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
Commerically 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, Houggaard, & 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, & Pizzoni, 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, Kroyer, 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 nyctalopia, photophobia, poor colour vision, and reduced acuity from birth.

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 approxi-
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.

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 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).

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.

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References


