Editorial

Questioning Optical Coherence Tomography

Richard F. Spaide, MD - *New York, New York*

Any sufficiently advanced technology is indistinguishable from magic.

Arthur C. Clarke

The increasing sophistication of modern technology is impressive to even the most jaded, but after a while it gets easier to think of technological devices, or in the case of ophthalmic imaging equipment, as black boxes that accomplish specific tasks. The problem with black boxes is that we may fail to appreciate the logical underpinnings of how they actually work. The results may seem a bit like magic, but we are rational creatures and to avoid the failings of magical thinking we can end up doubting or questioning the output. For example, it is common to hear someone present a new imaging finding and invariably someone from the audience will express doubt that the new finding is anything but an artifact. Questioning is good; it is the basis of a really big black box, science. However, artifacts are explainable if one understands the functioning of the imaging device. So a logical response to any assertion of a finding being an artifact is to ask: what physical principles would account for the creation of the proposed artifact?

In optical coherence tomography (OCT), light is split into 2 separate paths. One is directed into the tissue being evaluated, while the other travels an equal length route and is used as a reference. In the other arm, light backscattered (reflected back) by tissue has the potential to interfere with light in the reference arm, if the 2 are highly correlated, which is another way of saying they are coherent. To limit the axial range sampled short coherence light, typically having a coherence length of 5–7 μm, is used. That is how the axial resolution of OCT devices is derived. Lateral resolution is controlled by the size of the spot illuminating the tissue. Given the wavelengths used and the numerical aperture of the illuminating system in commercial OCT devices, the spot is usually no smaller than 14 μm in diameter. Commercially available OCT instruments use similar light sources and have similar detection systems, as these largely are dictated by price of the underlying optoelectronic components. With that knowledge one would expect the imaging of the outer retina, a layered structure vitally important in light detection, to be roughly similar from 1 instrument to another. How similar is the question? In this issue, Terasaki et al[1] teaches us that the images from various OCT instruments are very similar. Question asked, question answered, and the answer is rational given what we know about the physics of OCT.

The most erroneous stories are those we think we know best – and therefore never scrutinize or question.

Stephen Jay Gould

The interpretation of what those lines represent has an interesting, and what appears to be a flawed, history. In 1991, OCT was first described,[2] and because the instrument could only perform 2 A-scans per second, an autopsy eye was imaged. By 1997, the speed and resolution of OCT imaging advanced considerably and Toth et al[3] compared OCT images of the monkey retina to light microscopic examination of the same. They determined that there were no OCT reflections from the outer retina of the monkey. In 1998, Huang et al[4] described a reflective structure in OCT images that they called the outer retina-choroid complex. To determine what accounted for this bright line they analyzed waveforms of the OCT image. Throughout the manuscript they attributed this reflective structure to either the inner segments (IS) of the photoreceptors, the retinal pigment epithelium, the inner choroid, or possibly the outer segments (OS) of the photoreceptors. In 2001, Drexler et al[5] published a paper concerning ultrahigh–resolution OCT, which was a giant step forward in optical resolution. They were able to visualize several bands in the outer retina, and they labeled these layers using designations that were quite different from what we use today. To investigate this issue further, Drexler et al[5] published articles from 2 studies showing correlation between the histology of retinal sections and the corresponding OCT images; 1 used the pig, and the other the monkey. In each study they used a negative image from the OCT. In this methodology stronger reflections produce darker portions of the image. In each article, the authors found the OS backscattered light, the IS backscattered light, but the boundary between the 2 (also known as the IS/OS boundary) did not. So the inner segments were dark, the OS were dark, and the line in between, the IS/OS boundary, was bright in the negative image.[6,7] In a clinical paper published contemporaneously by the same authors, a reference image of a human macula was shown, but in keeping with conventions in clinical imaging it was a positive image.[8] In that usage the stronger the reflection, the brighter the image appears. Unfortunately, the authors transposed the histologically confirmed labels from the negative image to the positive image. In the positive clinical picture a dark band was labeled as the IS, a nearby dark band was labeled as the OS, and the bright line in between was called the boundary between the IS and OS. This dark-bright-dark cadence was the same as the negative image, but unfortunately the authors were labeling a positive image. That would mean the IS/OS boundary reflected light, which the previous histologic correlations showed it didn't. Thus, the idea that the boundary between the IS and OS is a bright band is a mistake because of a labeling error.

Shortly thereafter, spectral domain OCTs became commercially available. There were no patent issues, so soon everyone could make high-resolution images. What should the layers be called? Well it seems that the names from previous papers served as a guide. So thereafter everyone called the bright band in the outer retina the boundary between the IS and OS, although that was not correct. That

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term is still used today and strongly influences how we think of retinal pathophysiology. No one questioned the rationale or the science behind the naming convention. Thousands of clinical papers published over the years using this terminology all have a basic inherent error. Only recently has re-evaluation of the outer retinal layers begun[9] (Fig 1, available at http://aaojournal.org). We are certain we are imaging something consistently from one OCT instrument to the next, but what we are imaging has yet to be settled.

References

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Correspondence:
Richard F. Spaide, MD, Vitreous, Retina, Macula Consultants of New York, 460 Park Ave. Fifth Floor, New York, NY 10022. E-mail: rickspaide@gmail.com.

Erratum

With apologies from the authors of "Vascular endothelial growth factor Trap-Eye for macular edema secondary to central retinal vein occlusion: six-month results of the phase 3 COPERNICUS study." Ophthalmology (2012;119:1024–32) in Figure 2 the *P* value of 0.0001 is incorrect; the correct *P* value is 0.001.

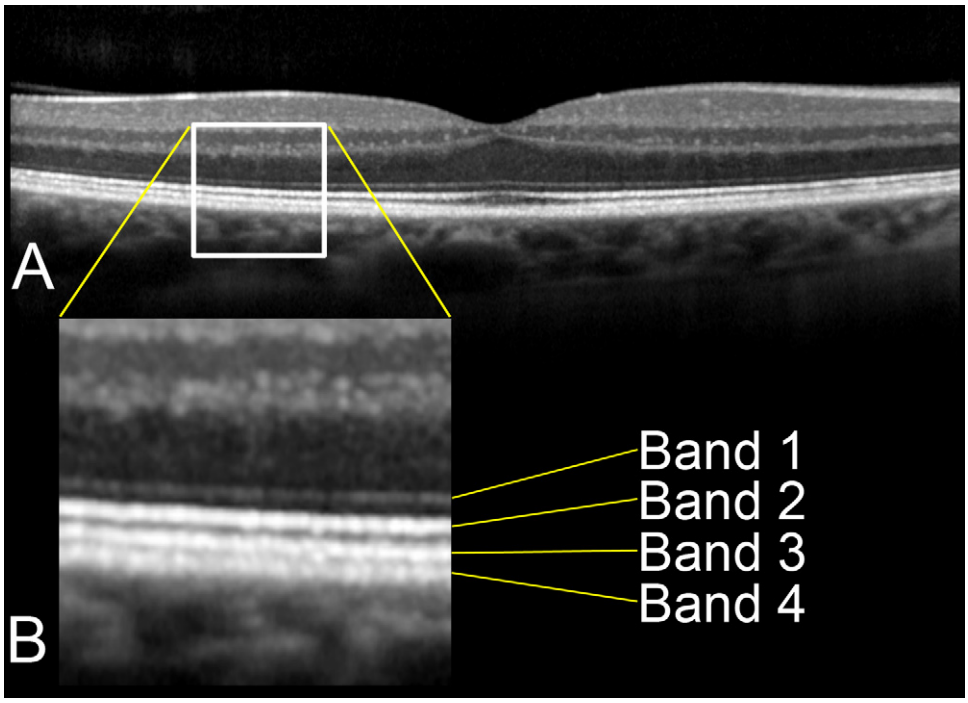

Figure 1. Bands in the outer retina and proposed anatomic correlates. Band 1, the external limiting membrane, is formed by the confluence of reflections from the tight junctions between the photoreceptors and the Müller cells. Band 2, is the ellipsoid portion of the inner segments and was formerly called the boundary between the inner and outer segments. Band 3 is the interdigitation between the apical processes from the retinal pigment epithelium and the cone outer segments, which stop well above the level of the retinal pigment epithelium. Band 4 is the retinal pigment epithelium (RPE), although it is possible this band also includes reflections from Bruch's membrane with or without the underlying choriocapillaris. Proposed names are Band 1, the ELM, Band 2, the Ellipsoid Zone, Band 3, the Interdigitation Zone, and Band 4, the RPE complex.