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Signal Strength Is an Important Determinant of Accuracy of Nerve Fiber Layer Thickness Measurement by Optical Coherence Tomography

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Abstract

Purpose—To investigate the effect of signal strength on the measurement of the retinal nerve fiber layer (RNFL) using optical coherence tomography (OCT).

Methods—Eyes with known or suspected glaucoma or non-glaucomatous optic atrophy were scanned twice within the same visit using Stratus OCT's Fast Nerve Fiber Layer Thickness (FNFLT) protocol. Only those eyes with two high quality scans (signal strengths of at least 5 and different from each other, no error messages, and no obvious segmentation errors) were included in the study. The RNFL thickness measurements from the initial and the repeat scans were compared and then correlated with the differences in signal strength. Subgroup analyses were performed similarly among patients with average RNFL thickness less than 90 microns and those with at least 90 microns.

Results—Scans with higher signal strengths are associated with greater RNFL thickness measurements if the signal strength is less than 7. Scans with signal strength of at least 7 have higher reproducibility. This is true among all patients as well as subgroups divided on the basis of average RNFL thickness. Additionally, we found that the greater the variability between the initial and repeat scans, the greater the variability in the RNFL thickness measurements. Scans with higher signal strengths have less variability, especially when the optic nerve is relatively healthy.

Conclusions—When measuring the RNFL thickness with the Stratus OCT, it is important to aim for a signal strength of at least 7. Visual field testing may be more reliable in some patients, especially when the optic nerve is significantly compromised.

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Keywords

Optical coherence tomography; signal strength; nerve fiber layer thickness

Optical coherence tomography (OCT) has become an increasingly important tool for detecting damage to the retinal nerve fiber layer (RNFL), which may precede the onset of detectable visual field defects in patients with glaucoma.[1] Using the principle of light interferometry, OCT provides a highresolution image of the retina and the optic nerve.[2,3] OCT may be more sensitive than visual field testing in detecting the progression of glaucoma in some cases,[3] and it has documented ability to differentiate between healthy and glaucomatous eyes.[5,6] Many investigators have observed relatively good reproducibility of the OCT RNFL segmentation algorithm.[7,8] The latest Stratus OCT software (Carl Zeiss Meditec, Dublin, CA), Version 4.0, also recognizes some scans of suboptimal quality and reports error messages. This further assures that quality measurements are used in clinical decision making.

A variety of scanning techniques exist on the Stratus OCT for measuring RNFL. Peripapillary RNFL thickness scans have been suggested as the preferred metric for measuring the extent of glaucomatous damage.[9] A commonly used protocol is the Fast Nerve Fiber Layer Thickness (FNFLT), which compares results to a reference normative database. The protocol generates A-scans along a 360-degree circular path located 1.74 mm from the center of the optic disc, producing a total of 3 separate scans during each test. It generates RNFL thickness measurement for each of twelve 30-degree sectors, then computes an average for each of four quadrants and an overall average.

However, we had previously demonstrated that signal strength, which is a proxy for the quality of the scan, may have a significant impact on the measurements of RNFL on the Stratus OCT.[10] Specifically, scans with lower signal strengths tend to underestimate the thickness of the RNFL. This variability is especially pronounced in patients with advanced optic nerve damage, even in scans without error messages.[10] Therefore, it is important to obtain scans of similar signal strengths in order to facilitate the longitudinal follow up of glaucoma.

A large number of scans evaluated in our previous study had signal strength of less than 5, which is the minimum value suggested by the manufacturer.[10] Therefore, we could not conclude that this variability in RNFL measurements existed if higher quality scans could be obtained. Assuming that variability could be reduced with higher quality scans, the minimum scan quality sufficient for clinically-acceptable reproducibility has not been precisely defined. In this report, to address these questions, we study the reproducibility of RNFL measurements in eyes in which higher quality scans could be obtained.

Methods

Patients undergoing RNFL thickness testing with the Stratus OCT Version 4.0 were retrospectively chosen from the imaging database of a general ophthalmology practice. The database was generated from April 2005 through February 2008. Approval for the analysis of OCT images was obtained from the Institutional Review Board of the University of Southern California. All data were managed in accordance with the regulations set forth in the Health Insurance Portability and Accountability Act.

Per the standard protocol at this ophthalmology practice, only patients with suspected or known glaucoma and non-glaucomatous optic atrophy were scanned by a trained technician using the FNFLT protocol through dilated pupils. Patients without any evidence or probability of RNFL damage on clinical examination, and those whose RNFL damage may be due primarily to retinal diseases such as arterial occlusion, were not evaluated with the FNFLT protocol. The trained technician controlled the placement of the scan circle and was instructed to center the scan around the optic nerve head. If the quality of the initial scan was felt to be improvable, a second scan was performed after lubricating eye drops were administered. The primary eye was defined to be the one with clinically definite or suspected optic nerve damage. For patients who had both eyes scanned, one eye was randomly chosen for analysis. Only eyes with at least two scans on the same day were selected for further analysis. Additionally, selected paired scans must meet the following inclusion criteria: 1) they must have signal strengths that are different from each other, and both must be at least 5; 2) no error messages such as “low analysis confidence,” “scan too high,” “scan too low,” or “missing data” which are automatically generated by the software using a proprietary algorithm; 3) no obvious segmentation errors; 4) if more than two scans were performed, the scans with the two highest signal strengths were selected. Interpretation of the OCT images was performed by a trained ophthalmologist (ZW).

The demographic information, signal strengths (SS_1 is the lower signal strength, SS_2 is the higher), and the associated RNFL thickness readings ($RNFL_1$ and $RNFL_2$, respectively, in microns) were recorded for each patient. Marginal RNFL thickness (MRT) is defined as $(RNFL_2\text{-}RNFL_1)/(SS_2\text{-}SS_1)$. Therefore, a positive MRT value means that the higher signal strength scan has a higher RNFL thickness reading, and vice versa. The MRT is treated as a dichotomous variable (either positive or negative). The p-values were calculated using binomial probability, with the null hypothesis that the measured RNFL thickness should be the same regardless of signal strength, i.e. MRT should be zero. No attempts were made to classify the optic nerves as normal, glaucomatous, or non-glaucomatous atrophy based on the scan results or other clinical information. However, subgroup analyses were performed similarly on patients whose average RNFL thickness (average of $RNFL_1$ and $RNFL_2$) were at least 90 microns and those whose average RNFL thickness were less than 90 microns.

Additionally, the correlation between the difference in signal strengths ($SS_2\text{-}SS_1$) and differences in RNFL measurements ($RNFL_2\text{-}RNFL_1$) were investigated using Spearman correlations. SS_2 represents the highest achieved signal strength for each eye. Its relationship to the differences in RNFL measurements ($RNFL_2\text{-}RNFL_1$) were also investigated using Spearman correlations to determine if higher quality scans was associated with less variability.

Results

A total of 897 patients were found in the database to have undergone at least two FNFLT scans on the same day. Among these, 571 (63.7%) did not have signal strengths of at least 5 on two separate scans. Of the remaining patients, 23 (2.6%) were eliminated due to error messages associated with one or both scans. Another 130 (14.5%) were excluded due to identical signal strengths on the two scans, and 8 (0.9%) had scans that were deemed likely to harbor segmentation errors. The remaining 165 patients met the inclusion criteria.

The average age of the patients was 64.7 ± 14.5 years. There were 76 (46.1%) men and 89 (53.9%) women. The primary eye was the right eye in 89 patients (53.9%) and the left eye in 76 (46.1%).

Table 1 summarizes the RNFL and signal strength data for all 165 patients using MRT as a dichotomous variable. The higher signal strength scan appeared to be associated with a thicker RNFL thickness measurement if both scans had signal strength of 7 or below, i.e. MRT was positive. In other words, scans with signal strength 7 were associated with higher RNFL thickness readings than those with signal strength 6, which were in turn higher than those with signal strength 5. However, if both scans had signal strengths of at least 7, this relationship was not statistically significant. This appeared to be true among patients with thinner RNFLs (<90 microns, Table 2) as well as those with thicker RNFLs (≥90 microns, Table 3).

Table 4 shows the Spearman correlations. Difference in signal strengths (SS_2-SS_1) was positively correlated to difference in RNFL thickness measurements ($RNFL_2$-$RNFL_1$) among all patients as well as among the subgroup of patients with RNFL thickness average of less than 90 microns, but not among the subgroup of patients with RNFL thickness average of at least 90 microns. This confirmed that higher signal strength scans were associated with greater RNFL thickness, especially among patients with thinner RNFLs. SS_2, the highest achieved signal strength for each eye, was negatively correlated with differences in RNFL thickness measurements among patients with thicker RNFL (at least 90 microns). After adjusting for differences in signal strength (SS_2-SS_1), SS_2 was also negatively correlated to the differences in RNFL thickness measurements for all patients, but still not among the subgroup of patients with thinner RNFL (less than 90 microns). After adjusting for SS_2, difference in signal strength (SS_2-SS_1) was significantly correlated to difference in RNFL thickness measurements for all patients and for both subgroups.

Discussions

In this study, we observed that signal strength was an important determinant of RNFL thickness measurement by the Stratus OCT, even when it was above the manufacturer's recommendation. It appeared that signal strength of at least 7 was required to reduce variability, regardless of the RNFL thickness. When the signal strength was above 7, no statistically correlations were found. This may be partly due to the relatively small sample size of scans with signal strength of 8 or above. In this retrospective study design, if the initial scan already achieved signal strength of 7, the technician was probably less likely to attempt a repeat scan.

As in our previous study, we again demonstrated that the greater the variability in the signal strength, the greater variability in RNFL thickness measurements. Higher signal strength scans appeared to be associated with thicker RNFL measurements. When high quality scans were achievable, the variability diminished, especially for cases in which the optic nerve was relatively healthy (RNFL ≥ 90 microns). However, when the RNFL was less than 90 microns, the positive correlation between differences in RNFL thickness measurements and difference in signal strengths became stronger. Additionally, the decreased variability associated with higher signal strength scans (SS_2) disappeared, i.e. the relationship between SS_2 and $RNFL_2$-$RNFL_1$ was not statistically significant in the subgroup of patients whose RNFL average was less than 90 microns (Table 4). The implication was that OCT may be less accurate and more dependent upon consistent and high signal strengths when the RNFL was compromised. This may be because the resolution of the Stratus OCT is 8-10 microns, which becomes a potentially greater percentage error in patients with thin RNFLs. Therefore, in patients advanced optic nerve damage, visual field testing may be more reliable in some cases.

OCT measures RNFL thickness by first defining its outer and inner boundaries by means of detecting differences of reflectivity between various layers. The vitreoretinal interface is easily recognized because the inner boundary of the RNFL has significantly greater reflectivity than the vitreous. However, the outer boundary between the more reflective RNFL and the less reflective deeper layers of the retina may be more difficult to discern. In a scan with higher signal strength, light penetrates deeper into the retina and increases the reflectivity of all layers. The result is that more retinal tissues would have a reflectivity higher than the threshold defined by OCT. Therefore, the apparent outer boundary of the RNFL is deeper into the retina in a scan with higher signal strength, increasingly the RNFL thickness measurement.

Our study demonstrates that greater signal strength, which is a proxy for higher scan quality, is essential in quantifying RNFL thickness using Stratus OCT's FNFLT protocol. Whenever possible, signal strength of at least 7 should be achieved. However, media opacity,[11] small pupils,[12] and dry eyes[13] are known to interfere with scan quality. Therefore, the ideal condition for performing RNFL scan can be achieved through a dilated pupil and an optimal corneal surface, either through instillation of artificial tears or with frequent blinking.[12,13] Our study may explain findings that phacoemulsification or pupillary dilation apparently increases RNFL thickness measurements.[14,15] Comparing the signal strengths is a convenient way to standardize comparison between two scans, even scans without any error messages. In cases where signal strength of at least 7 is not achievable, scans of similar signal strengths should be used to assess changes of RNFL thickness over time.

Different generations of OCT machines and software are known to produce measurements of considerable variability.[16,17] Whether the findings of the current study are applicable to newer generations of OCT machines (e.g. spectral domain OCT) is not known, but because the Stratus OCT is still in widespread use, these findings may have significant implications in the diagnosis and management of glaucoma.

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Table 1

Summary of Marginal RNFL Thickness (MRT) values for all patients (N=165, binomial probability)

SS_2 \ SS_1	5	6	7	8, 9, or 10
6	Positive = 46, Negative = 23, p=0.0020	--	--	--
7	Positive = 25, Negative = 7, p=0.0008	Positive = 23, Negative = 7, p=0.0019	--	--
8, 9, or 10	Positive = 8, Negative = 3, p=0.081	Positive = 4, Negative = 1, p=0.16	Positive = 5, Negative = 9, p=0.12	Positive = 1, Negative = 3, p=0.25

SS_1 = the lower of two signal strengths

SS_2 = the higher of two signal strengths

$RNFL_1$ = RNFL thickness measured by the scan with lower signal strength, microns

$RNFL_2$ = RNFL thickness measured by the scan with higher signal strength, microns

MRT = $(RNFL_2-RNFL_1) / (SS_2-SS_1)$

A positive MRT means that the RNFL thickness measurement is higher in the scan with the greater signal strength, and vice versa.

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Table 2

MRT values for patients with lower average RNFL thickness (<90 microns) (N=89, binomial probability)

SS_2 \ SS_1	5	6	7	8, 9, or 10
6	Positive = 26, Negative = 16, p=0.038	--	--	--
7	Positive = 15, Negative = 1, p=0.0002	Positive = 12, Negative = 3, p=0.014	--	--
8, 9, or 10	Positive = 4, Negative = 2, p=0.23	Positive = 3, Negative = 1, p=0.25	Positive = 2, Negative = 4, p=0.23	Positive = 0, Negative = 0

Table 3

MRT values for patients with higher average RNFL thickness (≥90 microns) (N=76, binomial probability)

SS_2 \ SS_1	5	6	7	8, 9, or 10
6	Positive = 20, Negative = 7, p=0.0066	--	--	--
7	Positive = 10, Negative = 6, p=0.12	Positive = 11, Negative = 4, p=0.042	--	--
8, 9, or 10	Positive = 4, Negative = 1, p=0.16	Positive = 1, Negative = 0, p=0.50	Positive = 3, Negative = 5, p=0.22	Positive = 1, Negative = 3, p=0.25

Table 4

Correlations between differences in RNFL thickness measurements ($RNFL_2$-$RNFL_1$) and SS_2 and differences in signal strength (SS_2-SS_1) using Spearman correlations.

	Spearman Correlation Coefficient with ($RNFL_2$ - $RNFL_1$)	p-value
SS_2		
All RNFL averages	-0.04	0.61
RNFL average < 90 microns	0.15	0.17
RNFL average ≥ 90 microns	-0.25	0.03
SS_2 - SS_1		
All RNFL averages	0.20	0.01
RNFL average < 90 microns	0.30	0.004
RNFL average ≥ 90 microns	0.09	0.46
SS_2 - adjusted for (SS_2-SS_1)		
All RNFL averages	-0.20	0.01
RNFL average < 90 microns	-0.09	0.41
RNFL average ≥ 90 microns	-0.32	0.006
(SS_2-SS_1) - adjusted for SS_2		
All RNFL averages	0.27	0.0004
RNFL average < 90 microns	0.28	0.008
RNFL average ≥ 90 microns	0.22	0.05