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A Practical Guide for Interpretation of Optical Coherence Tomography Retinal Nerve Fiber Layer Measurement

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INTRODUCTION

Structural damage in glaucoma often occurs before detectable loss in visual function.[1-3] Accurate assessment of the optic disk and retinal nerve fiber layer (RNFL) morphology, however, is not always an easy task. Optical coherence tomograph (OCT), confocal scanning laser ophthalmoscope (CSLO) and scanning laser polarimeter (SLP) are the 3 commonly used imaging instruments for objective measurement of the optic disk and RNFL in clinical and research settings. While SLP only measures the RNFL and CSLO primarily measures the optic disk, OCT provides cross-sectional imaging for both the RNFL and optic disk. Despite the recent introduction of spectral domain OCT,[4] the Stratus OCT is currently the most widely available OCT instrument. Misinterpretation of OCT RNFL analysis is not uncommon among clinicians who have not paid enough attention to the image quality and scan location. This article aims to provide a step-by-step approach for interpretation of Stratus OCT RNFL analysis printout in the evaluation of glaucoma and its progression.

STRATUS OCT

The principle of OCT is based on low coherence interferometry.[5] The first commercially available OCT unit was introduced by Carl Zeiss Meditec Inc (Dublin, CA). The first two generations of OCT (OCT 1 and OCT 2000) provide an axial resolution of 12 to 15 µm and a transverse resolution of 20 to 25 µm with a scan speed of 100 scan points per second. The Stratus OCT (Carl Zeiss Meditec Inc, Dublin, CA) is the third generation of OCT. It received food and drug administration approval in May 2002. Stratus OCT uses a low coherence super luminescent diode source with wavelength 820 nm giving an axial resolution of approximately 10 µm and a transverse resolution of 20 µm (spot size at retina). High diagnostic sensitivity and specificity in diagnosing glaucoma has been shown for OCT RNFL measurement.[6-9]

RETINAL NERVE FIBER LAYER ANALYSIS

In Stratus OCT, there are 4 scan protocols for measurement of the RNFL: (1) Fast RNFL thickness (3.4), (2) RNFL thickness (3.4), (3) RNFL thickness (2.27 × disk), and (4) RNFL map. The "fast RNFL thickness (3.4)" and "RNFL thickness (3.4)" perform 3 circle scans (with 256 and 512 scan points for each circle scan, respectively) with a diameter of 3.4 mm around the optic disk. The 3 RNFL measurements are then averaged. The "RNFL thickness (2.27 × disk)" allows the user to adjust the scan circle size with reference to the optic disk size. It acquires a circle scan with a diameter of 2.27 times the optic disk diameter. The default optic disk diameter is 1.5 mm and the size of scan circle is 1.5 × 2.27 = 3.4 mm. The "RNFL map" consists of six circle scans with radius of 1.44, 1.69, 1.90, 2.25, 2.73, 3.40 mm. It produces a RNFL map at the optic disk region.

The RNFL is automatically segmented and measured by the difference in distance between the vitreoretinal interface and a posterior boundary based on a predefined reflectivity signal level. OCT RNFL measurements have been demonstrated to be reproducible and reliable in normal and glaucomatous eyes.[10-12] Diagnosis of glaucoma with imaging instruments is commonly made with reference to normative data. The "fast

RNFL thickness (3.4)" and "RNFL thickness (3.4) are the most widely accepted scan protocols because normative reference ranges are available. No normative data has yet been collected for the "RNFL thickness (2.27 × disk)" and "RNFL map" rendering these scan protocols less popular for clinical assessment of RNFL loss.

INTERPRETATION OF RNFL ANALYSIS PRINTOUT – A STEP-BY-STEP APPROACH

Step 1: Identify the Scan Protocol

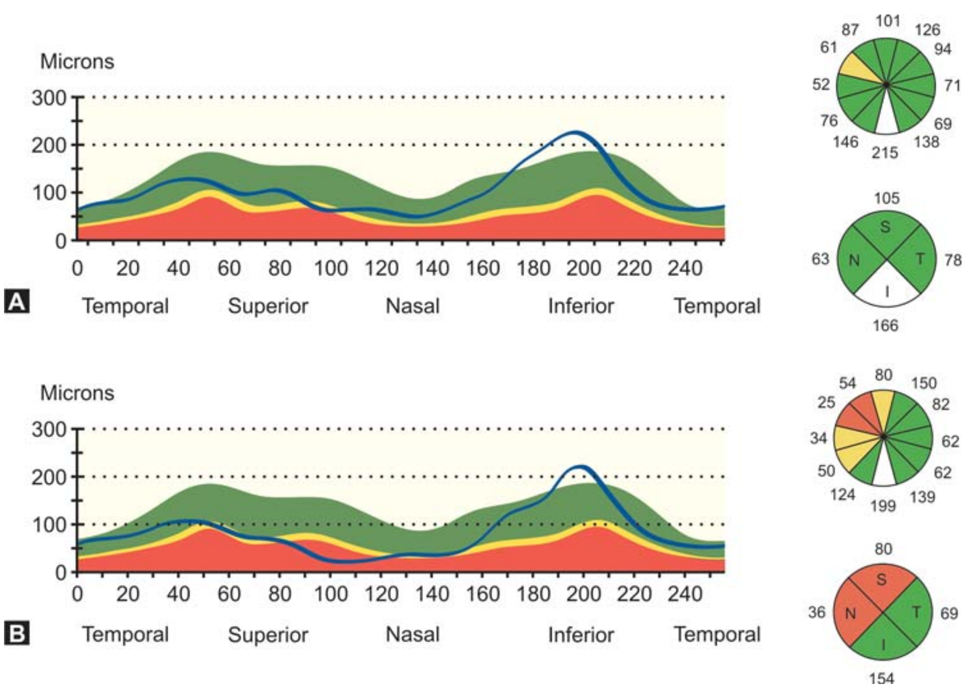
Analysis printouts of the "fast RNFL thickness (3.4)" and "RNFL thickness (3.4)" have similar display layouts. It is important to differentiate one from another because RNFL measurements obtained from the "fast RNFL thickness (3.4)" are generally greater than those from the "RNFL thickness (3.4)".[13] Selecting the same scan protocol is crucial for follow-up assessment.

Step 2: Check the Scan Quality and Signal Strength

Interpretation of RNFL measurement is impossible if the scan quality is suboptimal. Scan quality should be checked for every OCT image with particular attention to the segmentation of RNFL and the signal strength. False impression of RNFL loss could occur if the signal strength is poor (Figs 1A and B). The value of signal strength ranges between 1 and 10 with 10 represents the best and 1 the worst image signal. Poor signal strength is often related to incorrect scan focus or media opacity (e.g. cataract). It is notable that entering the axial length and spherical equivalent in the Stratus OCT does not change the scan focus of the instrument. Manual adjustment of the focusing knob is always necessary. While a signal strength of at least 5 is usually required (manufacturer recommendation),[14] signal strength is directly related to the RNFL thickness (Fig. 2).[15-16] Acquiring scan with maximal possible signal strength is recommended for RNFL measurement.

Step 3: Check the Scan Position

It is essential to position the center of the scan circle at the optic disk center. RNFL measurement error varies with the direction and distance of scan displacement.[17-18] The superior and inferior RNFL measurements are most vulnerable to scan displacement errors (Figs 3A and B). The scan circle (appeared as a white circle in the red-free image) shown in the OCT printout may not correspond to the actual scan location. Nevertheless, it serves as a useful reference to detect scans with poor centration.



Figs 1A and B: Retinal nerve fiber layer profile of a glaucoma suspect patient (glaucomatous optic disk but normal visual field) obtained with signal strength of (A**)** 5 and (B**)** 10. A nerve fiber layer defect was falsely noted when the measurement was obtained with a lower signal strength (Figure adapted from Cheung CY, et al. Ophthalmology. 2008;115:1347-51)

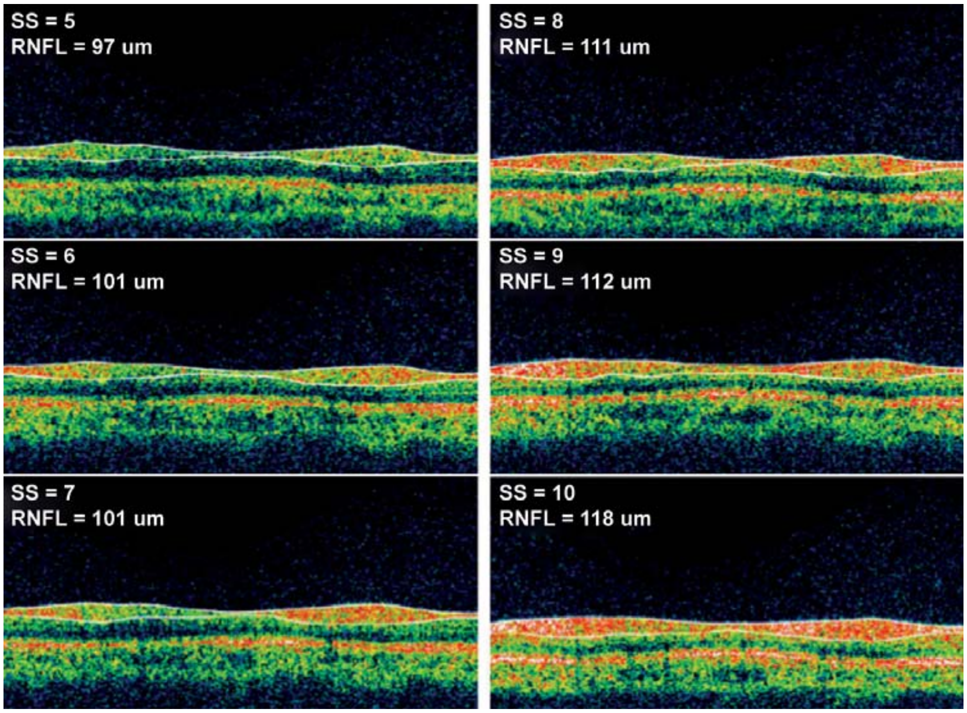
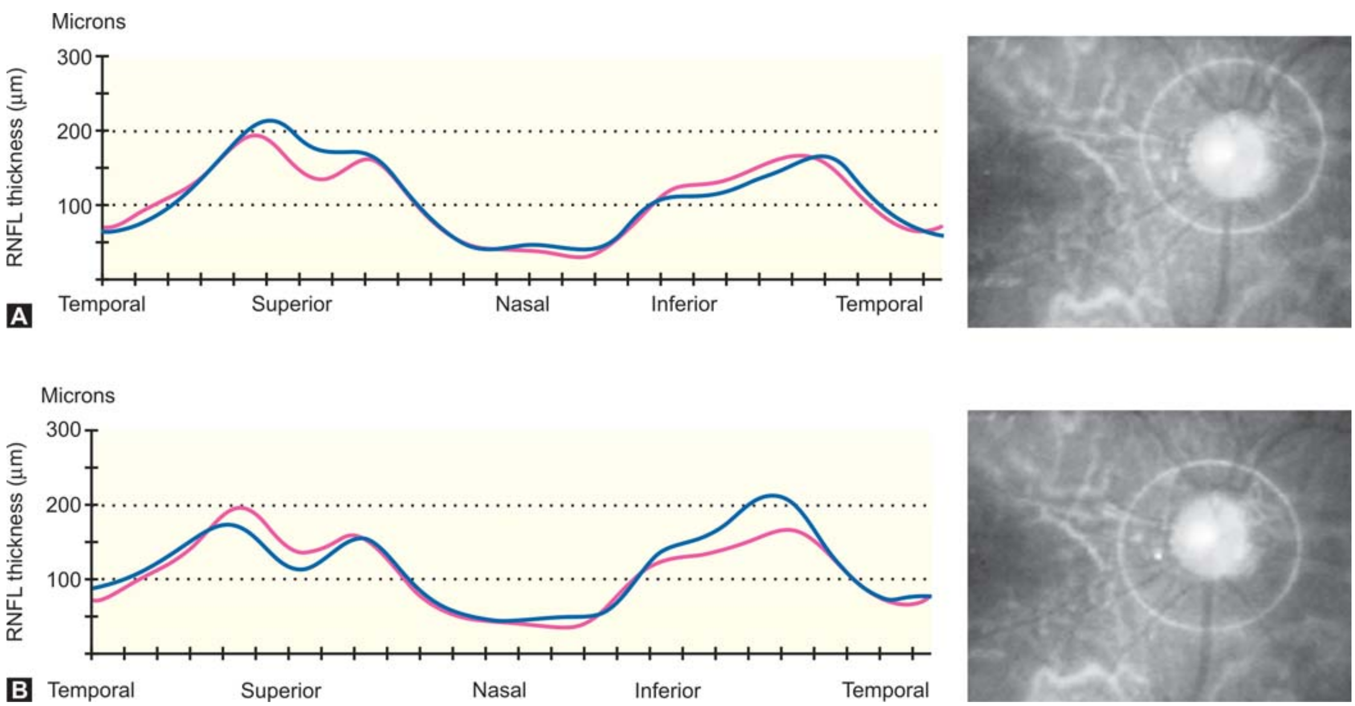
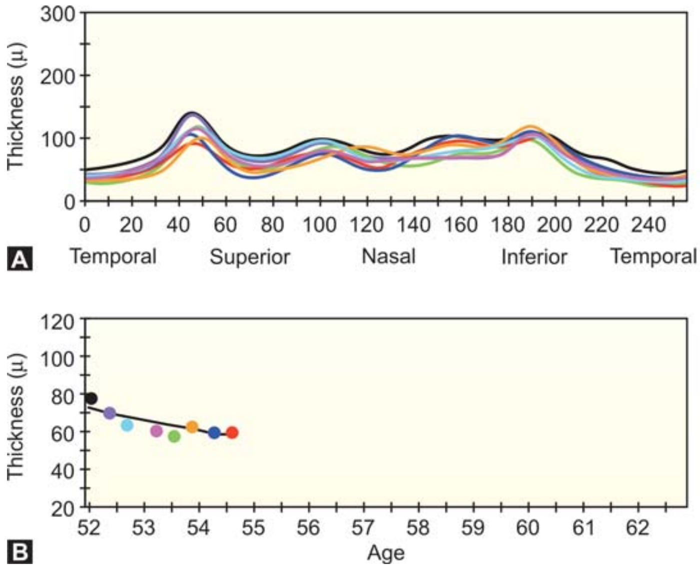


Fig. 2: OCT images demonstrating retinal nerve fiber layer (RNFL) segmentation and measurement by the Stratus OCT in the same eye with signal strength from 5 to 10. The average RNFL thickness increases with the signal strength (Figure adapted from Cheung CY, et al. Ophthalmology 2008;115:1347-51)



Figs 3A and B: The retinal nerve fiber layer (RNFL) profiles (centered and displaced scans) obtained by displacing the scan circle at an arbitrary distance during OCT imaging using the fast RNFL 3.4 scan protocol in the same eye are shown in the serial analysis printouts. The RNFL profile centered at the disk is shown in blue and those with scan circles displaced superiorly (A) and inferiorly (B) (demonstrated in the corresponding fundus photographs) are in red (Figure adapted from Cheung CY, et al. Eye. 2008 In press)



OD	SS,Q	AVG	SUP	INF
4/1/2006 10:55:41 AM (N=3)	10	78.92	91.00	88.00
8/19/2006 12:36:13 PM (N=3)	9	71.91	87.00	86.00
12/18/2006 11:44:16 AM (N=3)	8	64.87	82.00	71.00
6/14/2007 11:55:13 AM (N=3)	8	61.83	76.00	72.00
10/23/2007 10:38:40 AM (N=3)	9	58.74	71.00	66.00
2/25/2008 1:05:45 PM (N=3)	9	64.33	62.00	81.00
7/4/2008 12:50:23 PM (N=3)	9	60.94	61.00	79.00
11/3/2008 11:50:45 AM (N=3)	9	61.20	66.00	77.00

Rate of change: –5.846 +/– 4.479 µ/year*
Statistically significant P < 5%, seek clinical correlates

Figs 4A and B: (A) OCT guided progression analysis (GPA) printout showing the overlay of serial RNFL thickness profiles and the linear regression analysis of average RNFL thickness against time (age) in a glaucoma patient with significant trend of progression. The date and time, signal strength, average, superior and inferior RNFL thicknesses are shown in a table on the right. The rate of change was calculated and expressed in µm change per year with a p value. (B) Progression analysis with visual field index (VFI) against age

Step 4: Evaluate the RNFL Profile, Average and Sectoral RNFL Thicknesses

The normative display provides a useful reference to determine whether the RNFL measurements are within or outside the normal ranges. RNFL thickness is indicated in green, yellow or red which represents "within normal limit" (within 5-95% of normal distribution), "borderline" (within 1-5% of normal distribution) or "outside normal limit" (within 0-1% of normal distribution), respectively. The normative database is not race specific. It consists of RNFL measurements of 328 healthy individuals from 5 different ethnic groups (Caucasian, Hispanic, African-American, Asian, and Asian-Indian).[19]

INTERPRETATION OF RNFL PROGRESSION

A new RNFL progression analysis algorithm – the guided progression analysis (GPA), has been recently introduced in the Stratus OCT software (version 5.0). In contrast to an event-based analysis in which progression is detected as changes fall below a pre-set "threshold" compared with baseline, the OCT GPA is a trend-based analysis with progression analyzed and reported as change over time using serial RNFL measurements. At least 4 visits are required to generate the GPA report. The GPA overlays serial RNFL thickness profiles and performs linear regression analysis of average RNFL thickness against the duration of follow-up (age year) (Figs 4A and B). The slope of the regression line represents the rate of change of RNFL thickness and is expressed in µm per year. The current version of the software does not support progression analysis on clock hour RNFL measurements. Figure 4 demonstrates a glaucoma patient with progressive reduction of average RNFL thickness at a rate of –5.846 +/– 4.479 µm per year. Visual field progression is also noted by the visual field index analysis (Fig. 5). The agreement between optic disk/RNFL and visual field progression has been reported to be poor.[20-22] Both structural and functional tests should be considered in the assessment of glaucoma progression.

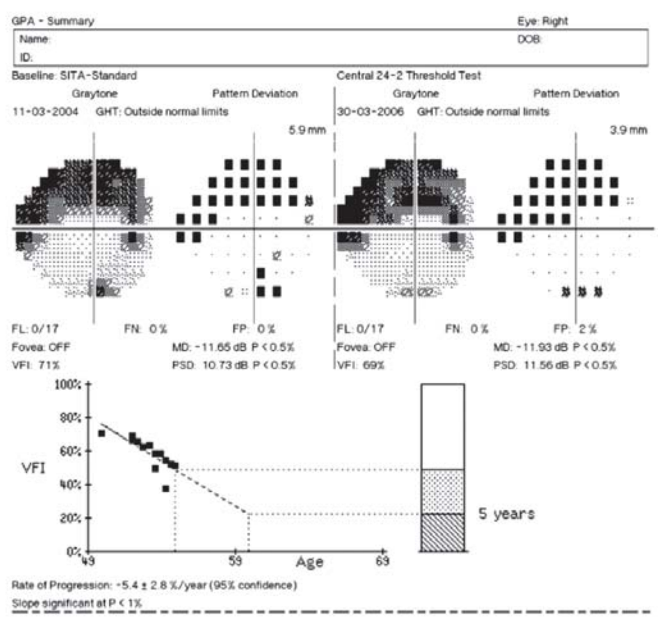


Fig. 5: Visual field progression as noted by the visual field index analysis

CONCLUSION

While clinical examination of the optic disk is indispensible in diagnosing glaucoma, RNFL evaluation is important in confirming the diagnosis and monitoring the progression of the disease. Measurement of RNFL with OCT may be even more sensitive than optic disk measurement in detecting glaucomatous damage.[23-24] With the recent availability of GPA, progressive changes of RNFL can be analyzed statistically. Information obtained from OCT, however, should always be interpreted carefully with reference to the image quality, scan location and reliability of RNFL segmentation.

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