Original Article

Reproducibility of retinal nerve fiber layer measurements across the glaucoma spectrum using optical coherence tomography

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Purpose: The purpose was to determine intra-session and inter-session reproducibility of retinal nerve fiber layer (RNFL) thickness measurements with the spectral-domain Cirrus optical coherence tomography (OCT)® (SD-OCT) in normal and glaucomatous eyes, including a subset of advanced glaucoma. **Materials and Methods:** RNFL measurements of 40 eyes of 40 normal subjects and 40 eyes of 40 glaucomatous patients including 14 with advanced glaucoma were obtained on the Cirrus OCT® (Carl Zeiss Meditec, Dublin, CA, USA) five times on 1-day (intra-session) and on five separate days (inter-session). Intraclass correlation coefficient (ICC), coefficient of variation (COV), and test-retest variability (TRT) values were calculated for mean and quadrant RNFL in each group separately. Reproducibility values were correlated with age and stage of glaucoma. **Results:** For intra-session reproducibility, the ICC, COV, and TRT values for mean RNFL thickness in normal eyes were 0.993, 1.96%, and 4.02 μm, respectively, 0.996, 2.39%, and 3.84 μm in glaucomatous eyes, and 0.996, 2.41%, and 3.70 μm in advanced glaucoma. The corresponding inter-session values in normal eyes were 0.992, 2.16%, and 4.09 μm, 0.995, 2.62%, and 3.98 μm in glaucoma and 0.990, 2.70%, and 4.16 μm in advanced glaucoma. The mean RNFL thickness measurements were the most reproducible while the temporal quadrant had the lowest reproducibility values in all groups. There was no correlation between reproducibility and age or mean deviation on visual fields. **Conclusions:** Peripapillary RNFL thickness measurements using Cirrus OCT® demonstrated excellent reproducibility in normal and glaucomatous eyes, including eyes with advanced glaucoma. Mean RNFL thickness measurements appear to be the most reproducible and probably represent the best parameter to use for longitudinal follow-up.

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Retinal nerve fiber layer (RNFL) thickness measurement has become a widely employed clinical technique for glaucoma assessment. Optical coherence tomography (OCT) provides objective, quantitative measurements of the retina and RNFL thickness.[1] The time-domain OCT Stratus® has been in clinical use since the past decade,[2-4]and has now incorporated a progression analysis software for follow-up of glaucoma patients.[5] However, the time-domain OCT was wrought with problems of motion artifacts, poor registration of the scan circle and less than optimum scans with low signal strength. The introduction of spectral domain OCT (SD-OCT) has improved scanning speed, and axial resolution has attempted to address these limitations by enabling high resolution, three-dimensional volume sampling.[6-8]

For any instrument to be a meaningful tool for diagnosis and follow-up in a progressive disease like glaucoma, it is essential that the test results have a high degree of reproducibility, to be sure that any change from either the normative database or in serial analysis over time is actual change and not just variability due to poor reproducibility of the measurements. Thus, it becomes imperative for preliminary validation of any instrument or test to determine the reproducibility, and specifically, the test-retest variability (TRT) values. The Stratus OCT has been reported to have lower reproducibility compared to spectral domain OCT in normal subjects.[9] It has also been reported to have the additional limitation of reduced reproducibility in glaucoma patients probably due to poor fixation leading to even greater motion artifacts.[10-12]

Previous studies on the spectral Domain OCT have demonstrated excellent reproducibility of the measurements in healthy eyes[13-17] and glaucoma patients.[18,19] However, most of these studies have combined all stages of glaucoma patients as a whole. It is difficult to assess progression on visual fields in patients with advanced glaucoma, due to the increased long-term fluctuation in test results seen in these patients. Monitoring them by a structural tool may prove to be an important adjunct in their management. Quantifying the reproducibility of the RNFL thickness measurements is an important step in evaluating the potential usefulness of SD-OCT for determining glaucomatous progression especially in those with advanced glaucoma. The aim of this study was to quantify the reproducibility of the spectral domain Cirrus OCT (Carl Zeiss Meditec, Dublin, CA, USA) for peripapillary RNFL thickness measurements in a subset of advanced glaucoma patients and to compare these values with normal subjects and glaucoma patients as a whole to assess the effect of disease severity on the reproducibility of these measurements.

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Materials and Methods

This was a prospective observational study including patients with open angle glaucoma and normal subjects presenting to the Glaucoma Clinic of a tertiary care ophthalmological Institute between July 2009 and September 2010. Normal subjects were selected from age and sex-matched healthy volunteers with no history of any ocular disease or surgery. Subjects fulfilling the inclusion criteria detailed below were prospectively recruited for the study. The study fulfilled all the guidelines required by and obtained clearance from the Institutional Ethics Committee (Vide No 786/PGI/2TRG/08 DT 23/10/2009). It adhered to the principles of the Declaration of Helsinki. Informed consent was obtained from all recruited individuals.

Each enrolled participant underwent a comprehensive ophthalmic examination including best-corrected visual acuity (BCVA), intraocular pressure (IOP) measured by Goldmann Applanation tonometry, slit lamp biomicroscopy, gonioscopy, and stereoscopic fundus evaluation on the slit-lamp using a 90.0-D lens. Color stereoscopic optic disc photographs and red-free nerve fiber layer photographs were taken on the Zeiss Fundus camera FF 450 with Visupac System 451 (Carl Zeiss Ophthalmic Systems, Jena, GmBH, Germany). Optic discs were assessed by two graders independently, who were masked to the patients' identity and other examination results. All subjects underwent baseline Standard Achromatic Perimetry on the Humphrey's Field Analyzer 750 II (Carl Zeiss-Humphrey Systems, Dublin, CA) using the 24-2 testing protocol by SITA-Standard strategy.

Normal participants were recruited if they fulfilled the following criteria: Age above 18 years, no history of ocular or neurologic disease or surgery that might interfere with test results (e.g. diabetic retinopathy, uveitis, significant cataract etc.), IOP ≤ 21 mm Hg, BCVA of 20/40 or better, open angles on gonioscopy, normal optic discs, and normal visual fields. Normal optic discs were defined as those with no features suggestive of glaucomatous optic neuropathy (such as cup-disc ratio >0.6, any diffuse or focal neuroretinal rim thinning, any disc hemorrhage, and/or any RNFL defects on the red-free photograph). Normal visual fields were defined as mean deviation (MD) and pattern standard deviation values within 95% normal confidence limits, and a glaucoma hemifield test classified as "within normal limits."

Glaucoma patients were included if they had the same features as normal, except for optic discs suggestive of glaucoma, and 2 consecutive abnormal visual field tests corresponding to the disc damage. Advanced glaucoma was defined according to standard grading by Hodapp-Parrish-Anderson[20]as those patients having MD worse than − 12 dB and >50% of points depressed below 5% level. Early glaucoma was defined as those with MD <−6.0 dB while moderate glaucoma was defined as those with MD between − 6> and − 12.0 dB.

One eye of each subject was included in the analysis. If both eyes of glaucoma patients were eligible for inclusion, the worse eye was enrolled. In case of normal subjects, the right eye was enrolled if both eyes were eligible.

Optical coherence tomography scanning was performed using the spectral domain Cirrus™ OCT (Carl Zeiss Meditec, Dublin, CA, USA; software version-3.0.0.64). The same Cirrus OCT instrument was used by the same operator for all testing sessions. Pupils were dilated. The subject was seated with his/her chin in a chin rest and the machine properly aligned. The subject was then instructed to fixate with the eye being measured on the internal fixation target to bring the optic nerve head within view of the examiner real-time. The Z-offset was adjusted to bring the OCT image into view.

The Optic Disc 200 × 200 scan was used to acquire a cube of side 6 mm while the patient was fixated so that the optic disc was near the center of the scan. Each Optic Disc Scan captures a 6 × 6 × 2-mm "cube" of data consisting of 200 A-scans from 200 linear B-scans (40,000 points) in ~ 1.5 s (27,000 A-scans/s). Cirrus OCT® extracts the RNFL thickness values in a circle centered on the optic disc. The machine does not depend upon the operator correctly placing the scan reproducibly because it includes an automated graph-based algorithm (AutoCenter™) that identifies the center and border of the optic disc in peripapillary images. This allows the RNFL thickness to be measured at the same location each time.

To be acceptable for inclusion, the OCT scans had to fulfill the following criteria: The fundus image must have been clear enough to see the optic disc and scan circle or spokes, the scan must have been properly centered on the optic disc, the signal strength had to have been >7, color saturation must have been even and dense across the entire scan. Care was taken to ensure no missing areas in the scan due to blinks or eye motion.

Five sets of RNFL measurements were made in quick succession in 1-day to measure the intra-test variability. The patient was not moved from his position on the chin rest and the OCT settings were not changed between these tests. This procedure was repeated on 5 different days, within 3 months. For intrasession variability of the scan, the 5 sessions performed on the 1st day were analyzed. For intersession variability, the average of 5 scans on each day was used.

Statistical techniques

The desired sample size in any reproducibility study depends on the number of measurements per subject, the lower confidence interval and the value of the intraclass correlation coefficient (ICC) deemed acceptable. With a lower confidence interval of not less than 0.75for an ICC of 0.8, we calculated the required sample size to be at least 39 subjects, with 5 measurements taken per subject.

Between subject, between-session and within-session variance components were calculated for each of the RNFL components by restricted maximum likelihood variance component analyses (MIXED procedure). ICCs were calculated using these variance components. The ICC is a statistic that summarizes the reproducibility of a measurement process for a given group of subjects. Coefficient of variation (COV) was calculated as standard deviation of variability divided by mean thickness expressed as a percentage, separately for intrasession and inter-session parameters. TRT was calculated (in microns) as twice the square root of the variance components. Each of these were calculated as both intersession and intrasession parameters, separately for the groups comprising normal subjects, glaucomatous patients as a whole, and patients with early, moderate, and advanced

glaucoma. Values for mean RNFL thickness as well as RNFL thickness in four different quadrants were computed. Spearman's ICCs were calculated for all three groups to evaluate any relationship between the measured COV and mean RNFL thickness, MD, and age.

Results

A total of 42 normal subjects (42 eyes) and 48 glaucomatous patients (48 eyes) were enrolled for the study. After excluding poor quality scans and subjects with incomplete follow-up visits, 80 eyes (40 normal, 40 glaucomatous) were included in the final statistical analysis.

The demographic data of the subjects are presented in Table 1. A subset of patients with advanced glaucoma is also shown. Intrasession reproducibility values are depicted in Table 2. The intrasession COV of mean RNFL thickness in glaucoma eyes was higher than that in normal eyes, but not very different from that in the advanced glaucoma subset. For quadrants, ICC was 0.9 or higher and COV was under 6% in all groups. Mean RNFL thickness measurements showed least variability in both groups. Reproducibility values were worst for the temporal quadrant in all groups.

The inter-session reproducibility is shown in Table 3. The COV and test-retest variability values for all RNFL thickness measurements were higher in glaucoma patients compared to normals, but the advanced glaucoma subset was similar to the overall glaucoma group. For quadrants, ICC was 0.89 or higher and COV was under 8% in all groups. As in the intra-session measurements, reproducibility values were best for mean RNFL thickness measurements and worst for the temporal quadrant measurements in all groups.

Correlation between COV and age, mean RNFL thickness and MD on visual fields is depicted in Table 4. There was no statistically significant correlation found between any parameter and COV of mean RNFL thickness for either intra-session or inter-session measurements.

Discussion

The Stratus OCT has been shown to demonstrate greater variability in measurements in glaucoma eyes compared to normal.[10-12,21] Budenz *et al*.[22] reported good reproducibility using the Stratus OCT in glaucoma eyes also, but out of the 59 patients taken as glaucoma, 15 had a normal visual field, so it is likely that their glaucoma patient cohort comprised eyes with very early disease.

Published reports using various spectral domain OCT machines in normal eyes[13-17]have demonstrated excellent reproducibility of RNFL measurements. Lee *et al*.[23] analyzed the TRT of RNFL thickness measurements by the spectral OCT/scanning laser ophthalmoscope (SLO) in normal and glaucoma patients with early disease (average MD − 4.99 ± 4.96 dB). The ICC and COV for mean RNFL thickness were 0.988 and 1.9% in normals, and 0.993 and 2.0% in glaucoma patients, respectively. Gonzales-Garcia[24,25]reported reproducibility of RNFL measurements using RTVue spectral domain OCT in healthy and glaucomatous eyes with early glaucoma (average MD of − 1.85 ± 2.8 dB). The reproducibility in both groups was similar, with COV and ICC 1.54% and 0.97 in healthy eyes, and 1.9% and 0.97 in glaucomatous eyes.

Wu *et al*.[26] studied intra-session reproducibility values of RNFL thickness using the Spectralis OCT in normal and glaucoma patients with varied severity (average MD was − 11.01 ± 8.76 dB). Their reported ICC and COV in the glaucoma subset was 0.996 and 1.74%, respectively. Ji-Peng *et al*.[27] reported intra-session reproducibility of RNFL measurements using the RTVue SD-OCT machine in subsets of glaucoma stratified according to disease severity. In the advanced glaucoma subset (MD − 22.97 ± 8.43 dB), the ICC and COV for average RNFL thickness were 0.97 and 4.59%, respectively, compared to 0.99 and 2.63%, respectively, in normal eyes. Using the spectral OCT/SLO, Mansoori *et al*.[18] reported intra-session ICC and COV for advanced glaucoma patients as 0.998 and 1.3%, while the inter-session values were 0.988 and 3.28%, respectively.

Our study included patients with advanced glaucoma, where there is increased fluctuation on visual fields, necessitating objective testing. Apart from the present study, there is only one study of intra-session and inter-session reproducibility of RNFL thickness in glaucoma patients using Cirrus OCT by Mwanza *et al*.[28] Though their study included advanced glaucoma subjects, they did not report the reproducibility values for the advanced glaucoma subset

Table 1: Baseline data

	Normal subjects (*n*=40)	Glaucoma patients (*n*=40)		
		Early glaucoma (*n*=6)	Moderate glaucoma (*n*=20)	Advanced glaucoma (*n*=14)
Male (% total)	42.5	50.0	53.8	78.6
Mean age±SD (years)	60.87±16.41	61.8±8.3	61.9±10.7	61.14±14.80
Mean deviation (mean±SD) (dB)	−1.57±1.19	−3.8±1.1	−8.6±1.8	−16.71±4.15
RNFL thickness (mean±SD) (μm)				
Mean RNFL	90.50±10.91	76.2±14.3	72.1±12.3	65±11.45
Superior RNFL	114.86±17.79	88.8±16.4	83.9±21.2	79±22.71
Nasal RNFL	71.68±9.84	72.3±10.8	67.2±10.7	59±9.54
Inferior RNFL	116.20±18.64	91.0±32.3	83.6±22.9	75±21.29
Temporal RNFL	59.31±10.67	51.6±11.9	53.8±18.3	46±8.99

SD: Standard deviation, RNFL: Retinal nerve fiber layer

Table 2: Intra-session reproducibility

	Interclass correlation coefficient (95% CI)				COV (%)				Test-retest variability(μm)			
	Normal	Early glaucoma	Moderate glaucoma	Advanced glaucoma	Normal	Early glaucoma	Moderate glaucoma	Advanced glaucoma	Normal	Early glaucoma	Moderate glaucoma	Advanced glaucoma
Mean RNFL	0.993 (0.991-0.994)	0.995 (0.994-0.997)	0.996 (0.995-0.997)	0.996 (0.994-0.997)	1.96	2.35	2.39	2.41	4.02	3.90	3.81	3.70
Superior RNFL	0.988 (0.986-0.991)	0.993 (0.992-0.995)	0.995 (0.992-0.996)	0.995 (0.993-0.997)	3.05	3.77	3.94	4.18	8.14	7.72	7.56	7.00
Nasal RNFL	0.973 (0.967-0.979)	0.975 (0.971-0.981)	0.977 (0.971-0.981)	0.978 (0.968-0.985)	4.01	4.87	4.92	4.56	6.30	7.90	7.65	6.15
Inferior RNFL	0.986 (0.982-0.988)	0.995 (0.993-0.996)	0.993 (0.991-0.994)	0.994 (0.992-0.996)	3.31	3.94	3.98	4.20	9.34	8.65	7.84	7.26
Temporal RNFL	0.977 (0.972-0.982)	0.971 (0.966-0.978)	0.976 (0.969-0.978)	0.954 (0.934-0.969)	3.05	5.23	5.45	5.37	19.19	19.60	18.7	17.99

RNFL: Retinal nerve fiber layer, CI: Confidence interval, COV: Coefficient of variation

Table 3: Inter-session reproducibility

	Interclass correlation coefficient (95% CI)				COV (%)				Test-retest variability (μm)			
	Normal	Early glaucoma	Moderate glaucoma	Advanced glaucoma	Normal	Early glaucoma	Moderate glaucoma	Advanced glaucoma	Normal	Early glaucoma	Moderate glaucoma	Advanced glaucoma
Mean RNFL	0.992 (0.988-0.995)	0.994 (0.993-0.998)	0.995 (0.993-0.997)	0.990 (0.995-0.998)	2.16	2.52	2.64	2.70	4.09	3.98	3.88	4.16
Superior RNFL	0.987 (0.980-0.993)	0.996 (0.990-0.999)	0.995 (0.990-0.996)	0.994 (0.988-0.998)	3.49	4.15	4.47	4.93	8.43	7.65	7.45	7.60
Nasal RNFL	0.984 (0.957-0.973)	0.969 (0.948-0.987)	0.968 (0.948-0.981)	0.975 (0.947-0.991)	4.26	5.02	5.62	4.84	6.85	8.16	8.08	7.10
Inferior RNFL	0.990 (0.985-0.994)	0.992 (0.991-0.997)	0.994 (0.991-0.997)	0.993 (0.985-0.997)	3.31	4.24	4.50	4.96	9.77	9.03	9.15	7.42
Temporal RNFL	0.989 (0.983-0.994)	0.981 (0.969-0.991)	0.974 (0.959-0.985)	0.891 (0.766-0.960)	3.17	5.27	6.09	7.90	20.11	20.29	20.46	18.20

RNFL: Retinal nerve fiber layer, CI: Confidence interval, COV: Coefficient of variation

Table 4: Correlation between COV*, age and MD#

	Normal		Glaucoma		Advanced glaucoma	
	Age	MD	Age	MD	Age	MD
Intra-session COV of mean RNFL thickness						
Spearman's correlation coefficient r	0.145	0.188	0.226	−0.95	−0.016	−0.047
P$	0.372	0.246	0.160	0.559	0.956	0.874
Intersession COV of mean RNFL thickness						
Spearman's correlation coefficient r	0.022	−0.006	0.059	−0.085	−0.076	−0.221
P$	0.755	0.933	0.410	0.229	0.530	0.065

*COV: Coefficient of variation, #MD: Mean deviation on visual fields, $*P*: Significance, RNFL: Retinal nerve fiber layer

separately. For the overall glaucoma group, the ICC and COV values for average RNFL thickness measurements were 0.986 and 1.9% for intra-visit, and 0.972 and 2.7% for inter-visit measurements, respectively.

Our study had a subset of advanced glaucoma (average MD − 16.71 ± 4.15 dB) and demonstrated good reproducibility for both intra-session and inter-session measurements. We found that the temporal quadrant measurements showed least reproducibility with maximum COV and TRT in both inter-session and intra-session measurements. This is in concordance with some studies[26,18] but differs from those by Ji-Peng *et al*.[27] and Mwanza *et al*.[28] who reported least reproducibility for the nasal quadrant. The reason for this difference is not clear, but it could be that our cohort of patients had more advanced glaucoma and, therefore, the temporal quadrant was affected more than in the other reports with earlier glaucoma.

Nevertheless, all studies show that the mean RNFL thickness parameter showed least variability across repeated measurements, within the same session or in different sessions. This was probably because, as the area which is sampled gets larger, more and more measurements get added into the mean for that area. Therefore, the larger the area sampled, the less likely is the variability. The RNFL measurements in four different quadrants, though reproducible in themselves, showed greater variability than the mean RNFL thickness. Probably, the average RNFL thickness measurement should be the parameter to consider when evaluating advanced glaucoma patients for structural progression. In our study, the test-retest variability values for mean RNFL thickness in both normal and glaucomatous subjects did not exceed 5 μm, and thus, a change in excess of this may be interpreted as being due to causes other than the inherent variability of the instrument.

We found no significant difference in the inter-session reproducibility compared to the intra-session values. This implies that RNFL thickness measurements over different sessions do not introduce significant added variability over that seen across different measurements in the same session.

Further studies using different instruments and operators would help to compare the reproducibility of measurements taken at different places. However, this study does demonstrate excellent reproducibility of RNFL measurements on the Cirrus OCT in advanced glaucoma patients. This indicates that there may be a significant advantage in following up patients with advanced glaucoma on the Cirrus OCT even if baseline measurements have been taken on the Stratus OCT. This study appears to be a small step in validating this particular spectral domain OCT instrument for further use in the management of glaucoma, especially in the assessment of progression in patients with advanced disease.

References

1. Huang D, Swanson EA, Lin CP, Schuman JS, Stinson WG, Chang W, *et al*. Optical coherence tomography. Science 1991;254:1178-81.
2. Schuman JS, Hee MR, Puliafito CA, Wong C, Pedut-Kloizman T, Lin CP, *et al*. Quantification of nerve fiber layer thickness in normal and glaucomatous eyes using optical coherence tomography. Arch Ophthalmol 1995;113:586-96.
3. Kamal DS, Bunce C, Hitchings RA. Use of the GDx to detect differences in retinal nerve fibre layer thickness between normal, ocular hypertensive and early glaucomatous eyes. Eye (Lond) 2000;14 (Pt 3A):367-70.
4. Wollstein G, Schuman JS, Price LL, Aydin A, Stark PC, Hertzmark E, *et al*. Optical coherence tomography longitudinal evaluation of retinal nerve fiber layer thickness in glaucoma. Arch Ophthalmol 2005;123:464-70.
5. Leung CK, Cheung CY, Weinreb RN, Qiu K, Liu S, Li H, *et al*. Evaluation of retinal nerve fiber layer progression in glaucoma: A study on optical coherence tomography guided progression analysis. Invest Ophthalmol Vis Sci 2010;51:217-22.
6. Leung CK, Chiu V, Weinreb RN, Liu S, Ye C, Yu M, *et al*. Evaluation of retinal nerve fiber layer progression in glaucoma: A comparison between spectral-domain and time-domain optical coherence tomography. Ophthalmology 2011;118:1558-62.
7. Sung KR, Kim JS, Wollstein G, Folio L, Kook MS, Schuman JS. Imaging of the retinal nerve fibre layer with spectral domain optical coherence tomography for glaucoma diagnosis. Br J Ophthalmol 2011;95:909-14.
8. Mwanza JC, Oakley JD, Budenz DL, Anderson DR, Cirrus Optical Coherence Tomography Normative Database Study Group. Ability of cirrus HD-OCT optic nerve head parameters to discriminate normal from glaucomatous eyes. Ophthalmology 2011;118:241-8.e1.
9. Kim JS, Ishikawa H, Sung KR, Xu J, Wollstein G, Bilonick RA, *et al*. Retinal nerve fibre layer thickness measurement reproducibility improved with spectral domain optical coherence tomography. Br J Ophthalmol 2009;93:1057-63.
10. Wu Z, Vazeen M, Varma R, Chopra V, Walsh AC, LaBree LD, *et al*. Factors associated with variability in retinal nerve fiber layer thickness measurements obtained by optical coherence tomography. Ophthalmology 2007;114:1505-12.
11. Antón A, Castany M, Pazos-Lopez M, Cuadrado R, Flores A, Castilla M. Reproducibility of measurements and variability of the

classification algorithm of Stratus OCT in normal, hypertensive, and glaucomatous patients. Clin Ophthalmol 2009;3:139-45.

12. Youm DJ, Kim H, Shim SH, Jang HJ, Kim JM, Park KH, *et al*. The effect of various factors on variability of retinal nerve fiber layer thickness measurements using optical coherence tomography. Korean J Ophthalmol 2012;26:104-10.
13. Hong JT, Sung KR, Cho JW, Yun SC, Kang SY, Kook MS. Retinal nerve fiber layer measurement variability with spectral domain optical coherence tomography. Korean J Ophthalmol 2012;26:32-8.
14. Carpineto P, Nubile M, Agnifili L, Toto L, Aharrh-Gnama A, Mastropasqua R, *et al.* Reproducibility and repeatability of Cirrus™ HD-OCT peripapillary retinal nerve fibre layer thickness measurements in young normal subjects. Ophthalmologica 2012;227:139-45.
15. Hirasawa H, Tomidokoro A, Araie M, Konno S, Saito H, Iwase A, *et al.* Peripapillary retinal nerve fiber layer thickness determined by spectral-domain optical coherence tomography in ophthalmologically normal eyes. Arch Ophthalmol 2010;128:1420-6.
16. Serbecic N, Beutelspacher SC, Aboul-Enein FC, Kircher K, Reitner A, Schmidt-Erfurth U. Reproducibility of high-resolution optical coherence tomography measurements of the nerve fibre layer with the new Heidelberg Spectralis optical coherence tomography. Br J Ophthalmol 2011;95:804-10.
17. Hong S, Kim CY, Lee WS, Seong GJ. Reproducibility of peripapillary retinal nerve fiber layer thickness with spectral domain cirrus high-definition optical coherence tomography in normal eyes. Jpn J Ophthalmol 2010;54:43-7.
18. Mansoori T, Viswanath K, Balakrishna N. Reproducibility of peripapillary retinal nerve fibre layer thickness measurements with spectral domain optical coherence tomography in normal and glaucomatous eyes. Br J Ophthalmol 2011;95:685-8.
19. Cremasco F, Massa G, Gonçalves Vidotti V, Pedroso de Carvalho Lupinacci Á, Costa VP. Intrasession, intersession, and interexaminer variabilities of retinal nerve fiber layer measurements with spectral-domain OCT. Eur J Ophthalmol 2011;21:264-70.
20. Hodapp E, Parrish RK, Anderson DR. Clinical Decisions in Glaucoma. St. Louis: CV Mosby; 1993. p. 52-61.
21. Arthur SN, Smith SD, Wright MM, Grajewski AL, Wang Q, Terry JM, *et al.* Reproducibility and agreement in evaluating retinal nerve fibre layer thickness between Stratus and Spectralis OCT. Eye (Lond) 2011;25:192-200.
22. Budenz DL, Chang RT, Huang X, Knighton RW, Tielsch JM. Reproducibility of retinal nerve fiber thickness measurements using the stratus OCT in normal and glaucomatous eyes. Invest Ophthalmol Vis Sci 2005;46:2440-3.
23. Lee SH, Kim SH, Kim TW, Park KH, Kim DM. Reproducibility of retinal nerve fiber thickness measurements using the test-retest function of spectral OCT/SLO in normal and glaucomatous eyes. J Glaucoma 2010;19:637-42.
24. González-García AO, Vizzeri G, Bowd C, Medeiros FA, Zangwill LM, Weinreb RN. Reproducibility of RTVue retinal nerve fiber layer thickness and optic disc measurements and agreement with Stratus optical coherence tomography measurements. Am J Ophthalmol 2009;147:1067-74, 1074.e1.
25. Vizzeri G, Weinreb RN, Gonzalez-Garcia AO, Bowd C, Medeiros FA, Sample PA, *et al.* Agreement between spectral-domain and time-domain OCT for measuring RNFL thickness. Br J Ophthalmol 2009;93:775-81.
26. Wu H, de Boer JF, Chen TC. Reproducibility of retinal nerve fiber layer thickness measurements using spectral domain optical coherence tomography. J Glaucoma 2011;20:470-6.
27. Li JP, Wang XZ, Fu J, Li SN, Wang NL. Reproducibility of RTVue retinal nerve fiber layer thickness and optic nerve head measurements in normal and glaucoma eyes. Chin Med J (Engl) 2010;123:1898-903.
28. Mwanza JC, Chang RT, Budenz DL, Durbin MK, Gendy MG, Shi W, *et al.* Reproducibility of peripapillary retinal nerve fiber layer thickness and optic nerve head parameters measured with cirrus HD-OCT in glaucomatous eyes. Invest Ophthalmol Vis Sci 2010;51:5724-30.

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