

# Effect of head tilt on repeatability of optic nerve head parameters using Cirrus spectral-domain optical coherence tomography

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## Abstract

- **AIM:** To assess the repeatability of measuring optic nerve head (ONH) parameters using the Cirrus optical coherence tomography (OCT), as well as to assess the effect of head tilt on these measurements.

- **METHODS:** Thirty healthy participants with no evidence of glaucoma were recruited for the study. Visual acuity, intraocular pressure, standard automated perimetry and ocular examination were performed for each participant. One eye was then randomly selected and scanned undilated with the Cirrus OCT in 3 positions (neutral, 30° right tilt and 30° left tilt).

- **RESULTS:** Data collected from 29 eyes were used for analysis. One patient was omitted due to poor scan quality. The repeatability of the ONH parameters was analyzed using analysis of variance, coefficient of variation (COV) and intraclass correlation coefficient (ICC). Analysis of variance showed no statistically significant difference between 3 scans in a single position. There was good agreement between measurements (ICC 0.919–0.996, COV 1.94%–5.48%). Even with the presence of head tilt, repeated scans in the 3 positions showed good agreement as well (ICC 0.888–0.996, COV 2.04%–5.39%).

- **CONCLUSION:** Serial measurements of ONH parameters using the Cirrus OCT are found to have good repeatability. The ONH parameters with Cirrus OCT also maintain good repeatability despite head tilt.

- **KEYWORDS:** glaucoma; imaging; artifacts; optical coherence tomography; head movements

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## INTRODUCTION

Glaucoma is a family of chronic, progressive and potentially blinding optic neuropathies characterized by distinctive morphological changes of the optic nerve head (ONH) and retinal nerve fibre layer (RNFL), associated with corresponding visual field changes<sup>[1]</sup>. The first index of suspicion for glaucoma is often the abnormal appearance of the ONH-which would prompt a clinician towards further diagnostic testing.

Optical coherence tomography (OCT) is an invaluable tool in the workup and management of glaucoma. Using Stratus time domain OCT, RNFL as well as the measurement of ONH parameters were found to be important in glaucoma detection, while a combination of ONH and RNFL parameters improved the diagnostic accuracy for glaucoma detection<sup>[2]</sup>. With the advent of the spectral-domain OCT, we have been able to attain higher resolution images at faster speeds than before<sup>[3]</sup>. There are several spectral-domain OCTs available; one of the most commonly used clinically is the Cirrus OCT (Carl Zeiss Meditec, Dublin, CA, USA).

The Cirrus spectral-domain OCT utilizes a super luminescent diode laser with a center wavelength of 840 nm, and has a scan speed of 27 000 A-scans per second. The built-in algorithm used automatically calculates the geometric optic disc center from the ONH margin using a graph-based method and positions a circle of diameter 3.46 mm evenly around the disc center. ONH parameters and peripapillary RNFL measurements are thus calculated. As the process is fully automated, operator error as well as the impact of eye motion on measurements may be reduced.

Repeatability is an important factor to consider in the applicability of a diagnostic tool in clinical practice. It refers to the closeness of agreement between independent results obtained with the same method on identical test material under the same conditions. It is particularly important for the accurate diagnosis of glaucoma as well as the monitoring for

progression of the disease. Good repeatability would assist in detecting small structural changes over time in most eyes.

One of the factors we have observed that could potentially affect repeatability is a degree of head tilt produced during the acquisition of scans. This is despite the patients' and operators' best efforts to keep the head straight. While it has been found that head tilt can significantly affect peripapillary RNFL measurements using the Cirrus OCT [4]. The effect of head tilt on ONH parameters using spectral domain has not been studied.

The objective of our study was to assess the repeatability of measuring ONH parameters using the Cirrus OCT, as well as to assess the effect of head tilt on the repeatability.

### SUBJECTS AND METHODS

The study was approved by the National Healthcare Group Domain Specific Review Board (DSRB), Singapore, the conduct of which is overseen by National Healthcare Group Research Ethics Committee. The research was conducted in accordance with the tenets set forth in the Declaration of Helsinki. All participants gave informed consent, and were recruited consecutively from March to October 2013 at the Department of Ophthalmology, Tan Tock Seng Hospital, Singapore.

All participants underwent a complete ophthalmic evaluation, which included past medical and ophthalmic history, best corrected Snellen visual acuity (VA) testing, intraocular pressure measurement, slit lamp examination, and Humphrey visual field testing using the Swedish Interactive Threshold Algorithm (SITA) Fast 24-2 protocol. Inclusion criteria for the study were normal ocular examination, normal visual field examination, aged 21 years or older, and best corrected VA of 20/40 or better. The exclusion criteria were preexisting retina or optic nerve pathology, previous surgery for glaucoma or retinal pathology, significant media opacity and inability to provide informed consent.

A computer-generated list was used to randomize each participant to have either their left or right eye scanned for the study. Each eye was scanned undilated in 3 positions (neutral, 30° right tilt then 30° left tilt). In each position of head tilt, an extra scan was repeated with the eye patched. Effort was made with a goniometer to standardize the 30° head tilt. In instances where the subject could not maintain this amount of tilt, we accepted the maximum amount of tilt the subject could maintain while still keeping the target in view. Participants who were uncomfortable maintaining the head tilt were allowed to sit back to rest before returning to the OCT machine in between scans. This helped to simulate an actual clinical setting.

Consecutive OCT scans were taken using the Cirrus OCT optic disc cube function. After adjusting for refractive error, the ONH was centered on the live scanning laser ophthalmoscopic image using the internal fixation cross. The

centering (Z-offset) and enhancement (polarization) were optimized before the scan was acquired. All participants were assessed for good scan quality-with signal strength better than 6, no RNFL discontinuity or misalignment, no involuntary saccade, no blinking artifacts, and absence of RNFL algorithm segmentation failure without misalignment or movement artifacts. The scans were obtained for each participant within a single visit. Two trained operators carried out all the scans.

If good scan quality was not achieved, the scan was immediately repeated as per usual clinical practice. The ONH parameters were then analyzed using Cirrus Software version 6.0.2.81. The following ONH parameters were derived: rim area = the area of the neuroretinal rim (mm<sup>2</sup>); disc area = total area within the disc margin (mm<sup>2</sup>); average cup-to-disc ratio (CDR) = the square root of the cup area divided by the disc area; vertical CDR = the ratio of the cup diameter to the disc diameter in the vertical meridian; and cup volume = the volume of the cup (mm<sup>3</sup>).

**Statistical Analysis** Data analysis was carried out using IBM SPSS Statistics (version 19, IBM Corp, New York, USA). Mean and standard deviation was calculated for the average of the 3 measurements for each of the disc parameters. Assessment of repeatability was carried out by the following methods: repeated measures analysis of variance (ANOVA) was used to check for differences among the three measurements; two way mixed, single-measure intraclass correlation coefficient (ICC)<sup>[5]</sup> was used to look for consistency between measurements; coefficient of variation (COV) was calculated as the ratio of the standard deviation (SD) to the mean (expressed as a percentage); and intrasession test-retest variability was calculated by multiplying the within-subject SD by  $1.96 \cdot \sqrt{2}$  [6].

### RESULTS

Thirty patients were recruited for the study. One participant had poor scan quality of 6/10 and segmentation errors despite multiple attempts and data was thus excluded from the study.

In total, 29 eyes from 29 participants were analyzed. The mean age of the participants was 27.6 (±6.8)y. There were 8 females and 21 males. There were 28 Ethnic Chinese patients, and one Malay patient. The mean measurements for each ONH parameter are shown in Table 1.

In Cirrus OCT optic disc parameter measurements, analysis of variance in repeated measurements did not show statistically significant differences when comparing 3 scans taken in a single position (neutral, right tilt and left tilt) in any of the parameters. There was good agreement between measurements in a single position with an ICC of 0.919-0.996. The summaries for the two-way mixed, single-measure ICC for absolute agreement for the disc parameters are shown in Table 2.

**Effect of head tilt on Cirrus OCT**

**Table 1 Mean values of ONH parameters in each position**

Position	Parameters	Mean	Standard deviation
Neutral	Rim area (mm <sup>2</sup> )	1.25	0.20
	Disc area (mm <sup>2</sup> )	1.86	0.41
	Average cup disc ratio	0.53	0.15
	Vertical cup disc ratio	0.48	0.15
	Cup volume (mm <sup>3</sup> )	0.20	0.15
Right tilt	Rim area (mm <sup>2</sup> )	1.27	0.19
	Disc area (mm <sup>2</sup> )	1.89	0.41
	Average cup disc ratio	0.52	0.16
	Vertical cup disc ratio	0.49	0.16
	Cup volume (mm <sup>3</sup> )	0.20	0.15
Left tilt	Rim area (mm <sup>2</sup> )	1.26	0.20
	Disc area (mm <sup>2</sup> )	1.88	0.42
	Average cup disc ratio	0.53	0.15
	Vertical cup disc ratio	0.49	0.15
	Cup volume (mm <sup>3</sup> )	0.20	0.15

ONH: Optic nerve head.

**Table 2 ONH parameters ICC for absolute agreement**

Position	Parameters	ICC	95%CI		
			Lower	Upper	Width
Neutral	Rim area (mm <sup>2</sup> )	0.963	0.933	0.981	0.048
	Disc area (mm <sup>2</sup> )	0.982	0.966	0.991	0.025
	Average cup disc ratio	0.996	0.992	0.998	0.006
	Vertical cup disc ratio	0.985	0.972	0.992	0.020
	Cup volume (mm <sup>3</sup> )	0.996	0.993	0.998	0.005
Right tilt	Rim area (mm <sup>2</sup> )	0.919	0.858	0.958	0.100
	Disc area (mm <sup>2</sup> )	0.969	0.945	0.984	0.039
	Average cup disc ratio	0.994	0.990	0.997	0.007
	Vertical cup disc ratio	0.981	0.965	0.990	0.025
	Cup volume (mm <sup>3</sup> )	0.995	0.990	0.997	0.007
Left tilt	Rim area (mm <sup>2</sup> )	0.963	0.933	0.981	0.048
	Disc area (mm <sup>2</sup> )	0.984	0.971	0.992	0.021
	Average cup disc ratio	0.995	0.991	0.998	0.007
	Vertical cup disc ratio	0.987	0.977	0.994	0.017
	Cup volume (mm <sup>3</sup> )	0.995	0.991	0.997	0.006

ONH: Optic nerve head; ICC: Intraclass correlation coefficient.

Within each position of tilt, the ICC was found to be consistently highest for cup volume but lowest for rim area. The COV was 1.94% -5.48% . Intra-session test-retest variability ranged from 0.025-0.154 (Table 3).

Taking head tilt into account, we compared single scans

**Table 3 ONH parameters test-retest variability and COV**

Position	Parameters	Intrasession test-retest variability	COV (%)
Neutral	Rim area (mm <sup>2</sup> )	0.105	3.05
	Disc area (mm <sup>2</sup> )	0.154	2.99
	Average cup disc ratio	0.028	1.94
	Vertical cup disc ratio	0.051	3.84
	Cup volume (mm <sup>3</sup> )	0.025	4.54
Right tilt	Rim area (mm <sup>2</sup> )	0.154	4.38
	Disc area (mm <sup>2</sup> )	0.203	3.88
	Average cup disc ratio	0.032	2.22
	Vertical cup disc ratio	0.062	4.57
	Cup volume (mm <sup>3</sup> )	0.031	5.48
Left tilt	Rim area (mm <sup>2</sup> )	0.108	3.10
	Disc area (mm <sup>2</sup> )	0.146	2.79
	Average cup disc ratio	0.030	2.04
	Vertical cup disc ratio	0.047	3.47
	Cup volume (mm <sup>3</sup> )	0.030	5.27

ONH: Optic nerve head; COV: Coefficient of variation.

taken in each of the 3 positions. Repeated measurements analysis of variance did not show any statistically significant differences among the three measurements in any of the parameters. We found there to be good agreement between measurements as well (ICC: 0.888-0.996), with COV: 2.04%-5.39%. Intrasession test-retest variability was 0.026-0.249. ICC was again highest for cup volume and lowest for rim area. Despite the head tilt, the vertical cup disc ratio still had good repeatability, with ICC of 0.974 (Table 4).

An extra scan was taken in each position of head tilt with the eye patched, to analyze the effect of the vestibulo-ocular reflex (VOR) on eye position. The VOR is expected to cause the eye to compensate (straighten) more when the eye is unpatched, as compared to when the eye is patched. Paired *t*-test was used to compare differences between patched and unpatched data for the 1st tilt (right tilts and left tilts) and the corresponding patched data. The differences in measurements were all very small (2<sup>nd</sup> decimal place), and there were no statistically significant differences in the patched and unpatched data.

**DISCUSSION**

In the evaluation of glaucoma, both structural and functional changes result from loss of retinal ganglion cells and their axons. The degree of structural (neuroretinal rim, RNFL) and functional visual field loss is used to grade the likelihood and severity of primary open angle glaucoma both in the clinical setting and in clinical trials [7-8]. Combining structural and functional testing improves the diagnostic ability to detect

**Table 4 Comparing 1<sup>st</sup> scans taken in 3 positions-neutral, right tilt and left tilt positions**

Type	Parameters	ICC	95%CI			Intrasection test-retest variability	COV (%)
			Lower	Upper	Width		
1 <sup>st</sup> scan (single measure ICC)	Rim area (mm <sup>2</sup> )	0.888	0.805	0.942	0.137	0.189	5.39
	Disc area (mm <sup>2</sup> )	0.954	0.918	0.977	0.059	0.249	4.77
	Average cup disc ratio	0.995	0.991	0.998	0.007	0.030	2.04
	Vertical cup disc ratio	0.974	0.952	0.987	0.035	0.067	5.02
	Cup volume (mm <sup>3</sup> )	0.996	0.993	0.998	0.005	0.026	4.67

ICC: Intraclass correlation coefficient; COV: Coefficient of variation.

glaucoma [9], hence emphasizing the importance of reliable diagnostic tools. In subjects with ocular hypertension with RNFL defects and normal conventional achromatic visual fields, the most valuable optic disc variables for early detection of glaucomatous optic nerve damage were found to be the vertical CDR corrected for optic disc size, total neuroretinal rim area, rim-to-disc area ratio, and cup-to-disc area ratio corrected for disc size<sup>[10]</sup>.

The Cirrus spectral-domain OCT has been found to have good glaucoma discrimination capability [11]. With regards to peripapillary RNFL measurement, the Cirrus OCT has been extensively analyzed and found to have excellent repeatability in normal subjects and glaucoma patients<sup>[12-13]</sup> with a high inter-operator and intersession reproducibility<sup>[14]</sup>. In our study, our main finding is that there is good repeatability between several measurements taken in a single position, whether in neutral or in a tilted head position. There was a high ICC, low COV and low intra-session test-retest variability. This was found to be the highest for cup volume and lowest for rim area, using both ICC and COV parameters. The difference in correlation coefficients is small and unlikely to be significant. From this, we can conclude that most of the valuable optic disc variables can be measured in a reliably repeatable manner with the use of the Cirrus OCT. Of note, optic disc area had high ICC of 0.954. This is important, as several of the parameters should be considered while bearing the disc size in mind.

With regards to the measurement of cup disc parameters, the time domain OCT has been more extensively evaluated compared to the spectral domain OCT. The reproducibility of ONH parameters with the time domain OCT was found to be variable, with some studies reporting ICCs of as low as 33.3% for rim area<sup>[15]</sup> to as high as 97% for CDR<sup>[16]</sup>. Lin *et al*<sup>[17]</sup> however, found ONH measurements to be highly reproducible, with ICCs ranging between 86% and 95.9%, with the exception of disc area (73%).

Using the newer spectral domain OCT, the Cirrus OCT was found to have good repeatability in healthy eyes<sup>[18]</sup>, and good intervisit and intravisit measurement reproducibility in

glaucoma patients [19]. The RTVue OCT has also been evaluated and found that to have good reproducibility in both healthy participants and patients [20]. Our findings of good repeatability of ONH parameters in healthy participants are in keeping with other findings of repeatability using the spectral domain OCT. Although the ICCs are generally higher than what was obtained with the time domain OCT, it is not the intention of this paper to compare repeatability of Cirrus OCT with the time domain OCT.

Repeatability of ONH parameters is important. Although CDR measurements can be easily performed by most ophthalmologists and do not require additional imaging equipment, the single measurement has limited value in the estimation of glaucomatous damage if not adjusted for disc size [21], with a tendency for overdiagnosis in large discs and under diagnosis in small discs [22]. The examination of the ONH clinically has disadvantages such as high interobserver variability and low reproducibility. The use of the disc damage likelihood scale (DDLS) has been reported to provide a more accurate assessment of the optic disc damage than the conventional CDR measurement [23]. Nevertheless, interobserver variability is a potential limitation of DDLS and training is essential for low interobserver variability and high reproducibility. Hence, an evaluation tool that facilitates the measurement of optic disc parameters and can capture them in a repeatable manner is very useful, reducing error induced by interobserver variability. Good repeatability for the ONH parameters would thus assist in improving the sensitivity for serial measurements and detecting changes in the ONH over time.

Another major finding of our paper is that the repeatability of measurement of ONH parameters is not affected by head tilt-when comparing a scan in neutral position compared to a scan in head tilt. ONH parameters are not "sector-based", and hence the minimal effect of head tilt is predictable. In this study, we did not evaluate quadrant and clock-hour neuroretinal rim thickness, for which head tilt may affect repeatability of measurements. The serially measured rim area, disc area, average cup disc ratio and cup volume were

found to have good repeatability with high ICC and low COV. It was interesting to find that the vertical cup disc ratio also displayed good repeatability between positions, with an ICC of 0.974. We believe that this may be due in part to mechanisms of compensatory ocular counter torsion, as well as due to the small degree of head tilt in our study and small CDR measurements, resulting in no significant effect on vertical CDR.

Our paper is the first paper to evaluate the effect of head tilt on the measurement of ONH parameters. With evidence that head tilt affects measurement of peripapillary RNFL quadrants using Cirrus OCT as reported by Hwang *et al*<sup>[4]</sup>, it is important to evaluate the effect of head tilt on ONH parameters as well. If a significant effect of head tilt on the measurements was found, the use of this machine as a diagnostic tool would be limited if it were without a function to correct for head tilt. The updated Cirrus OCT with a retinal tracking system was found to enhance the repeatability of RNFL thickness measurements despite eye movement<sup>[24]</sup>. In addition, the Guided Progression Analysis (GPA) program also adjusts scan location and rotation. Therefore, the latest Cirrus OCT may be able to compensate for head tilt in the measurements of both ONH parameters and RNFL thickness.

This study has several limitations. We used only normal subjects, and the sample size is small. Hence, the clinical applications of the study are limited. Furthermore, only good quality scans were included, which may not reflect actual clinical settings where poor quality scans are sometimes obtained inadvertently (signal strength may be good, but RNFL segmentation errors present). The participant population was also a generally young group. They may represent a more compliant group who may have obeyed instructions better *e.g.* not to blink for a few seconds, compared to the usual middle aged and older population who are evaluated for glaucoma. Hence, the good repeatability of ONH parameters may not be reflected as well in usual clinical practice. Nonetheless, it is important to know that if done properly, the Cirrus OCT can achieve good repeatability for ONH parameters.

In conclusion, this study highlights the use of ONH parameters as a complementary tool to improve the sensitivity of detection of glaucoma and its progression. While head tilt can cause artifacts in the measurement of RNFL thickness using the Cirrus OCT, the ONH parameters maintain good repeatability despite head tilt and are helpful in the assessment of glaucoma.

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