The use of optical coherence tomography in neuro-ophthalmology

Carmen K. M. Chan, *MRCP, FRCSEd (Ophth)*
Neuro-ophthalmology service, Hong Kong Eye Hospital; Department of Ophthalmology & Visual Sciences, The Chinese University of Hong Kong, Hong Kong.

Correspondence and reprint requests:
Dr. Carmen Chan, Hong Kong Eye Hospital, 147K Argyle Street, Kowloon, Hong Kong. Email: kmcc2001@hotmail.com

Abstract

In recent years, optical coherence tomography has become an indispensable tool for ophthalmologists. In neuro-ophthalmology, this form of tomography is particularly useful for the structural documentation of peripapillary retinal nerve fiber layer thickness and optic nerve head morphology. The spectral-domain optical coherence tomography has advantages over the older, time-domain, optical coherence tomography and other instruments used to measure retinal nerve fiber layer thickness. Such other instruments for this purpose entail use of the confocal scanning laser ophthalmoscope and scanning laser polarimetry. Optical coherence tomography can aid diagnosis, disease monitoring and in some cases, give prognostic information about optic neuropathies. It is particularly useful for the diagnosis of functional visual loss, differentiation of optic neuropathy and maculopathy, and discriminating real disc swelling from pseudopapilledema. Signal strength and movement artefacts affect the reliability of its images and measurements. The available technology is rapidly changing and it is important to keep up with latest developments so as to utilize this tool fully and interpret the findings correctly.

Key words: Ophthalmoscopy; Optic disk; Optic neuropathy, ischemic; Tomography, optical coherence

Introduction

What is optical coherence tomography?

Optical coherence tomography (OCT) is a non-invasive, non-contact technology which can be used to obtain cross-sections of the anterior and posterior segments of the eye. For the posterior segment, in addition to obtaining cross-sectional images of the retina, the instruments may have built-in algorithms to automatically measure retinal thickness, peripapillary retinal nerve fiber layer thickness (PRNFLT), and quantify optic nerve head (ONH) morphology (e.g. disc size and cup-disc ratio).

History and scientific principles of optical coherence tomography

The Massachusetts Institute of Technology, USA developed OCT technology in the early 90s.[1] The first commercial OCT instrument for the eye became available in 1996, however its use was limited by its slow scanning speed. The clinical use of OCT only took off with the advent of the Stratus OCT (Carl Zeiss, 2002), with improved scanning speed and definition. In OCT, low coherence interferometry is used to measure optical delay on a micron scale. The technology is analogous to obtaining images with an ultrasound B scan, but instead of ultrasound, it uses near-infrared rays with a wavelength of 820 nm, generated by a superluminescent diode. Stratus OCT is an example of a time-domain technology. From 2006, spectral-domain OCT (SD-OCT) became commercially available; SD-OCT is also known as Fourier domain OCT, and is marketed as HD-OCT or 3D-OCT. The SD-OCT technology is spectrometer-based and uses Fourier transformation to convert the obtained signals to images. Compared with time-domain OCT, SD-OCT offers higher scanning speeds and definition (**Table 1**) and movement artefacts are greatly reduced.

Currently there are many commercially available instruments using SD-OCT technology to image the posterior segment, for example the Cirrus OCT (Carl Zeiss Meditec), the Spectralis (Heidelberg Engineering), 3D OCT-2000 (Topcon), the RTVue (Optovue Inc), and others. By contrast, the Visante OCT (Carl Zeiss Meditec) is an instrument dedicated to the imaging of the anterior segment. An example of the Cirrus OCT printout of the ONH analysis of

a patient with nonarteritic anterior ischemic optic neuropathy (NAION) is shown in **Figure 1**.

Optical coherence tomography versus other modalities for assessment of optic nerve pathology

In neuro-ophthalmology, OCT can be used objectively to assess the **structure** of the ONH and PRNFL. This is analogous to looking at the optic disc by fundoscopy or taking stereoscopic disc photographs, but OCT has the advantage of giving reproducible and quantifiable measurements, with low inter- and intra-observer variability. Other objective assessments of optic nerve pathology, e.g. the relative afferent pupillary defect and visual-evoked potential, are used for assessment of optic nerve **function**. The objective assessment of structure and function complement each other. To give a complete picture, they have to be performed in conjunction with subjective assessment of optic nerve function e.g. visual acuity, color vision, visual field examination.

Optical coherence tomography versus other instruments for retinal nerve fiber layer assessment

Apart from OCT, PRNFLT can also be measured by the confocal scanning laser ophthalmoscope (CSLO) e.g. Heidelberg Retinal Tomograph (HRT3), and scanning laser polarimetry (SLP), e.g. GDx nerve fiber analyzer. Both CSLO and SLP were originally developed for glaucoma assessment. The CSLO is an instrument designed primarily to analyze ONH morphology. It uses a confocal diode laser to scan the surface of the retina and creates a 3-dimensional topography of the retinal surface. It then estimates the PRNFLT from the height above a standard reference plane. OCT-PRNFLT has a better structure-function correlation compared to that measured by CSLO, both in glaucoma[2] and in non-glaucomatous optic neuropathies.[3]

The SLP uses a near-infrared diode laser, which emits polarized light. The RNFL has birefringent properties and causes a phase shift of the polarized light that is proportional to the RNFLT. The SLP estimates the PRNFLT from retardation of birefringence. In different types of optic neuropathies, the structure-function correlation of OCT-PRNFLT has been shown to be similar to or better than SLP-PRNFLT measurements.[4-6]

A comparison of the 3 imaging modalities is displayed in **Table 2**. Due to its ability to image the macula / retina as well as the ONH, and measure PRNFLT, in recent years OCT has become increasingly popular relative to the other two instruments.

Clinical use of optical coherence tomography in neuro-ophthalmology

For optic neuropathies, OCT can aid diagnosis, disease monitoring and in some cases, give prognostic information.

Diagnosis

OCT can be used to confirm a chronic optic neuropathy but does not usually give information on the underlying cause. PRNFL thinning is an objective biomarker of optic atrophy. Notably, optic atrophy takes about 6 to 8 weeks to develop after an acute insult.[7] Thus, immediately after an acute severe traumatic optic neuropathy causing no light perception and in the presence of an absolute afferent pupillary defect, the PRNFLT is usually normal unless there is disc swelling. Thus, for the assessment of acute optic neuropathies this technique is of limited value, except to detect subtle disc swelling. Moreover, optic atrophy can develop secondary to retinal or extensive macular disease, such that PRNFL thinning is not diagnostic of a primary optic neuropathy.

Functional visual loss

OCT is particularly useful in cases of long-standing visual loss with no apparent cause revealed by clinical examination. If a patient complains of chronic severe unilateral visual loss with no apparent afferent pupillary defect, the clinical suspicion of a cause other than optic neuropathy can usually be confirmed by normal and symmetrical PRNFLT findings. If the electroretinography (ERG) [full field ± multifocal] is also normal, then functional visual loss is high on the list of differential diagnoses. Pattern-reversal visual-evoked potentials can also be used in the diagnosis of functional visual loss, though intelligent malingerers can voluntarily alter visual-evoked potential results,[8] e.g. by defocusing.

Table 1. Time-domain vs spectral-domain optical coherence tomography.		
	Time-domain	**Spectral-domain**
Scanning speed	400 A-scans per sec	1024 A-scans in 0.04 sec
Scanning mode	Sequential: 1 pixel at a time	Simultaneous 1024 pixels at a time
Resolution	10 microns	5 microns

Table 2. Comparison of optical coherence tomography (OCT), confocal scanning laser ophthalmoscope (CSLO) and scanning laser polarimetry (SLP).			
	Spectral-domain OCT e.g. Cirrus OCT	**CSLO e.g. HRT 3**	**SLP e.g. GDx NFA (ECC)**
Retinal nerve fiber layer thickness	√√√	√	√√
Optic nerve head morphology	√	√√	X
Macula / retina	√√	X	X

Abbreviations: HRT 3 = Heidelberg Retinal Tomograph; GDx NFA (ECC) = GDx nerve fiber analyzer (enhanced corneal compensation).
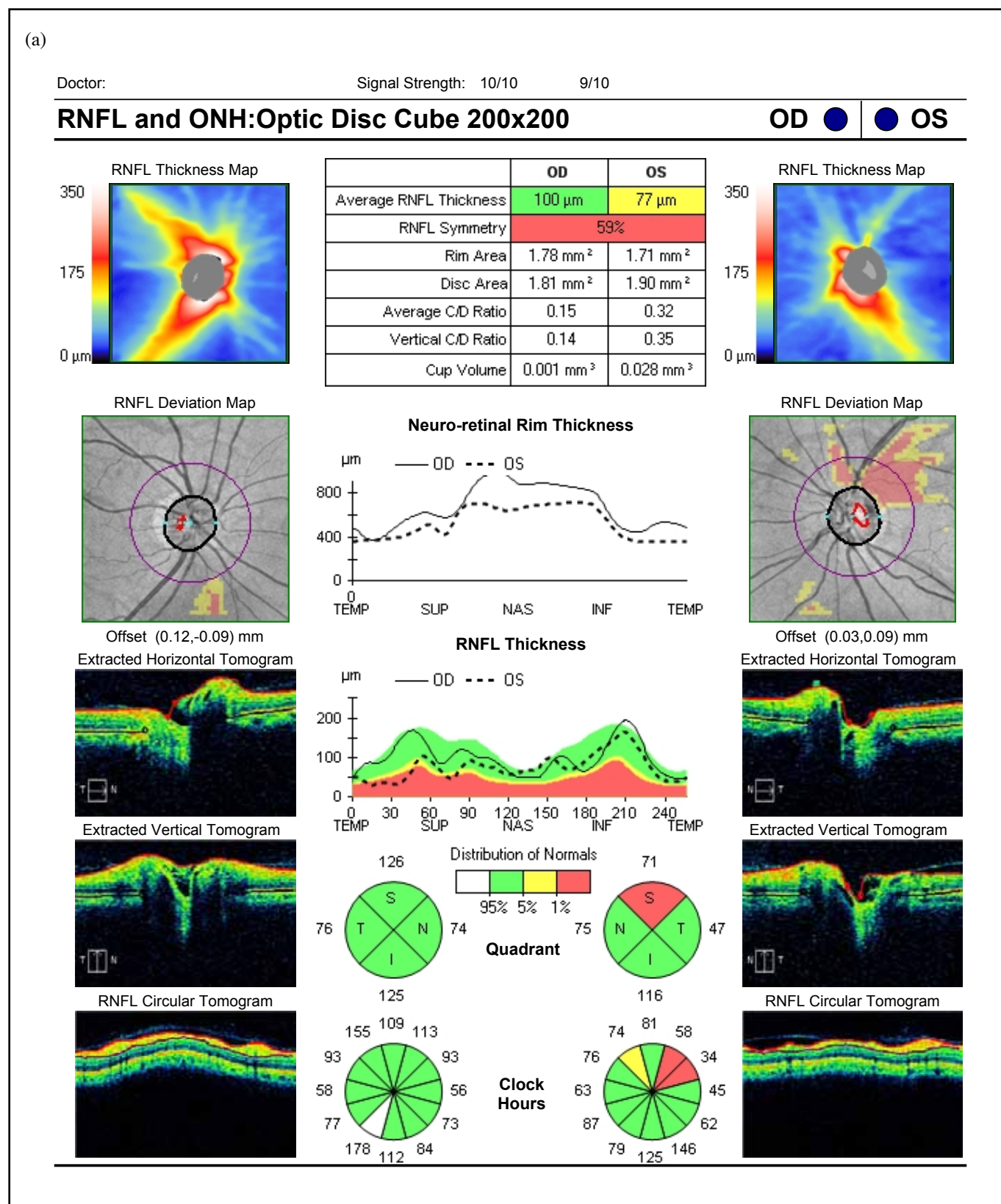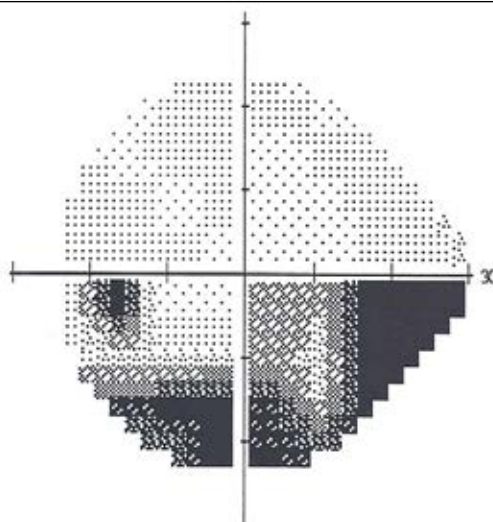
Figure 1. (a) Cirrus OCT 'optic disc cube' scan of a patient with a history of NAION of the left eye 3 years earlier. In the left eye, there is thinning of the superotemporal sectors of the peripapillary RNFL, particularly well-demonstrated on the 'RNFL deviation map'. This corresponds to an inferior arcuate visual field defect on the Humphrey visual field (24-2) as shown in (b), and retinal thinning of the superior macula (c). Also note the nearly cupless disc of the fellow (right) eye in (a). Images in (a) and (c) were generated with Cirrus OCT software version 5.0.0.326.

Abbreviations: OCT = optical coherence tomography; NAION = nonarteritic anterior ischemic optic neuropathy; RNFL = retinal nerve fiber layer, ONH = optic nerve head.
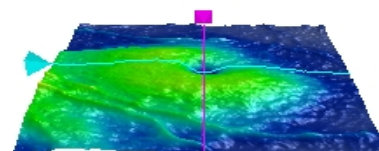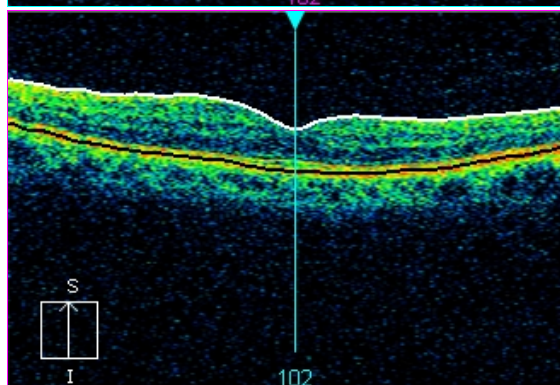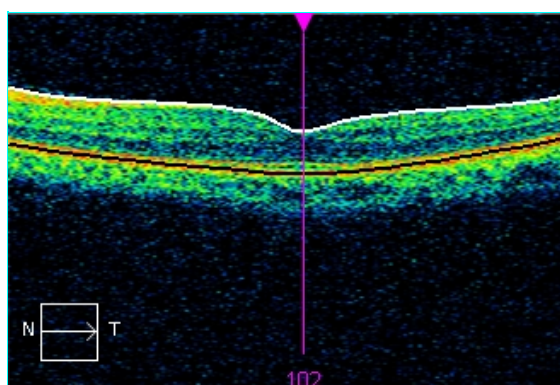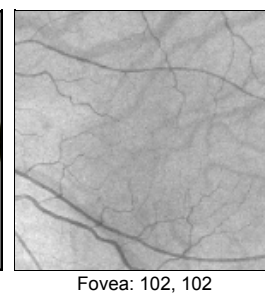
(b)

(c)

Macula Thickness : Macular Cube 200x200   OD ○   ● OS

Overlay: ILM - RPE Transparency: 50 %

ILM-RPE Thickness (µm)   Fovea: 102, 102

ILM - RPE

ILM

Distribution
of Normals
99%
95%
5%
1%
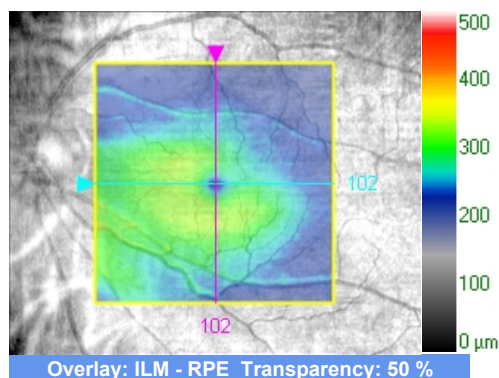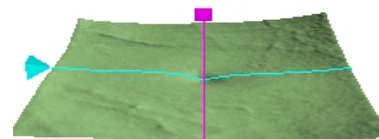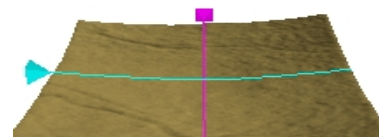
RPE
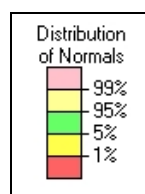
	Central Subfield Thickness (µm)	Cube Volume (mm³)	Cube Average Thickness (µm)
ILM - RPE	276	9.3	258

Optic neuropathy versus maculopathy

OCT, especially SD-OCT, can detect subtle abnormalities of the macula, which may not be apparent on clinical examination.[9,10] An example is shown in **Figure 2.** Traditionally occult maculopathies can also be diagnosed using multifocal electroretinography (mfERG) or pattern electroretinography (PERG), but OCT is quicker and requires less cooperation than for mfERG or PERG.

Real disc swelling versus pseudopapilledema

Karam and Hedges[11] have shown that with a single measurement, OCT-PRNFLT could not distinguish between congenitally crowded discs and mild papilledema due to increased intracranial pressure. However with serial measurements, in congenitally crowded discs the PRNFLT should remain stable, whilst in papilledema, it might increase (due to increased severity) or decrease (due to resolution of papilledema from normalization of intracranial or advent of secondary optic atrophy). On the contrary, a recent study by Johnson et al[12] demonstrated that OCT can be used to distinguish optic disc swelling from pseudopapilledema due to ONH drusen. This was achieved qualitatively by comparing the internal optic disc contour, and qualitatively by comparing nasal RNFLT and subretinal hyporeflective space thickness.

Disease monitoring

OCT-PRNFLT is useful for monitoring disease progression in chronic optic neuropathies, in conjunction with visual acuity, color vision and visual field examination. However, it is of less use in conditions with optic disc swelling (e.g. in idiopathic intracranial hypertension [IIH]) because it cannot distinguish resolving disc edema from the development of optic atrophy.[13] On the other hand, serial objective quantification of ONH morphology could be useful in IIH monitoring and this has been demonstrated with HRT.[14] With the advent of ONH analysis software (e.g. Cirrus OCT), it is anticipated that OCT can also be used in a similar way.

Prognosis

In a study by Danesh-Meyer et al,[15] the authors evaluated the OCT-PRNFLT before surgery in 35 patients with compressive neuropathy from parachiasmal lesions. They found that patients with objective PRNFL loss at the time of surgery were less likely to have post-surgery recovery of visual acuity or visual field defects. This is entirely consistent with the observation that patients with established optic atrophy from compressive optic neuropathies are less likely to recover their optic nerve function after relieving the compression. It has been demonstrated that on Stratus OCT, eyes with no light perception vision from non-glaucomatous optic neuropathies had a residual peripapillary PRNFLT of about 45 microns.[16] Therefore a patient with an optic neuropathy of any cause and a PRNFLT of less than 50 microns is unlikely to enjoy significant recovery of vision. In rare cases, even patients with very thin PRNFL can have reasonable central vision, but these patients usually have very constricted visual fields. An example is illustrated in **Figure 3.**

Other specific conditions

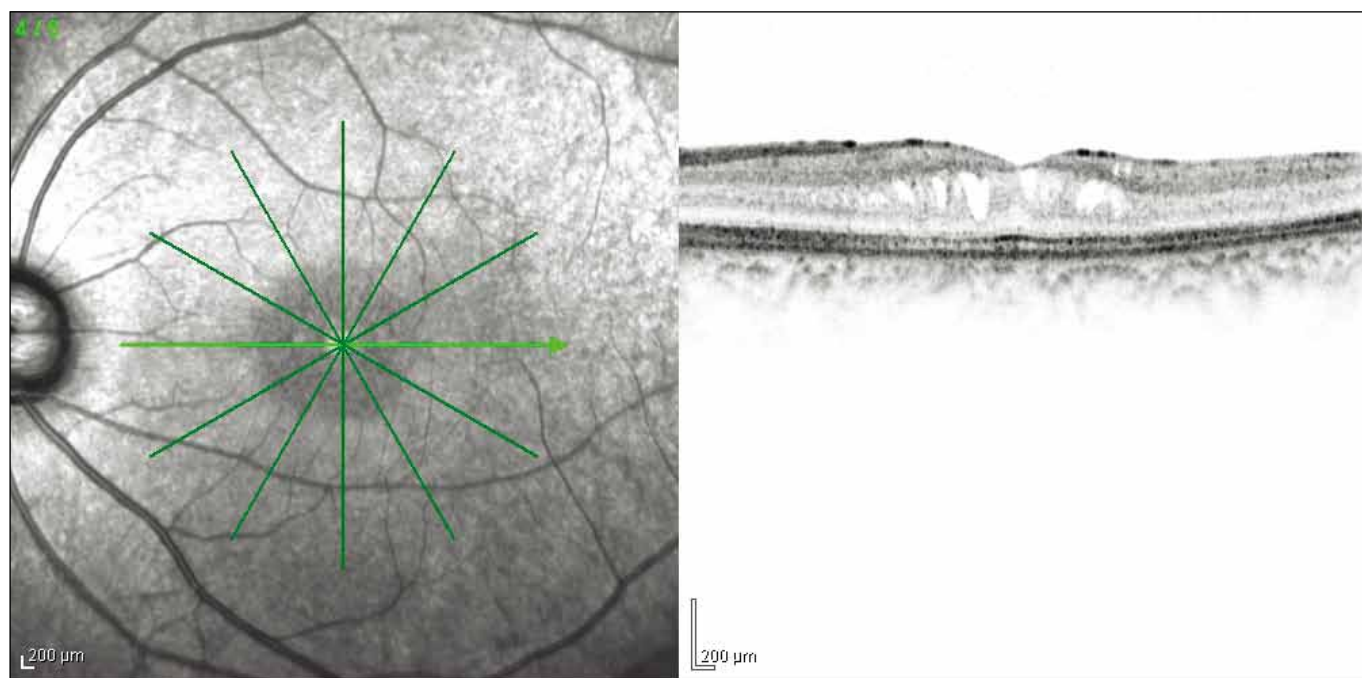In addition to the conditions already mentioned, there are

Figure 2. Spectralis optical coherence tomography (OCT) scan of the left macula of a 33-year-old man who was referred for investigation of visual loss of unknown cause. He did not give a definite history of subjective visual loss but had bilaterally reduced vision (20/50) with a 'normal' ocular examination. OCT scan of both eyes revealed subtle cystoid macula edema. Together with abnormal cone and rod responses on full-field electroretinogram, the diagnosis was retinitis pigmentosa (sine pigmento) with cystoid macular edema.

(a)
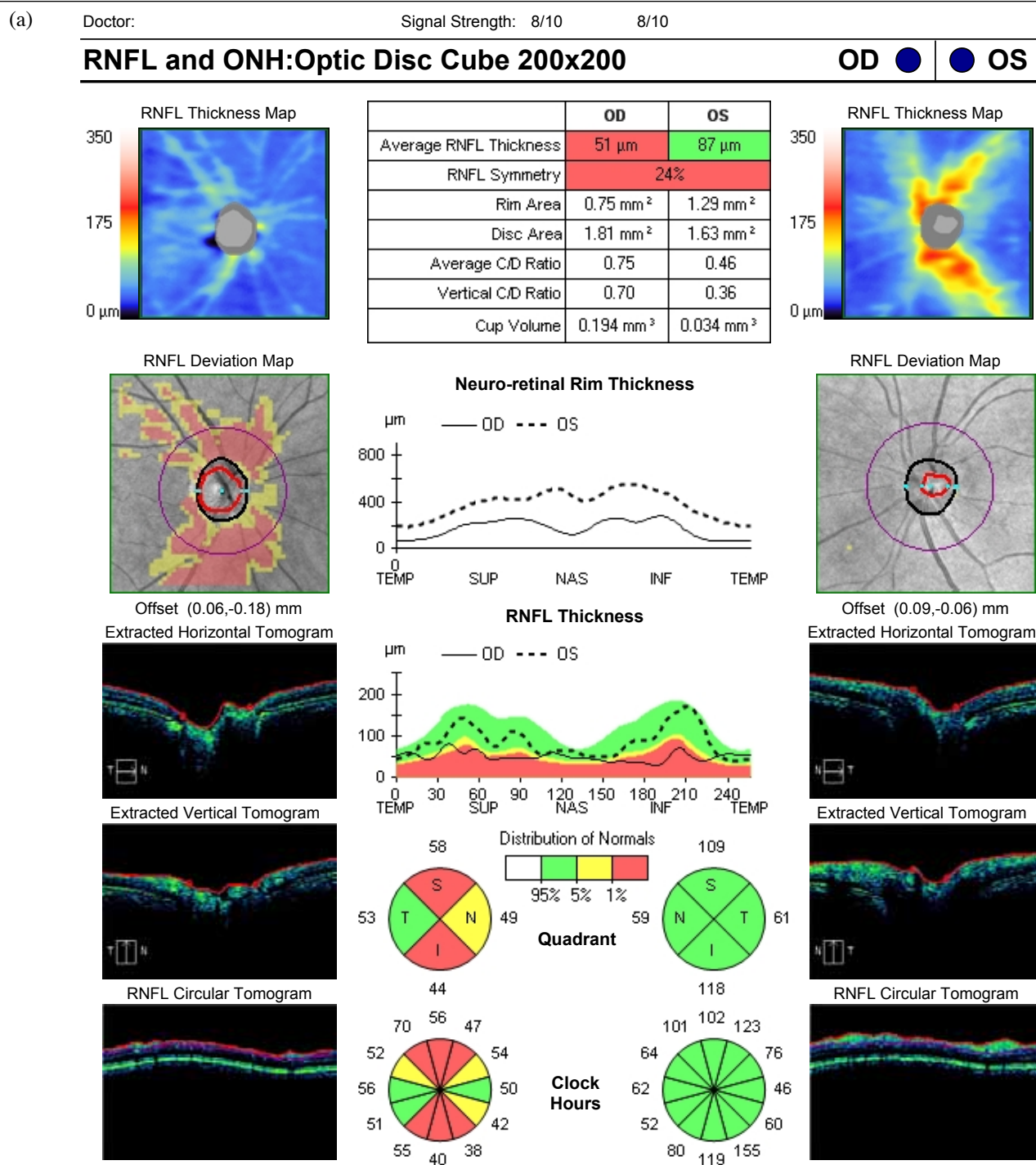
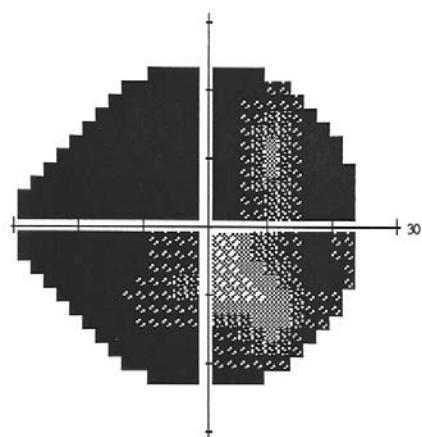Figure 3. (a) Cirrus OCT 'optic disc cube' scan of a patient with a history of non-arteritic anterior ischemic neuropathy of the right eye 3 years earlier. Despite a residual average peripapillary retinal nerve fiber layer thickness of only 51 microns in the right eye, he retained a visual acuity of 20/40, but the visual field was very constricted, as shown in (b) (Humphrey visual field 24-2 of right eye).

published reports about the use of OCT in almost all types of optic neuropathies.[17,18] A few specific conditions of particular interest are mentioned below.

Optic neuritis / multiple sclerosis
This is one area in neuro-ophthalmology where the use of OCT is widely reported. Not surprisingly, there is PRNFL thinning after optic neuritis. More interestingly, even in the eyes of multiple sclerosis patients with no prior history of optic neuritis, the PRNFL is thin.[19] PRNFL thinning has also been reported in Alzheimer's and Parkinson's disease.[20] Such findings indicate that loss of retinal ganglion cells may reflect more widespread degenerative changes in the brain.

Non-arteritic anterior ischemic optic neuropathy
Classically, NAION patients have smaller optic cups ('cupless discs'), which was quantitatively demonstrated with OCT.[3] Using OCT, Hedges et al[21] demonstrated the presence of subfoveal fluid in the acute stage of NAION and suggested that resolution of the subfoveal fluid may account for some of the visual recovery after NAION. More recently, using OCT and HRT, Danesh-Meyer et al[22] demonstrated that eyes with NAION and arteritic anterior ischemic optic neuropathy had significantly different disc topography than in open-angle glaucoma (at a given level of retinal ganglion cell loss). This was an example of using OCT to delineate the cause of optic neuropathy, instead of just confirming its presence.

Leber's hereditary optic neuropathy
Using OCT ONH analysis, Ramos Cdo et al[23] demonstrated that Leber's hereditary optic neuropathy (LHON) carriers had larger ONHs than LHON-affected eyes. In addition, among the LHON-affected eyes, larger discs correlated with visual recovery and had better visual outcomes. The authors postulated that a large disc size could have a protective role in patients with LHON mutations.

Retrogeniculate lesions
Using OCT, Jindahra et al[24] demonstrated that in patients with congenital and acquired homonymous hemianopia due to occipital lesions had thinning of PRNFL in the corresponding sectors of both optic discs. This was a demonstration of trans-synaptic retrograde degeneration of retinal ganglion cells following retrogeniculate visual pathway lesions.

Practical considerations

An OCT measurement is only reliable if the signal strength is good and there is a lack of movement artefacts.

Signal strength
A signal strength of at least 7/10 is generally considered acceptable on the Stratus OCT or Cirrus OCT. There are many factors which affect signal strength.

Media opacity
Obviously corneal scars, cataract and vitreous opacities affect signal strength, but it has been shown that cataracts can also cause underestimation of PRNFLT.[25] Similarly,

contact lenses should be removed before the examination, as they reduce signal strength and measured PRNFLT.[26] If the corneal surface is dry, topical lubrication can be applied during the assessment. The corneal surface should be optimal before performing OCT, so it is advised not to undertake prior contact lens examinations (e.g. gonioscopy) or use contact lens electrodes (e.g. Burian Allan electrodes for ERG).

Pupil size
Studies have shown that a pupil size of 3 mm or more does not significantly affect OCT measurements,[25,27] but obtaining a satisfactory image is much easier with a dilated pupil, especially if the media is not absolutely clear.

Refractive error
It is more difficult to obtain a good signal strength in patients with high myopia. In addition, such patients have a thinner PRNFL and may have a different distribution from emmetropic patients,[28,29] which means OCT results in these patients must be interpreted with caution.

Movement artefacts
Movement artefacts affect OCT results considerably; getting an eye to fixate on the target is especially difficult in patients with poor vision. If vision is good in the fellow eye, then an external fixation target (if available) can be used. Newer models (e.g. Spectralis) have active eye tracking, which minimizes movement artefacts. Scan displacement also affects OCT-measured PRNFLT, but some models e.g. Cirrus OCT, automatically detects the position of the ONH and can ensure that the scan is well-centered.

Result interpretation
In cases where it is impossible to obtain images of good signal strength, any measurement has to be interpreted with caution. Most instruments have built-in software which utilizes algorithms to place demarcation lines separating different ocular structures e.g. edge of optic disc or RNFL. The placement of such lines may be incorrect in poorly acquired images and it may be necessary to rectify the position of the demarcation lines manually before generating measurements.

Conclusion

In the past few years, OCT has become an indispensable tool for ophthalmologists, initially for retinal and glaucoma specialist, but now increasingly for neuro-ophthalmologists too. The available technology is rapidly changing and it is important to keep up with the latest developments, so as to utilize this tool fully and interpret the findings correctly.

Acknowledgment

Declaration

References

1. Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. Science. 1991;254:1178-81.
2. Bowd C, Zangwill LM, Medeiros FA, et al. Structure-function relationships using confocal scanning laser ophthalmoscopy, optical coherence tomography, and scanning laser polarimetry. Invest Ophthalmol Vis Sci. 2006;47:2889-95.
3. Chan CK, Cheng AC, Leung CK, et al. Quantitative assessment of optic nerve head morphology and retinal nerve fibre layer in non-arteritic anterior ischaemic optic neuropathy with optical coherence tomography and confocal scanning laser ophthalmoloscopy. Br J Ophthalmol. 2009;93:731-5.
4. Deleón-Ortega J, Carroll KE, Arthur SN, Girkin CA. Correlations between retinal nerve fiber layer and visual field in eyes with nonarteritic anterior ischemic optic neuropathy. Am J Ophthalmol. 2007;143:288-94.
5. Bertuzzi F, Suzani M, Tagliabue E, et al. Diagnostic validity of optic disc and retinal nerve fiber layer evaluations in detecting structural changes after optic neuritis. Ophthalmology. 2010;117:1256-64.
6. Horn FK, Mardin CY, Laemmer R, et al. Correlation between local glaucomatous visual field defects and loss of nerve fiber layer thickness measured with polarimetry and spectral domain OCT. Invest Ophthalmol Vis Sci. 2009;50:1971-7.
7. Topical diagnosis of acquired optic nerve disorders. In: Miller NR, Newman NJ, editors. Walsh & Hoyt's clinical neuro-ophthalmology. Philadelphia: Lippincott Williams & Wilkins; 1999: 134-65.
8. Manresa MJ, Bonaventura I, Martinez I, Gómez L, Aguilar M. Voluntary changes of visual evoked potentials in cases with hysteria and/or simulation [in Spanish]. Rev Neurol. 1996;24:285-6.
9. Witkin AJ, Wojtkowski M, Reichel E, et al. Photoreceptor disruption secondary to posterior vitreous detachment as visualized using high-speed ultrahigh-resolution optical coherence tomography. Arch Ophthalmol. 2007;125:1579-80.
10. Rodriguez-Padilla JA, Hedges TR 3rd, Monson B, et al. High-speed ultra-high-resolution optical coherence tomography findings in hydroxychloroquine retinopathy. Arch Ophthalmol. 2007;125:775-80.
11. Karam EZ, Hedges TR. Optical coherence tomography of the retinal nerve fibre layer in mild papilloedema and pseudopapilloedema. Br J Ophthalmol. 2005;89:294-8.
12. Johnson LN, Diehl ML, Hamm CW, Sommerville DN, Petroski GF. Differentiating optic disc edema from optic nerve head drusen on optical coherence tomography. Arch Ophthalmol. 2009;127:45-9.
13. Rebolleda G, Munoz-Negrete FJ. Follow-up of mild papilledema in idiopathic intracranial hypertension with optical coherence tomography. Invest Ophthalmol Vis Sci. 2009;50:5197-200.
14. Salgarello T, Falsini B, Tedesco S, Galan ME, Colotto A, Scullica L. Correlation of optic nerve head tomography with visual field sensitivity in papilledema. Invest Ophthalmol Vis Sci. 2001;42:1487-94.
15. Danesh-Meyer HV, Papchenko T, Savino PJ, Law A, Evans J, Gamble GD. In vivo retinal nerve fiber layer thickness measured by optical coherence tomography predicts visual recovery after surgery for parachiasmal tumors. Invest Ophthalmol Vis Sci. 2008;49:1879-85.
16. Chan CK, Miller NR. Peripapillary nerve fiber layer thickness measured by optical coherence tomography in patients with no light perception from long-standing nonglaucomatous optic neuropathies. J Neuroophthalmol. 2007;27:176-9.
17. Subei AM, Eggenberger ER. Optical coherence tomography: another useful tool in a neuro-ophthalmologist's armamentarium. Curr Opin Ophthalmol. 2009;20:462-6.
18. Mendoza-Santiesteban CE, Gonzalez-Garcia A, Hedges TR 3rd, et al. Optical coherence tomography for neuro-ophthalmologic diagnoses. Semin Ophthalmol. 2010;25:144-54.
19. Petzold A, de Boer JF, Schippling S, et al. Optical coherence tomography in multiple sclerosis: a systematic review and meta-analysis. Lancet Neurol. 2010;9:921-32.
20. Jindahra P, Hedges TR, Mendoza-Santiesteban CE, Plant GT. Optical coherence tomography of the retina: applications in neurology. Curr Opin Neurol. 2010;23:16-23.
21. Hedges TR 3rd, Vuong LN, Gonzalez-Garcia AO, Mendoza-Santiesteban CE, Amaro-Quierza ML. Subretinal fluid from anterior ischemic optic neuropathy demonstrated by optical coherence tomography. Arch Ophthalmol. 2008;126:812-5.
22. Danesh-Meyer HV, Boland MV, Savino PJ, et al. Optic disc morphology in open-angle glaucoma compared with anterior ischemic optic neuropathies. Invest Ophthalmol Vis Sci. 2010;51:2003-10.
23. Ramos Cdo V, Bellusci C, Savini G, et al. Association of optic disc size with development and prognosis of Leber's hereditary optic neuropathy. Invest Ophthalmol Vis Sci. 2009;50:1666-74.
24. Jindahra P, Petrie A, Plant GT. Retrograde trans-synaptic retinal ganglion cell loss identified by optical coherence tomography. Brain. 2009;132:628-34.
25. Savini G, Zanini M, Barboni P. Influence of pupil size and cataract on retinal nerve fiber layer thickness measurements by Stratus OCT. J Glaucoma. 2006;15:336-40.
26. Youm DJ, Kim JM, Park KH, Choi CY. The effect of soft contact lenses during the measurement of retinal nerve fiber layer thickness using optical coherence tomography. Curr Eye Res. 2009;34:78-83.
27. Savini G, Carbonelli M, Parisi V, Barboni P. Effect of pupil dilation on retinal nerve fibre layer thickness measurements and their repeatability with Cirrus HD-OCT. Eye (Lond). 2010;24:1503-8.
28. Kang SH, Hong SW, Im SK, Lee SH, Ahn MD. Effect of myopia on the thickness of the retinal nerve fiber layer measured by Cirrus HD optical coherence tomography. Invest Ophthalmol Vis Sci. 2010;51:4075-83.
29. Leung CK, Mohamed S, Leung KS, et al. Retinal nerve fiber layer measurements in myopia: An optical coherence tomography study. Invest Ophthalmol Vis Sci. 2006;47:5171-6.