

# Repeatability of Optic Nerve Head Parameters Measured by Spectral-Domain OCT in Healthy Eyes

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■ **BACKGROUND AND OBJECTIVE:** To evaluate the repeatability of optic nerve head (ONH) measurements by spectral-domain optical coherence tomography.

■ **PATIENTS AND METHODS:** Three scans were acquired in 32 healthy subjects during one session. Using Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, CA), the cup-to-disc ratio (CDR), disc area, rim area, cup volume, and horizontal and vertical CDRs were investigated. Repeatability was assessed by the coefficient of variation (COV), the test–retest intrasession variability, and the intraclass correlation coefficient (ICC).

■ **RESULTS:** Good repeatability was achieved for all parameters, with a COV of 4.23% or less and ICCs of 0.98 or greater for all measurements. Test–retest intrasession variability was 0.024 for CDR, 0.121 mm<sup>2</sup> for disc area, 0.087 mm<sup>2</sup> for rim area, 0.017 mm<sup>3</sup> for cup volume, and 0.048 for horizontal and vertical CDR.

■ **CONCLUSION:** In healthy eyes, Cirrus HD-OCT provides repeatable measurements of ONH parameters.

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## INTRODUCTION

Optical coherence tomography (OCT) is a non-invasive imaging technique for creating in vivo cross-sectional images of biological tissue.<sup>1</sup> Detailed structural images result, for which quantitative analyses have been developed to support clinical interpretation. Time-domain OCT (TD-OCT) using Stratus OCT

(Carl Zeiss Meditec, Dublin, CA) is well established in clinical practice, but the emphasis is now shifting to the more recent spectral-domain OCT (SD-OCT) devices, which have faster acquisition rates and higher axial resolutions.<sup>2,3</sup> The increase in the speed of the SD-OCT devices has facilitated the collection of more data, resulting in higher sampling densities and true volumetric imaging.

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In the context of optic nerve pathologies, OCT has been used to evaluate the peripapillary retinal nerve fiber layer (RNFL) in many diseases, including glaucoma, nonarteritic anterior ischemic optic neuropathy, optic neuritis, and Leber's hereditary optic neuropathy.<sup>4-8</sup> In all of these pathologies, OCT has been able to detect and follow changes in RNFL thickness. Recently, SD-OCT has been reported to improve the already good repeatability of conventional TD-OCT in measuring RNFL thickness.<sup>9,10</sup>

OCT can also be used to analyze optic nerve head (ONH) parameters, such as disc area, rim area, or cup-to-disc ratio, with good repeatability and reproducibility.<sup>11,12</sup> This feature has received less attention, although several studies have shown that ONH analysis improves our ability to discriminate between healthy and glaucomatous eyes.<sup>13-16</sup> Moreover, ONH parameters have been reported to play an important role in other diseases, such as Leber's hereditary optic neuropathy and dominant optic atrophy.<sup>17,18</sup> Given the importance of ONH analysis and the recent development of dedicated software to be used for this purpose with Cirrus HD-OCT (Carl Zeiss Meditec), a commercially available imaging device that uses the SD-OCT technology, we were prompted to investigate the repeatability of its measurements in a sample of healthy eyes.

## PATIENTS AND METHODS

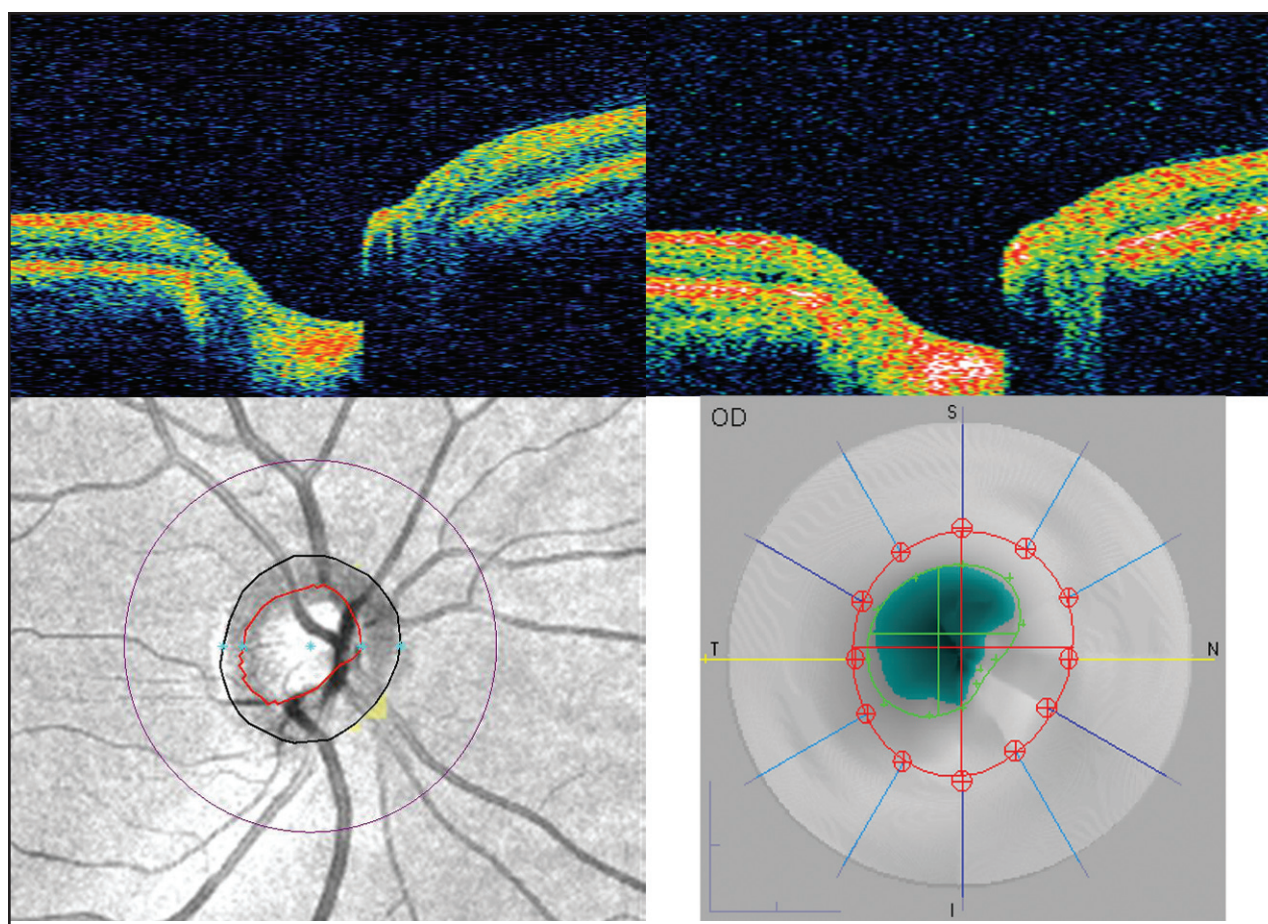
Thirty-three eyes of 33 healthy subjects were prospectively enrolled in a private practice setting for this observational case series. The study population consisted of consecutive patients with minor refractive disorders. All subjects underwent a complete ophthalmologic examination, including visual acuity measurement, intraocular pressure measurement, slit-lamp biomicroscopy, and indirect ophthalmoscopy, to determine eligibility. Inclusion criteria were: best-corrected visual acuity of better than 20/25, refractive error between -3 and +3 diopters of sphere or between -2 and +2 diopters of cylinder, normal intraocular pressure less than 21 mm Hg, normal appearance of the optic disc, no peripapillary atrophy at fundus examination, no significant ocular disease found by routine ophthalmological examination, and no history of glaucoma in the family and/or systemic diseases with possible ocular involvement, such as diabetes mellitus.

Three individual  $200 \times 200$  cube optic disc scans

were obtained with Cirrus HD-OCT (software version 5.0) within a single session, without pupil dilation. The subject remained seated between measurements, but was repositioned in the headrest for each measurement. Once the subject was properly aligned, the iris was brought into view and the scanning laser ophthalmoscopic image was focused by adjusting for refractive error. As the optic nerve head was centered on the live scanning laser ophthalmoscopic image using the internal fixation cross, centering (Z-offset) and enhancement (polarization) were optimized and then the scan was acquired. The Optic Disc Cube  $200 \times 200$  protocol comprises 200 B-scans; each B-scan comprises 200 A-scans, where an A-scan is the instantaneously acquired reflectivity profile of the back-scattered light acquired by the device. The profile has an axial depth of 2 mm, and is made up of 1,024 samples (pixels). A total of 27,000 A-scans are acquired per second. Each B-scan has a 6-mm horizontal field of view, and the 200 B-scans are stacked over a vertical distance of 6 mm. The resulting volume is therefore a set of  $200 \times 200 \times 1,024$  data points covering a volume of  $6 \times 6 \times 2$  mm.

The quality of Cirrus HD-OCT scans was assessed by an experienced examiner. To be considered of good quality, the scans had to have focused images from the ocular fundus, a signal strength of at least 6 (on a scale from 1 to 10), and no signs of involuntary eye movement during the scan (as evidenced by checking the en-face images for motion). Only scans without overt algorithm failure in detecting the ONH limits were included in the study. If a scan was classified as unacceptable, the patient was excluded from the study.

The ONH analysis was performed on this data set using 5.0 software. The ONH parameters reported result from a fully automatic algorithm that defines both the disc and cup margins within the three-dimensional data cube. The disc margin is defined as the termination of Bruch's membrane (also referred to as "neural canal opening" or "Bruch's membrane opening").<sup>19,20</sup> Increased resolution of Cirrus HD-OCT with respect to Stratus OCT (whose transverse resolution is 128 A-scans) can be observed in the figure. The cup margin is defined using a proprietary algorithm that measures the neuroretinal rim as it exits the eye. It is designed to emulate the cup margin, which would be manually defined by a clinician based on an ophthalmic examination. From these landmarks the following param-



**Figure.** Optic nerve head imaging by spectral-domain and time-domain optical coherence tomography (OCT). Top: horizontal scan of the same optic nerve head by spectral-domain OCT (left) and time-domain OCT (right). Bottom: optic disc and cup edges reconstructed by spectral-domain OCT (left) and time-domain OCT (right).

eters can be derived and were analyzed in this study: (1) cup-to-disc ratio (CDR) = average CDR, defined as the square root of the cup area divided by the disc area; (2) disc area = the total area within the disc margin ( $\text{mm}^2$ ); (3) rim area = the area of the neuroretinal rim ( $\text{mm}^2$ ); (4) cup volume = the volume of the cup ( $\text{mm}^3$ ); (5) horizontal CDR = the ratio of the cup diameter to the disc diameter in the horizontal meridian; and (6) vertical CDR = the ratio of the cup diameter to the disc diameter in the vertical meridian.

All participants gave their informed consent according to the Declaration of Helsinki and the study was approved by the internal review board of the University of Bologna Department of Neurological Sciences.

### Statistics

For the purposes of the current study, the term repeatability was used according to the definition of the British

Standards Institute, which considers it a part of accuracy.<sup>21</sup> Accuracy, as formally defined by BS ISO 5725-1, includes trueness and precision. Trueness is the inverse of bias and is determined by comparing the measurement result with the accepted reference (conventional true) value. Precision is the inverse of statistical uncertainty and is normally expressed in terms of standard deviation (SD). The factors involved include (1) the operator, (2) the equipment used, (3) the equipment calibration, (4) the environment, and (5) the elapsed time between measurements. Precision has two conditions: repeatability and reproducibility. Under repeatability conditions, factors such as (1) to (5) are considered to be constant and do not contribute to the variability of the measurement result. Under reproducibility conditions, the factors can vary. Repeatability and reproducibility are the two extremes of precision.

We assessed repeatability by means of the following methods:



TABLE 1  
Mean Value of the Optic Nerve Head Parameters<sup>a</sup>

Parameter	Mean $\pm$ SD
CDR	0.51 $\pm$ 0.14
Disc area (mm <sup>2</sup> )	1.91 $\pm$ 0.32
Rim area (mm <sup>2</sup> )	1.32 $\pm$ 0.21
Cup volume (mm <sup>3</sup> )	0.14 $\pm$ 0.11
Horizontal CDR	0.57 $\pm$ 0.16
Vertical CDR	0.47 $\pm$ 0.11

CDR = cup-to-disc area ratio; SD = standard deviation.

<sup>a</sup>All values represent the average of the three measurements.

1. Repeated measurements analysis of variance: this was automatically calculated using Instat software 3.0 (GraphPad Software, San Diego, CA) for each of the ONH parameters.
2. Intraclass correlation coefficient (ICC): this is defined as the ratio of the between-subjects variance to the sum of the pooled within-subject variance and the between-subjects variance. It was automatically calculated using SPSS software 12.01 (SPSS Inc., Chicago, IL).
3. Coefficient of variation (COV): this was calculated as the within-subject SD (ie, the square root of the average of the within-subject variance) divided by the overall mean and was expressed as a percentage.<sup>22,23</sup>
4. Intrasection test–retest variability: this was calculated by multiplying the within-subject SD by 2.77.<sup>23</sup>

## RESULTS

After excluding one subject due to poor quality of the scans (because errors resulted in the segmentation and 5.0 software does not have any editing capability), 32 eyes of 32 subjects (mean age: 56.4  $\pm$  19.2 years) were analyzed.

Analysis of variance did not disclose any statistically significant difference among the three measurements for any parameter. The mean value of each parameter is reported in Table 1. Results for ICC, intrasection test–retest variability, and COV are summarized in Table 2. For all parameters, the ICC was higher than 0.94 and the COV was lower than 4.5%.

A comparison to previous studies about ONH

repeatability of measurements obtained using Stratus OCT showed improved values in all cases.

## DISCUSSION

Previous studies performed to investigate TD-OCT measurements have shown that topographic analysis of the ONH is of utmost importance for the assessment of the optic disc for many reasons. First, combining RNFL and ONH parameters results in the highest diagnostic accuracy for glaucoma.<sup>16</sup> Second, ONH size influences the sensitivity of Stratus OCT with respect to glaucoma detection, because a decrease in sensitivity has been reported in subjects with larger discs.<sup>24</sup> Third, ONH parameters play a major role in the clinical course of other diseases such as nonarteritic anterior ischemic optic neuropathy, Leber's hereditary optic neuropathy, and dominant optic atrophy.<sup>17,18,25</sup> Fourth, optic disc size influences OCT RNFL thickness measurements in healthy eyes.<sup>26–28</sup> Hence, the development of specific software for ONH analysis on Cirrus HD-OCT is a remarkable update for this instrument.

Repeatability of ONH parameter measurements by Cirrus HD-OCT has been recently assessed in a sample of glaucomatous eyes by Mwanza et al., who reported excellent results.<sup>29</sup> Our study is the first to investigate repeatability of the same measurements in healthy eyes, an essential requisite to validate this software and develop future normative database for ONH parameters. Our data are in good agreement with those reported by Mwanza et al., although we found a slightly higher intravisit repeatability in most cases; for example, the COV of the disc area was 2.29% instead of 4.4% and the COV of the rim area was 2.38% instead of 6.6%. This difference may be related to the presence of peripapillary atrophy in glaucomatous eyes and its absence in our sample, and the higher mean age in Mwanza et al.'s study (70.7 compared to 56.4 years in ours), with possible higher prevalence of cataract. Our data also suggest that Cirrus HD-OCT increases the repeatability of ONH parameter measurements compared to Stratus OCT, as is shown in Table 2.<sup>11,12</sup> For example, disc area repeatability was higher than that reported by Kampeter et al. (COV = 1.99% vs 5.7% for Cirrus HD-OCT and Stratus OCT, respectively), and the same applies for CDR (COV = 1.84% vs 15.3% for Cirrus HD-OCT and Stratus OCT, respectively).<sup>12</sup>

Our findings, together with those reported by

TABLE 2  
ICC, Intrasection Test–Retest Variability, and COV of Each  
Optic Nerve Head Parameter Measured by Cirrus HD-OCT

Parameter	ICC (Lower 95% CI)		Intrasection Test–Retest Variability		COV (%)	
	Current Study	Paunescu et al. <sup>11</sup>	Current Study	Paunescu et al. <sup>11</sup>	Current Study	Kampptetter et al. <sup>12</sup>
CDR	0.99 (0.99)	0.97 <sup>a</sup>	0.024	0.055 <sup>b</sup>	1.68	15.3
Disc area (mm <sup>2</sup> )	0.98 (0.96)	0.66	0.121	0.637 <sup>b</sup>	2.29	5.7
Rim area (mm <sup>2</sup> )	0.98 (0.96)	0.81 <sup>a</sup>	0.087	0.332 <sup>b</sup>	2.38	7.3
Cup volume (mm <sup>3</sup> )	0.99 (0.99)	0.84 <sup>a</sup>	0.017	0.110 <sup>b</sup>	4.23	—
Horizontal CDR	0.99 (0.98)	0.87 <sup>a</sup>	0.048	0.083 <sup>b</sup>	3.03	8.5
Vertical CDR	0.98 (0.96)	0.90 <sup>a</sup>	0.048	0.083 <sup>b</sup>	3.65	8.4

ICC = intraclass correlation coefficients; COV = coefficient of variation; HD-OCT = high-definition optical coherence tomography; CI = confidence interval; CDR = cup-to-disc ratio.

<sup>a</sup>Measurements obtained with pupil dilation.

<sup>b</sup>Values obtained by multiplying the intravisit standard deviation reported in the original study by 2.77.

Cirrus HD-OCT is manufactured by Carl Zeiss Meditec, Dublin, CA.

Mwanza et al.,<sup>29</sup> reveal an additional advantage of SD-OCT technology, which has already been reported to improve the repeatability and reproducibility of peripapillary RNFL thickness measurements.<sup>9,10,30</sup> Although the most likely reason for the lower variability in Cirrus HD-OCT RNFL thickness measurements is the automatic positioning of the peripapillary circle around the ONH, which reduces the changes in RNFL thickness related to manual location of the circle,<sup>30</sup> the reason for the improved repeatability of ONH measurements is different and is likely to depend mostly on the higher number of scans used to reconstruct ONH topography. It should be remembered that Stratus OCT reconstructs ONH topography on the basis of six radial B-scans in a spoke-like pattern centered on the ONH; the OCT interpolates among the B-scans to provide measurements for the entire ONH. In the case of Cirrus HD-OCT, interpolation is minimal because ONH topography is reconstructed on the basis of as many as 200 B-scans (containing 200 A-scans each). A second explanation for improved repeatability may be the higher transverse resolution of each B-scan: with Stratus OCT the best repeatability has been achieved with the Fast ONH acquisition protocol<sup>12</sup> at 128 A-scans, whereas the transverse resolution of Cirrus HD-OCT is 200 A-scans. Given that the scans cover a 4- and 6-mm lateral field of view, respectively, the increased sampling density and better lateral resolution of the SD-OCT device are likely to support improved

analyses. The axial resolution of Cirrus HD-OCT (5  $\mu$ m) is also higher than that of Stratus OCT (7 to 10  $\mu$ m). Increased resolution leads to better visualization of the Bruch's membrane opening (Figure).

A comparison of our results to those of a previous study assessing the repeatability of ONH measurements provided by another SD-OCT device (RTVue; Optovue Inc, Fremont, CA) show a better COV for Cirrus HD-OCT versus RTVue for most parameters, including CDR ratio (1.68% vs 22.2%), cup volume (4.23 vs 29.1%), horizontal CDR (3.03 vs 14.1%), vertical CDR (3.65 vs 15.8%), and rim area (2.38% vs 2.68%), and a slightly worse COV for disc area (2.29 vs 0.27%). The differences probably depend on the fact that the RTVue uses a different method to obtain measurements of the ONH, whose disc margin is drawn manually on the en-face image for each scan; in addition, other factors, such as differences in age, refractive error, and inclusion of eyes with peripapillary atrophy (which was an exclusion criterion in our sample) might have played a role.<sup>10</sup>

Further studies are needed to determine whether the higher repeatability of ONH measurements can improve the diagnostic performance of SD-OCT. Recent articles evaluating RNFL thickness measurements have shown that the diagnostic sensitivity and specificity of Cirrus HD-OCT are similar to those of TD-OCT.<sup>30-33</sup> Similar results have been reported with another SD-OCT device.<sup>34</sup> Only one study found better values with

SD-OCT than TD-OCT.<sup>35</sup> Given that previous studies with Stratus OCT have reported increased sensitivity in detecting glaucoma after combining data from RNFL thickness and ONH measurements,<sup>16</sup> it is likely that combining the same data will enhance the diagnostic performance of Cirrus HD-OCT. Meanwhile, it has already been shown that there is no difference in the ability of ONH parameters and RNFL thickness measurements, as measured with Cirrus HD-OCT, to distinguish between healthy and glaucomatous eyes.<sup>36</sup>

The current study has some limitations. We did not include eyes with papilledema, optic disc drusen, optic atrophy (due to glaucoma or other causes), or peripapillary atrophy; hence our findings cannot be directly applied to these cases (a prospective study evaluating eyes with Leber's hereditary optic neuropathy, however, is being performed). Nor did we evaluate intersession reproducibility. These issues warrant further investigation.

We observed that ONH parameters measured by Cirrus HD-OCT show excellent repeatability in healthy eyes, with less variability compared to TD-OCT. Further studies are needed to detect the benefits resulting from this finding.

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