present generation of spectral-domain OCT allows the retina and the choroid to be imaged in unprecedented detail. It is expected that the future will bring more of the same, so the goal of the panel was to codify current understanding and provide a framework to integrate future developments. To aid the taxonomy of existing OCT findings, the panel reviewed the history of the findings and feature attributions, and then reviewed features visualized by current OCT instruments. Likely anatomic correlates received ready assent from panel members for many structures, whereas other features required careful logical parsing of numerous possibilities. In the absence of recognized specific evidence to assign an attribution, the term "zone" was used along with the local anatomic region. This avoided the problem of overspecification of the attribute in the absence of exacting proof. Future improvements in imaging with the expected enhanced resolution will provide better images, and the information obtained can be used to refine this proposed classification scheme.

Intracellular structures and interfaces between the different cellular and nerve fiber layers of the retina and other constituent structures can be resolved with OCT, but the layers easily seen and highlighted by stains in ordinary microscopy are not necessarily seen as reflective structures in OCT. The outer nuclear layer is a ready example. It is a densely packed layer that stains with typical stains or dyes used in histologic evaluation, but seems nearly devoid of any reflection by OCT imaging. This is an important complicating factor in properly assigning layer names. The number and clarity of visualization of the layers rapidly increased with the evolution of OCT, and the multiplicity of laboratories that were the sources of information resulted in a haphazard development of a nomenclature in describing the tomographic details.

Optical coherence tomography morphed from a research instrument available to a select few to a pervasive, everyday tool in clinical practice, with many treatment algorithms heavily dependent on the findings of tomographic imaging. Therefore, there is a pressing need for the construction of a pragmatic and consistent glossary of terms constituting an OCT lexicon. The present report represents the first coordinated, international, systematic, and structured exercise to codify a terminology to facilitate communication in this field.

This exercise has several limitations. First, the expert panel had a finite number of participants as dictated by pragmatic considerations. There is an extensive pool of recognized leaders in the field of ocular imaging who were not included. Second, the panel assigned names based on contemporaneous concepts; if history is any guide, they are likely to need revision in the future. This is the iterative nature of science. Third, the index of illustrative OCT sections were obtained with only 2 SD-OCT devices, using single averaged B-scans as the scanning protocol. The scan results of competing SD-OCT instruments has been found to be highly comparable, but there may be subtle variations in scanning performance from 1 instrument to another that may have influenced the outcome.

Through a consensus-driven process undertaken by the IN•OCT Panel, an initial nomenclature for the various hypo- and hyperreflective features visible in SD-OCT scans of normal eyes has been proposed. The members of the IN•OCT Panel consider this classification system to be a dynamic construct that requires continuous updating based on improvements in OCT technology and new discoveries. This classification system, however, may provide a method for harmonizing terminology in ongoing OCT research studies. We recommend adoption of this terminology by authors of future publications.

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Abbreviations and Acronyms:
IN•OCT = International Nomenclature for Optical Coherence Tomography; **RPE** = retinal pigment epithelium; **SD-OCT** = spectral-domain optical coherence tomography.

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