The Application of Optical Coherence Tomography (OCT) in Neurological Disease

Optical coherence tomography (OCT) was first described by Huang et al. in 1991 and was first used to image the retina in 1993. OCT technology has evolved rapidly enabling the production of in vivo high resolution cross-sectional and three-dimensional images of the ocular microstructure in real time. These OCT images closely reflect histological sections of the macula and fovea, hence the term “optical biopsy”. The technique was initially used for the diagnosis and management of ophthalmological diseases but over the last decade has been increasingly recognized for its applications in neurology.

Basic principles of OCT
OCT is the optical analogue of B mode ultrasound, except that instead of using acoustic waves it uses light reflections to acquire images. A laser generated beam of near infrared light is scanned across the retina and the magnitude and echo time delay of backscattered light is measured. In contrast to standard ultrasound, direct detection of light echoes is not possible because of their high speed. A correlation technique is therefore required and OCT systems are based on the principle of low coherence tomography which was first described by Sir Isaac Newton. Acquisition of the OCT signal is based on splitting of the coherent light beam into two parts: a sample and a reference beam which are the same length but follow two different paths. When reflected light from each of the two paths reaches the detector at the same time they induce an interference signal. The image is acquired by measuring the amplitude of this interference signal (Figure 1).

There are currently two types of commercially available OCT techniques, called time domain and spectral domain OCT.

Time domain OCT
The earlier time domain OCT machines use a superluminescent diode to direct low coherence light into the eye. The light beam is split into two parts by a beam splitter. One beam is directed into the eye and is reflected back from the different layers of the retina. The other reference beam is reflected by a reference mirror. A series of A scans are sequentially acquired one after another producing a final cross-sectional image, or B scan, with a resolution of approximately 8-10 µm.

Spectral Domain OCT
The first retinal images with spectral domain OCT were reported in 2002 and the technique became commercially available in 2006. Imaging is approximately 50 times faster than...
time domain OCT with an acquisition speed of approximately 25,000 axial scans per second and an axial image resolution of approximately 5-7µm. There is also a significant reduction of artefact from ocular movements. Spectral domain also exceeds time domain OCT in its ability to form three dimensional maps of the retina and optic nerve. It is based on fast fourier transformation and it allows all echoes of light from the different retinal layers to be measured simultaneously and the interference signal is a function of their wavelength. This eliminates the need for a moving reference mirror.

OCT in ophthalmology

A detailed review of OCT in ophthalmology is beyond the scope of this article but some examples are mentioned here. OCT has the potential to permit early diagnosis of glaucoma, even in the absence of clinical signs or visual symptoms. The early detection of structural damage to the retinal nerve fibre layer (RNFL) helps to identify those patients who require preventative therapy.\(^{6}\)

OCT measures RNFL thickness in MS is reliable and reproducible.\(^ {11}\)

When an acute lesion affects the optic nerve during an episode of optic neuritis there is transaction of axons followed by retrograde axonal degeneration culminating in loss of retinal ganglion cells and axons in the RNFL, which manifest as loss of macular volume (Figure 2) and thinning of the RNFL (Figure 3).

Optic neuritis is a common manifestation of MS and is the first symptom in up to 20% of patients and will occur in as many as 70% of patients at some point during the course of the disease.\(^ {12},13\)

The retina has often been described as the window into the central nervous system (CNS) and the afferent visual system represents an exciting prospect for MS researchers specifically with regards to the processes of neurodegeneration and repair. This is because the retina is unique in the CNS in that it contains unmyelinated axons, which comprise the retinal nerve fibre layer (RNFL), the most proximal part of the afferent visual system and therefore changes primarily represent axonal loss. OCT measurement of RNFL thickness in MS is reliable and reproducible.\(^ {11}\)

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correlated significantly with optic nerve area. In a 12 month longitudinal study, Costello et al. demonstrated that 74% of patients had RNFL thinning after acute optic neuritis and the majority of this occurred within the first three to six months, the temporal sector being the earliest involved. They also suggested a threshold for RNFL thickness of 75 µm below which visual function, as measured by automated perimetry, declined linearly.

Fisher et al. demonstrated that low contrast letter acuity scores were significantly correlated with average RNFL thickness and every one line decrease in low contrast letter acuity was associated with an average 4mm thinning of the RNFL.

Subsequently, several studies have shown that average RNFL thickness can differentiate between MS subtypes with lower values in progressive forms of MS when compared with patients with clinically isolated syndromes suggestive of MS, and overall disability, as measured by the expanded disability status scale (EDSS), correlates with the RNFL thickness.

In 2010, Henderson et al. performed a prospective study on 23 patients with acute unilateral optic neuritis. Patients underwent OCT, visual assessments and visual evoked potentials (VEPs) at 3, 6, 12 and 18 months. They found that 90% of the retinal nerve fibre degeneration occurred within a mean 2.38 months from onset of the disease and that poorer visual function was associated with greater decline in RNFL thickness during the first three months. They also performed sample size calculations which have paved the way for future neuroprotection trials using OCT as a primary outcome measure.

With the emergence of high resolution SD-OCT it is now possible to segment the different retinal layers. Of particular interest is the retinal ganglion cell layer (GCL) as a potential marker for neuronal loss. The Balcer group has developed a segmentation algorithm and in a study of 122 MS patients and 31 controls found that the GCL and inner plexiform layer (IPL) (Figure 4) were significantly decreased in MS eyes versus controls and in MS optic neuritis eyes versus non-optic neuritis eyes. GCL atrophy is comparable to grey matter atrophy in MRI and may emerge as a structural marker of disease progression in the future.

OCT in neuromyelitis optica

OCT has also been considered as a biomarker for axonal loss in neuromyelitis optica (NMO). Mean RNFL thickness is significantly reduced in optic neuritis eyes in NMO patients compared with controls and RNFL atrophy after optic neuritis is more severe in NMO than in MS.

Ratchford et al. estimated that one episode of optic neuritis in NMO causes 24 µm more RNFL atrophy than in relapsing remitting MS. In NMO, mean RNFL thickness correlated with EDSS and visual disability.

OCT in Alzheimer’s disease & Parkinson’s disease

OCT may have applications in other neurodegenerative conditions. Several groups have demonstrated RNFL thinning in Alzheimer’s disease patients when compared with age-matched controls. These changes occur early during the course of the disease and correlate with the severity of cognitive impairment. Thinning of the RNFL has also been reported in Parkinson’s disease. Inzelberg et al. demonstrated a significant reduction in inferotemporal peripapillary RNFL thickness when compared with age-matched controls. Currently the functional and clinical implications of these structural abnormalities are unknown.

Conclusion

OCT is a relatively new technique that has greatly advanced our understanding, diagnosis and management of ocular diseases. The introduction of spectral domain instruments has improved acquisition speeds and allows high resolution, three-dimensional images to be produced. It is able to provide quantitative measurements of retinal structures with a high degree of reproducibility.

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