Editorial

Correlation of optical coherence tomography with retinal histology

Correlación de la tomografía de coherencia óptica con la histología retiniana

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Optic coherence tomography (OCT) is a fundamental tool in clinical practice. Its introduction has revolutionized imaging tests in ophthalmology and made OCT irreplaceable for studying and diagnosing specific diseases as well as for taking therapeutic decisions and making post-surgery functional assessments. It renders 2- or 3-dimensional sections, measuring the delay in the transmission of light reflected over a reference mirror and the amount of light absorbed or reflected by the retina layers on the basis of the interferometry principle.1 Due to increased acquisition speed, spectral domain or Fourier tomographs are able to reduce artifacts caused by ocular movements and enhance the definition of the various retina layers.2

Since the use of spectral domain OCT (SD-OCT) has become widespread we have become acquainted with terms such as hyper-efringent lines and their correlation with the retina layers. However, there is no consensus about said histological correlation between groups and not even within the same group. The light is reflected the most in the layers where the fibers or membrane structures are distributed perpendicular to the impinging light, or at intercellular junctions. If tissue elements run parallel to the light beam, the light dispersion or reflection would be smaller. Accordingly, due to its distribution which runs at right angles to the light beam, the retina nervous fiber layer generates a hyper-efringent light in the internal retina. The nuclear and plexiform layers are defined as lines with low or mean refraction. As a correct interpretation of OCT is highly relevant in the diagnostic, treatment and prognosis of retinal diseases, it is crucial to determine the exact nature of each of the strips observed in the OCT.

In high resolution tomographs, the external retina appears as four hyper-efringent parallel lines separated by mean reflectance lines. The innermost line, which is least obvious in the tomographic image, corresponds to the external limiting membrane (ELM). The following line is that which we refer to as the junction line between the inner and outer photoreceptor segments (IS-OS). However, why should the junction between both produce such a wide hyper-efringence strip? As the joint between the inner and outer segment is limited, it would involve a narrow line of reflection below the resolution capacity of existing SD-OCT. However the size of the so-called IS-OS strip is similar to that of the other strips. On the other hand, if the reflection of said strip would be due to the membrane of the outer segment discs, it would appear throughout the length, reaching the pigment epithelial cells. In addition, we have assigned it a high value and related it with the recovery of visual acuity in various retinal diseases after surgery. Perhaps we have not pondered enough the possibility that the

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disappearance of the outer segments need not have a prognostic value for functional recovery. There are many diseases in which these segments disappear, such as in the first hours after a retina detachment. However, the outer segments are structures that can be generated once again when the photoreceptor has recovered its function. In addition, it must be taken into account that in the foveal area the length of the inner and outer photoreceptor segments is relatively similar. How could we explain that the arrangement of this line is closer to the ELM than to the retina pigment epithelium (RPE)?

Under the well-known junction line of the inner and outer segments we have another hyper-efrangent line which either represents the outer segment terminals or what is known as Verhoeff’s membrane, described by said author and relating it to the apical junctions of the RPE cells. However, if this hyper-efrangement line actually corresponds to the apical RPE junctions, why should it be separated from the fourth hyper-efrangement, which represents the RPE cells and Bruch’s membrane? And if it is only the outer segment terminals, why is it so clearly differentiated?

In a paper published in Retina in 2011, Richard Spaida and Christine Curcio assessed the anatomic correlation with the hyper-efrangent lines usually observed in our tomographs. Using reproductions of the foveal and perifoveal region of the external retina, they correlated their schemas with the findings obtained with Spectralis (Heidelberg, Germany) and Cirrus (Carl Zeiss, USA) tomographs. With their model, they have concluded that said IS-OS is no such thing. Instead, it is a line representing the ellipsoids of the cones located in the outermost portion of the inner photoreceptor segment. Ellipsoids are full of mitochondria and these membranous structures, which in the cone are arranged in a particular manner with a longer and thinner morphology, could be the cause of the hyper-reflectiveness lines. The same interpretation of this strip was made with high resolution tomographs and aberration correction. If this strip actually represents ellipsoids, its importance in OCT analysis remains vital because the loss of mitochondria inexorably determines the death of photoreceptors. The third line does not seem either to represent what we thought it did. At the level of the apical portion of the RPE cells, the epithelial cell establishes its contacts with cones by means of apical extensions, forming sheaths that cover the outer cone segment which has been defined as the “contact cylinder”. If this is the junction that gives rise to reflectiveness, it would explain that the third and fourth layer at the central foveal level are virtually joined because the aposition between the cells at the foveal level is much greater. In their analysis, said authors reach the conclusion that the first hyper-efrangent layer is ELM; the second represents the photoreceptor ellipsoids, which could be named as “inner segment ellipsoids” (ISE); the third represents the sheaths of the pigment epithelium cell extensions with the outer portion of the outer segments, while the fourth strip is mainly generated by the RPE. However, said authors expressed their inability to establish the contribution made by the Bruch membrane. As it is in fact a basal membrane due to its thinness and composition, it is unlikely that the Bruch membrane could produce a noticeable hyper-reflectiveness strip when joined to the RPE. The need to clarify and standardize the names of OCT layers on a histological basis is essential in order to develop appropriate interpretations to determine the diagnostic and treatment of retinal diseases. Just like other tasks, this one can give rise to debate, besides the fact that the authors made clear that their results are only preliminary. A definitive establishment of the correlation between OCT and histology must be taken into account when we analyze the results of our OCT scans in the clinic.

In the near future, the advent of new OCT systems with greater wavelengths will enable an improved analysis of deep structures which are as yet hardly known and studied, such as the choroids. Spaida et al. have modified the SD-OCT data acquisition in order to improve the visualization of the choroids, enabling the measurement of its thickness and the differentiation between the choriocapillary and the large vessels layer. Similarly, it is possible to identify a hyper-reflectiveness line that could represent the Bruch membrane (its thickness is below the resolution capacity of existing SD-OCT) when it is separated from the RPE or in eyes with RPE atrophy (Fig. 1).

The density of the vascular structure of the choroids and its pigmentation restrict the penetration of current OCT system waves. However, in cases with RPE and choroids atrophy, the identification of the sclera is possible. The limits of OCT are yet to be established as the new OCT systems with greater wavelengths (close to 1060 nm) have higher penetration capability and can obtain images at the same time from the vitreous up to the sclera, with high resolution and in minute detail, thus enabling us to study the range from the vitreous–retina interface to the choroidal thickness, as can be seen in Fig. 2.

The correlation of hyper-reflectiveness lines with their corresponding retinal structures in different diseases is a

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**Fig. 1** – Retina scan focused on the choroids, hypothetically showing the Bruch membrane (Topcon 3D-OCT 2000).

**Fig. 2** – Image obtained with the Topcon Swept-Source prototype which produces scans that are longer (12 mm), have higher resolution (axial resolution of 8 μs in the tissue) and with greater penetration (we can see up to the sclera).
challenge that would help us to improve the diagnostic and prognosis of retinal diseases.

REFERENCES