Optical Coherence Tomography: A review of current technology and its implications for clinical applications

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Abstract
Optical Coherence Tomography (OCT) has become an invaluable tool in many ophthalmology departments and is in use in some optometric practices where it is applied in the examination of a variety of acquired and genetic ophthalmologic conditions, including age-related macular degeneration and diabetic retinopathy. While image interpretation may initially seem simple, proper interpretation relies on a thorough understanding of the theoretical background of image generation. This review utilizes case examples to enhance this understanding.

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Background

OCT imaging system

Commercially available OCT systems are based on low-coherence interferometry, generally using a broadband infrared laser diode with a centre wavelength of 840 nm. In contrast to most laser sources, the low-coherent light in OCT is not restricted to a narrow range of wavelengths and the bandwidth is typically in the range of 20-40 nm. In experimental systems the bandwidth is even broader. A broad bandwidth is required in OCT, as the axial resolution is inversely proportional to the bandwidth (Marschall, Sander, Mogensen, Jørgensen, & Andersen, 2011; Xi, Mei, Brauler, Zhou, & Ren, 2011). Current commercial systems have an axial resolution of approximately 5 µm, making it theoretically possible to visualise individual cells. The image in Figure 1 shows an OCT scan performed under favourable conditions, but where resolution on a cellular level is still not achieved. This is due to the resolution in the transversal plane which in the absence of adaptive optics, is limited by the optics of the eye to approximately 15 µm.

The laser beam used in an OCT system is split into two pathways: one within a reference arm and one directed towards the eye. The OCT image is generated using light back-reflected from these two pathways i.e. from a reflector in the reference arm and from the tissue being examined (Marschall et al., 2011). These two reflections form an interference pattern which is subsequently analysed with a spectrometer grating within the OCT system. Previous time domain OCT systems utilized a moving mirror in the reference arm, limiting acquisition speed, but with the introduction of a fixed reference and analysis of the interference pattern by spectroscopy, the scanning speed is increased, making it possible to obtain up to 50,000 A-scans per second. In experimental systems even higher speeds can be achieved. Further signal processing is performed via Fourier transformation of the spectroscopic data and the instrument is thus termed Spectral-Domain (SD) or Fourier Domain (FD) OCT. The software shows the images as cross-sectional B-scans, each composed of approximately 500 to 4096 A-scans, and as a consequence of the high acquisition speed, multiple A-scans or B-scans from the same location may be averaged to reduce random noise and the speckle noise inherent in OCT, thereby improving signal to noise ratio (Sander, Larsen, Thrane, Hougaard, & Jørgensen, 2005). Averaged images of B-scans have been used for the majority of the examples shown, but it should be noted that averaging is not useful in subjects with severely impaired fixation where a reasonable acquisition time may be impossible.

The image quality of Spectral-Domain OCT varies from the top to the bottom of the acquisition window seen on the screen and correspondingly, from the inner to the outer retina. The degradation with depth is due to a decrease in signal to noise ratio and resolution and is related to the Fourier transformation (Spaide, Koizumi, & Pozzoni, 2008; Xi et al., 2011). The frequency pattern on the spectrometer, at the top of the image is represented by a low frequency and corresponds to the most optimal resolution and sensitivity, while the deeper retinal structures imaged at the bottom in the imaging window are represented by a high frequency and lower quality.

Qualitative evaluation of OCT

The image quality from the retinal layers should be maximised and therefore it is important that the OCT scan is placed as high as possible in the acquisition window on the computer screen during the examination. The quality of the OCT image may be estimated by the overall signal to noise ratio given by the software of the respective OCT system software, but in clinical use, the examiner's visual impression of the OCT image is the best guideline.

The differences in signal intensity between the retinal layers allow identification of classical histological layers. On the OCT image nuclear layers are low-reflecting and synaptic layers are high-reflecting. A qualitative marker of the OCT image quality is the appearance of retinal vessels (see Figure 1). The vessels are seen as bright dots in the inner layers with a shadow beneath them. If the quality of the OCT image is high, the shadow is distinct.

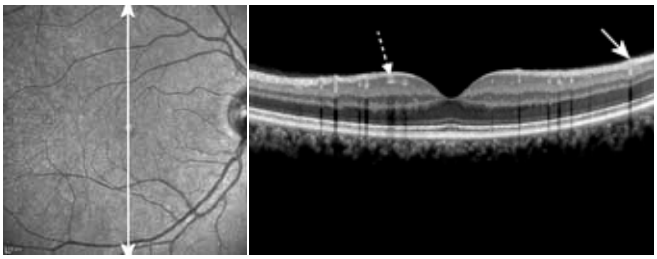

Figure 1. A vertical OCT scan through the fovea of a healthy subject. The whole scan (also called a B-scan) is composed of 768 A-scans. Beneath the high-reflecting retinal nerve fibre layer, the retinal vessels are seen as bright dots in the inner retinal layers with sharply defined shadows below (arrow). Some vessels are sectioned along the scan and the vessel section is elongated in the B-scan (dashed arrow).

Scatter and signal intensity

Both for acquired and inherited disease, the status of the outer retinal layers is of major importance, as changes in these layers may be correlated with visual loss (see Figure 2, left) (Christensen, et al., 2010; Christensen, Krøyer, Sander, Larsen, & la Cour, 2009). The photoreceptor layer, i.e. the nuclei of rods and cones, appears dark and beneath it the external limiting membrane is

seen as a high-reflecting but very thin line which appears less intense than other reflecting layers. The external limiting membrane is visible in the majority of OCT scans. Where this is not the case, it indicates decreased OCT image quality or severe pathology. The inner (IS) and outer segments (OS) of the photoreceptors appear dark, and between them the high-reflecting junction between the inner and outer segments stands out as a bright line. Very recent evidence reveals that the appearance of this line may be due to mitochondria in the outermost portion of the inner segment of the photoreceptors (Spaide & Curcio, 2011). The IS/OS line is dome-shaped in the fovea, as the outer segments below the line are longer in the fovea. It should be continuous through the scan, except for a tiny point in the fovea where small interruptions may be present. An example from a patient with reduced visual function is shown in Figure 2 (right), where an interruption is seen in the junction between inner and outer photoreceptor segments, probably due to a photoreceptor atrophy of genetic origin. This sign, sometimes referred to as a "bubble" is pathognomonic for achromatopsia, an autosomal recessive hereditary eye disorder resulting in nystagmus, photophobia, poor colour vision, and reduced acuity from birth.

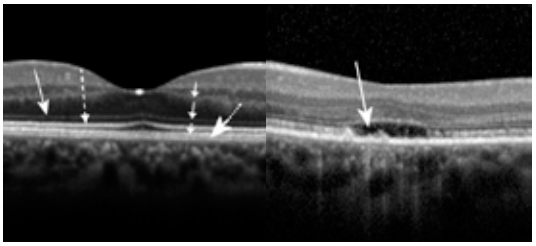

Figure 2. Left: Enlarged foveal region of a healthy subject in high-resolution comprised of 1536 A-scan on the original B-scan. In the outer retina, the layers on an OCT image include the nuclear layer of the photoreceptors (dark), the external limiting membrane is seen as a thin grey line (arrow), the inner segments of the photoreceptors (dark), the junction between the inner and outer segments (dashed arrow), the outer segments (dark) and an interdigitating zone of outer segments and the retinal pigment epithelium (repeated arrow) and as the outermost layer, the bright zone of retinal pigment epithelium (dotted arrow). The basement membrane of the pigment epithelium, Bruch's membrane, is a bright line but is not seen unless a pigment epithelium detachment lifts the overlying RPE. Right: OCT of a patient with presumed achromatopsia. The external limiting membrane is visible throughout the scan, while the junction between the inner and outer segments is absent in the centre (arrow).

OCT is used extensively for the evaluation of retinal thickness in diseases causing retinal oedema. The qualitative and quantitative evaluation of intraretinal and subretinal fluid aids in determining whether therapy with intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF) is indicated. In patients with a gross thickening of the retina, the image quality is often decreased with low signal intensity, probably due to large amounts of fluid and increased scatter, and thereby a decrease in the amount of light reflected directly back to the detector. Figure 3 shows an example of a diabetic patient who presented with significant central retinal oedema which had not responded to macular photocoagulation. The Snellen visual acuity was 0.2. The left hand side of Figure 3 shows low signal intensity, and the morphology of the outer retinal layers, and therefore the potential for improved visual function, cannot be determined. The patient was treated with anti-VEGF, and one week later the oedema was nearly resolved and the retinal thickness approximately normalized (Figure 3, right). The signal intensity increased, indicating that the low signal intensity before injection was related to intraretinal scatter and not to cataract or other media opacities. It was also observed that the normal dark band of photoreceptor nuclei was absent, and the IS/OS junction was not visible. Although a brief improvement in visual acuity was seen 1 month after treatment, the final visual acuity was unchanged despite several additional treatments. The absence of a visible IS/OS junction indicates poor prognosis for improvement in visual acuity after resolution of oedema.

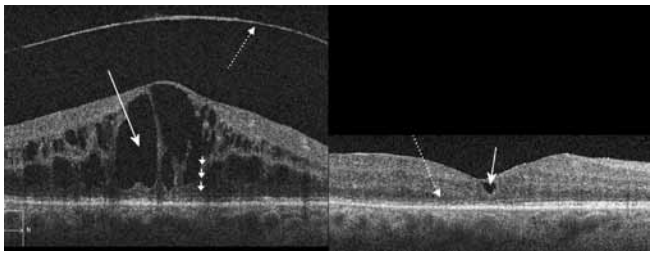

Figure 3. OCT from a patient with persistent macular oedema. Left: The patient had persistent oedema (arrow) despite previous photocoagulation and at the top of the image the posterior hyaloid membrane is seen (dashed arrow). The overall signal to noise ratio calculated by the software was decreased from a maximal value of 10 to 6, a decrease is often seen with extensive oedema. Due to the low signal intensity and absorbance of the thickened retina, interpretation of the status of the deeper retinal layers is difficult (repeated arrow). Right: After treatment with anti vascular endothelium factor (anti-VEGF) the oedema decreased markedly. The small cyst (arrow) in the centre disappeared later. Note the lack of the dark photoreceptor layer in the fovea (dashed arrow) and the low intensity of the inner and outer segment signal compared to a healthy subject (Figure 2, left). Both these features indicate lack of normal morphology. The overall signal to noise ratio increased to 9 out of 10 as the intraretinal scatter and absorbance from the oedema was diminished.

Absorption

The central wavelength of the laser allows some penetration of the retina down to and including the retinal pigment epithelium and Bruch's membrane. To some degree it is also possible to visualise the choriocapillaris and choroidal vessels. In cases of accumulation of intraretinal material, the visualisation of the choroid may be severely obscured due to the light absorption of the material. Figure 4 shows an OCT of a patient with Best's disease. In this genetic disease, lipofuscin accumulates in the retinal pigment epithelium and an egg-yolk appearance is seen in the fundus (Figure 4, left) and at the same time the choroid is no longer visible in the OCT due to the high absorbance of the accumulated lipofuscin (Figure 4, right).

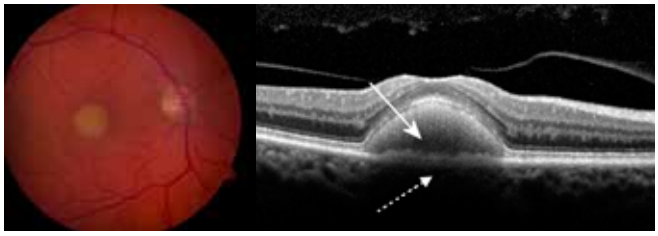

Figure 4. A patient with Best's disease. Left: The accumulation of yellow deposit (lipofuscin) is seen in the fovea on the fundus image. Right: The OCT shows the same accumulation located in the outermost retina (arrow), and the signal from the choroid is no longer detectable (dashed arrow). Beneath the dome-shaped elevation, the signal intensity is low at the level of the retinal pigment epithelium probably due to absorbance by the overlying layer, but pathologic changes in the retinal pigment epithelium may also be a cause.

Figure 5 shows a patient with dry age-related macular degeneration, with large drusen in the fovea. Due to the separation of the retinal pigment epithelium from Bruch's membrane, Bruch's membrane is now seen as a distinct thin line beneath the greyish drusenoid deposits.

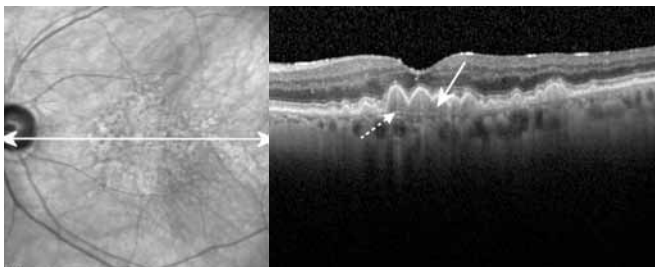

Figure 5. A patient with dry AMD. Left: Fundus photo. The arrow shows the direction of the OCT. Right: Numerous large drusen are seen beneath the fovea (arrow). Bruch's membrane is seen as a thin line at the bottom of the drusen (dashed arrow).

Visualisation of the choroid by inverted images

As the spectral domain instruments use Fourier transformation in the transformation of a frequency signal to a time-delay representation, two images are formed (+1 solution and -1 solution of the Fourier transformation). Many examiners have noticed a disturbing mirror image at the top of the acquisition window. In fact, this theoretical problem may be utilized to increase the quality of the examination of the choroid. For most instruments, by moving the objective lens of the OCT closer to the examiner's eye, this second inverted image can be seen more clearly (Spaide et al., 2008). Direct viewing of the inverted image is possible via a system termed Enhanced Depth Imaging (EDI) where the standard distance from the objective to the eye now corresponds to the mirror image and the mirror image is presented on the computer screen as a normal OCT image, with the vitreous on the top and the retinal pigment epithelium at the bottom of the image. An example from a healthy subject is seen in Figure 6 and clearly

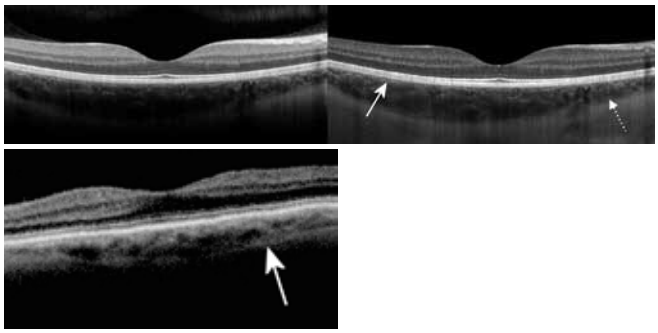

Figure 6. OCT scan of a healthy subject. Top left: Standard OCT. Top right: Enhanced Depth Imaging mode. With this procedure, the intensity of the outer retina, the choroid and the sclera is enhanced, revealing the choriocapillaris (arrow) and the choroidal-scleral interface (dashed arrow). Bottom: Another way of improving visualisation of outer layers is to increase the centre wavelength. A healthy subject was imaged with an experimental system using swept laser technology (Technical University of Denmark) with a centre wavelength of 1050 nm. The choroidal-scleral interface is just visible in this picture. This is an emerging technology designed to enhance visualisation of deeper structures.

illustrates the improved visualisation of the small capillaries of the choroid, the larger choroidal vessels and the choroid/sclera interface. The full importance of choroidal thickness remains to be explored, but it is known that the thickness decreases with increasing axial length and may also be related to retinal disease (Fujiwara, Imamura, Margolis, Slakter, & Spaide, 2009). Lately, improved visualization of the choroidal layer has been achieved by using a swept-source laser. With this approach the central wavelength is changed to 1050 nm, which allows penetration into the deeper tissues (Hirata et al., 2011).

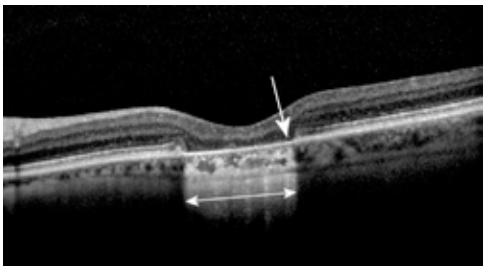

Figure 7. OCT scan of a patient with Stargardt's disease where central atrophy leads to severe loss of visual function. In the foveal region, all layers from the outer retina are missing (arrow), including the outer photoreceptor layer, inner and outer segments. The choroid and the sclera are seen with high intensity (two-headed arrow), illustrating the decreased absorbance of the overlying layers.

Stargardt's disease

In this final example (Figure 7) a patient with Stargardt's disease illustrates several important features. Stargardt's is a disease of genetic origin leading to severe visual deterioration with a total atrophy of all outer retinal layers in the foveal region. Due to the loss of retinal tissue, and therefore decreased absorbance, the choroid and the sclera are clearly visualised. In this case an Enhanced Depth Image was not required, and the scan was obtained with a standard procedure.

Summary

The previous examples illustrate that the interpretation of OCT images should be based on evaluation of the image quality and tissue properties regarding scatter and absorbance. The outer retinal layers are of particular interest for visual function and should be examined carefully for atrophy and discontinuity. For quantitation of retinal and choroidal thickness, centration is important but should not be pursued at the cost of assessment of the qualitative features described above.

Acknowledgements

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References

Christensen, U. C., Krøyer, K., Sander, B., Jørgensen, T. M., Larsen, M., & la Cour, M. (2010). Macular morphology and visual acuity after macular hole surgery with or without internal limiting membrane peeling. *British Journal of Ophthalmology*, 94, 41-47. doi:10.1136/bjo.2009.159582

Christensen, U. C., Krøyer, K., Sander, B., Larsen, M., & la Cour, M. (2009). Prognostic significance of delayed structural recovery after macular hole surgery. *Ophthalmology*, 116, 2430-2436. doi:10.1016/j.ophtha.2009.06.001

Fujiwara, T., Imamura, Y., Margolis, R., Slakter, J. S., & Spaide, R. F. (2009). Enhanced depth imaging optical coherence tomography of the choroid in highly myopic eyes. *American Journal of Ophthalmology*, 148, 445-450. doi:10.1016/j.ajo.2009.04.029

Hirata, M., Tsujikawa, A., Matsumoto, A., Hangai, M., Ooto, S., Yamashiro, K.,…Yoshimura, N. (2011). Macular choroidal thickness and volume in normal subjects measured by swept-source optical coherence tomography. *Investigative Ophthalmology & Visual Science*, 52, 4971-4978. doi:10.1167/iovs.11-7729

Marshall, S., Sander, B., Mogensen, M., Jørgensen, T.M., & Andersen, P.E. (2011) Optical coherence tomography-current technology and applications in clinical and biomedical research. *Analytical & Bioanalytical Chemistry,* 400, 2699-2720. doi:10.1007/s00216-011-5008-1

Sander, B., Larsen, M., Thrane, L., Hougaard, J. L., & Jørgensen, T. M. (2005). Enhanced optical coherence tomography imaging by multiple scan averaging. *British Journal of Ophthalmology*, 89, 207-212. doi:10.1136/bjo.2004.045989

Spaide, R. F., & Curcio, C. A. (2011). Anatomical correlates to the bands seen in the outer retina by optical coherence tomography: literature review and model. *Retina*, 31, 1609-1619. doi:10.1097/IAE.0b013e3182247535

Spaide, R. F., Koizumi, H., & Pozzoni, M. C. (2008). Enhanced depth imaging spectral-domain optical coherence tomography. *American Journal of Ophthalmology,* 146, 496-500. doi:10.1016/j.ajo.2008.05.032

Xi, P., Mei, K., Brauler, T., Zhou, C., & Ren, Q. (2011). Evaluation of spectrometric parameters in spectral-domain optical coherence tomography. *Applied Optics,* 50, 366-372. doi:10.1364/AO.50.000366