



香港眼科醫學院

Advances in quantitative morphological assessment of glaucomatous optic neuropathy with optical coherence tomography

Christopher K. S. Leung,^{1,2} MD, MB ChB, Clement C. Y. Tham,^{1,2,3} FRCS, Dennis S. C. Lam,^{1,2} MD, FRCOphth

¹Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong, China.

²Hong Kong Eye Hospital, Kowloon, Hong Kong, China.

³Queen Mary Hospital, Pokfulam Road, Hong Kong, China.

Correspondence and reprint requests:

Clement C. Y. Tham, Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong, China. Tel: (852) 2855 3788; Fax: (852) 2816 7093; E-mail: clemtham@hkstar.com

Evaluation of the retinal nerve fiber layer (RNFL) and optic nerve head (ONH) are key components for establishing the diagnosis of glaucoma. Changes in RNFL and ONH have been found to precede the onset of visual field loss, thereby providing early evidence of glaucomatous damage.¹⁻³ Morphological examinations of RNFL and ONH are also important for monitoring the course of the disease and the assessment of prognosis. However, accurate descriptions of these structural changes are not easy.

With the advent of modern imaging technology, reproducible and reliable RNFL and ONH measurements have been made possible. Three diagnostic imaging devices are commercially available for these measurements: optical coherence tomography (OCT), confocal scanning laser ophthalmoscopy and scanning laser polarimetry. Increasing attention has been focused on OCT for its unique capability of measuring both the RNFL and ONH.

From prototype to ultrahigh-resolution optical coherence tomograph

The principle of OCT is based on an optical measurement technique — low coherence interferometry and OCT imaging of the retina was first demonstrated in vitro by Huang et al in 1991.⁴ In vivo OCT imaging of the retina with a prototype OCT built upon a modified slit-lamp biomicroscope was subsequently reported.⁵ The OCT images were displayed on a gray-scale or false-color-scale based on the back-scattered signal intensity. Structures with high reflectivity signals were coded with bright colors (red and white), whereas those with low reflectivity were coded with dark colors (blue and black). Those with intermediate reflectivity were coded in green. In the retina, the RNFL, and the retinal pigment epithelium are highly reflectile (highly backscattering) structures and therefore they appear in red (**Figure 1**). The first commercially available OCT unit was developed by Carl

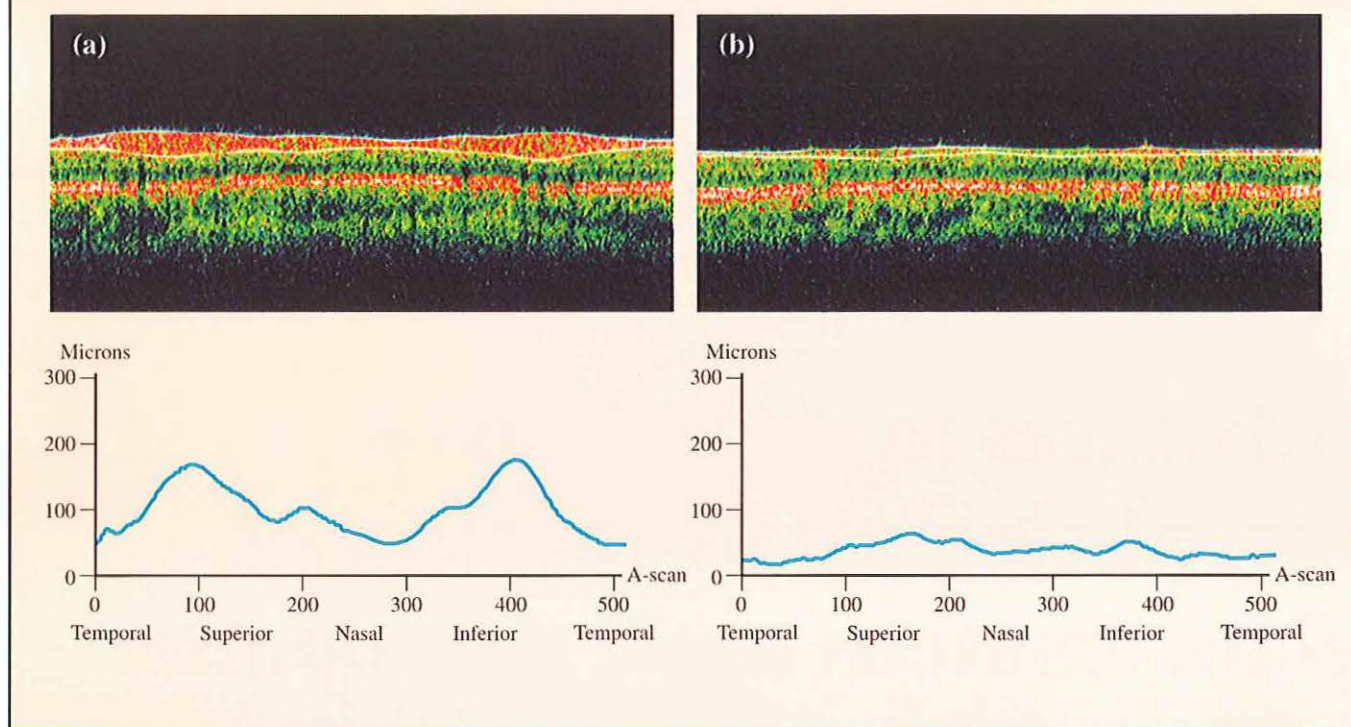


Figure 1. The peripapillary retinal nerve fiber layer profile in (a) a healthy eye; and (b) a glaucomatous eye. Normal retinal nerve fiber layer profile is characterized by the 'double hump' pattern with peaks at the superior and inferior sectors of the optic disc, and troughs at the nasal and temporal sectors. In a glaucomatous eye, there is diffuse or localized thinning of the retinal nerve fiber layer.

Zeiss Meditec Inc — OCT 1. This unit provides an axial resolution of 12 to 15 μm and a transverse resolution of 20 to 25 μm with 100 scan points. The latest commercially available version — Stratus OCT is the third generation of the commercially available models. This unit received USA Food and Drug Administration approval in May 2002. The axial resolution of an OCT image is dependent on the wavelength and bandwidth of the light source whereas the transverse resolution is determined by the focused spot size of the light beam. Stratus OCT uses a low coherence super luminescent diode source with a wavelength of 820 nm giving an axial resolution of 8 to 10 μm . On the other hand, the maximum transverse resolution is limited at approximately 10 μm because it is subjected to the constraints of the pupillary aperture and the optical aberrations of the eye.

Using a femtosecond titanium:sapphire laser with an ultra-broad spectral bandwidth centered at 800 nm as the imaging light source, a prototype of ultrahigh-resolution OCT that can provide an axial resolution of up to 3 μm is currently being investigated.⁶ OCT images with enhanced resolution allow better visualization and delineation of intraretinal layers that may improve the capabilities to detect early glaucomatous change.⁷

Assessment of glaucoma with optical coherence tomography — strengths and limitations

The major strengths of OCT are that it provides objective and quantitative measures of the RNFL and ONH, which

may improve the sensitivity and specificity for detection of glaucoma, and allows longitudinal monitoring for progression. The merits of OCT are recognized as being totally non-invasive and non-contact. In contrast to functional assessment with the automated visual field analyzer, which usually requires at least 10 minutes, OCT takes less than 2 minutes for a scan of the RNFL or ONH. RNFL and ONH measurements with different generations of OCT (OCT 1/ OCT 2000 and Stratus OCT) have been demonstrated to be reproducible in healthy and glaucomatous eyes.^{8,9} However, measurements obtained from different models may be different and it has been shown that the Stratus OCT is more sensitive to detecting glaucomatous change compared with the earlier models.¹⁰ OCT is not capable of detecting some important clinical signs, for example, optic disc hemorrhage and peripapillary atrophy, which have been found to be associated with glaucomatous change or progression. A clear OCT image is difficult to obtain in the presence of media opacity such as moderate cataract or vitreous opacity. Patient cooperation with steady fixation is required to avoid motion artefacts.

In addition, OCT is expensive and a learning curve exists for the operator to acquire high-quality scans. While OCT promises to provide a fast and objective approach to monitoring glaucoma progression, defining the normal reference range of change in longitudinal RNFL measurements and drawing the distinction between pathological change and physiological degeneration and measurement variability of RNFL over time remain major challenges.

References

1. Balazsi AG, Drance SM, Schulzer M, Douglas GR. Neuroretinal rim area in suspected glaucoma and early open-angle glaucoma. Correlations with parameters of visual function. *Arch Ophthalmol*. 1984;102:1011-4.
2. Jonas JB, Königsreuther KA. Optic disk appearance in ocular hypertensive eyes. *Am J Ophthalmol*. 1994;117:732-40.
3. Sommer A, Katz J, Quigley HA, et al. Clinically detectable nerve fiber atrophy precedes the onset of glaucomatous field loss. *Arch Ophthalmol*. 1991;109:77-83.
4. Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. *Science*. 1991;254:1178-81.
5. Hee MR, Izatt JA, Swanson EA, et al. Optical coherence tomography of the human retina. *Arch Ophthalmol*. 1995;113:325-32.
6. Gloesmann M, Hermann B, Schubert C, Sattmann H, Ahnelt PK, Drexler W. Histologic correlation of pig retina radial stratification with ultrahigh-resolution optical coherence tomography. *Invest Ophthalmol Vis Sci*. 2003;44:1696-703.
7. Wollstein G, Paunescu LA, Ko TH, et al. Ultrahigh-resolution optical coherence tomography in glaucoma. *Ophthalmology*. 2005;112:229-37.
8. Carpineto P, Ciancaglini M, Zuppari E, Falconio G, Doronzo E, Mastropasqua L. Reliability of nerve fiber layer thickness measurements using optical coherence tomography in normal and glaucomatous eyes. *Ophthalmology*. 2003;110:190-5.
9. Paunescu LA, Schuman JS, Price LL, et al. Reproducibility of nerve fiber thickness, macular thickness, and optic nerve head measurements using StratusOCT. *Invest Ophthalmol Vis Sci*. 2004;45:1716-24.
10. Bourne RR, Medeiros FA, Bowd C, Jahanbakhsh K, Zangwill LM, Weinreb RN. Comparability of retinal nerve fiber layer thickness measurements of optical coherence tomography instruments. *Invest Ophthalmol Vis Sci*. 2005;46:1280-5.