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Agreement between slit lamp examination and optical coherence tomography in estimating cup-disc ratios

J.M. MARTÍNEZ-DE-LA-CASA, F. SÁENZ-FRANCÉS, A.M. FERNÁNDEZ-VIDAL, C.D. MENDEZ-HERNANDEZ, L. PABLO-JÚLVEZ, J. GARCÍA-SÁNCHEZ, J. GARCÍA-FEIJOÓ

Department of Ophthalmology, Hospital Clínico Universitario San Carlos–Universidad Complutense, Madrid - Spain

PURPOSE. *To compare optical coherence tomography (OCT) cup-disc ratio measurements with those estimated by two independent examiners using the slit lamp in an evaluation of the optic nerve head (ONH).*

METHODS. *In 47 eyes each of 47 patients with glaucoma and 47 healthy subjects, the ONH was examined using the slit lamp with a 78 D lens. Two examiners subjectively determined the cup-disc area ratio (A-CDR), the horizontal cup-disc ratio (H-CDR), and the vertical cup-disc ratio (V-CDR). These measurements were compared to objective OCT readings obtained by a third examiner blind to the slit lamp results.*

RESULTS. *For the three variables determined, correlation indices between the OCT readings and the two sets of slit lamp measurements were significantly higher for the glaucoma group than the control group. In the patients with glaucoma, the OCT tended to underestimate A-CDR and overestimate H-CDR. For both these variables, Bland-Altmann analysis revealed significant differences between the two methods that persisted across the whole range of CDRs examined. In contrast, differences in V-CDR varied with disc size.*

CONCLUSIONS. *The OCT is a diagnostic tool that provides a complete automatic evaluation of the ONH. However, its measurements vary significantly from those obtained in subjective evaluations performed by experienced ophthalmologists. (Eur J Ophthalmol 2008; 18: 423-8)*

KEY WORDS. *Glaucoma, OCT, Slit lamp, Cup-disc ratio, Optic nerve head*

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INTRODUCTION

Ophthalmoscopic examination of the optic nerve head is one of the key tests performed during the diagnosis and follow-up of a patient with glaucoma. The high interobserver variability (1, 2) of ophthalmoscopy has been traditionally overcome by drawing the optic nerve head or by analyzing series of photographs to detect the structural changes produced during the course of disease. Thus, the current gold standard for evaluating the optic nerve head is the use of stereoscopic photographs (3-6).

New systems offering automatic analysis of the optic nerve head and the nerve fiber layer are starting to impact the glaucoma field (7-11). Instruments such as the scanning laser polarimeter (GDx VCC), Heidelberg retinal tomograph (HRT), optical coherence tomography (OCT), and the retinal thickness analyzer (RTA) provide quantitative data, as useful clinical support both for the diagnosis and follow-up of the disease.

The currently marketed OCT (Stratus OCT, Carl Zeiss Meditec, Dublin, CA) enables the clinician to acquire and analyze tomographs through 18 examination protocols. Of these, 8 are specifically designed to assess the nerve fiber layer and the morphology of the optic nerve head. Several studies have established the reproducibility of OCT measurements (12, 13). To date, however, no reports

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in the scientific literature have compared optic nerve measurements obtained through OCT and slit lamp stereoscopic examination in normal subjects and patients with glaucoma. Moreover, studies that have compared the use of other automatic instruments with the slit lamp have demonstrated significant measurement differences (14).
The main purpose of this study was to compare optic nerve head evaluations undertaken by OCT and by two experienced ophthalmologists using the slit lamp to directly examine the optic nerve head, as is usually done in clinical practice. Our study was designed to identify possible differences between these two analytical methods.

METHODS

Patients with glaucoma were recruited from the Glaucoma Unit of the Hospital Clínico San Carlos, Madrid. Control subjects were recruited among the patients' relatives and hospital personnel. The study protocol was approved by our institution's Review Board and complied with the guidelines of the Declaration of Helsinki. Informed consent was obtained from each subject before inclusion in our study. Eyes were considered to be glaucomatous if they had shown abnormal results in at least two consecutive visual field examinations and if there was evidence of progressive glaucomatous change, as determined by the appearance of the optic nerve head. Control subjects had intraocular pressures < 21 mmHg, normal visual fields, and non-glaucomatous appearing optic discs.
Exclusion criteria were a spherical equivalent greater than 5 diopters, or 3 or more diopters of astigmatism, a best-corrected visual acuity lower than 20/25, opacities in the cornea or lens impairing optic nerve head visualization, and alterations in optic nerve head morphology, such as oblique discs or peripapillary atrophy. We also excluded subjects who had undergone previous eye surgery (except cataract extraction) and those with visual field defects of causes other than glaucoma (e.g., demyelinating disease, non-glaucomatous neuropathy, or a central nervous system disorder). If both eyes of a patient or subject fulfilled all the inclusion and exclusion criteria, the right eye was selected.
Finally, we enrolled one eye each of 47 patients and 47 healthy subjects who fulfilled the inclusion criteria. Examinations were performed by four of the authors, who are all ophthalmologists with considerable experience in the glaucoma field (denoted Examiners 1 to 4). Examiners 1 and 2 (J.M.C. and A.F.V.) evaluated the optic nerve head using the slit lamp (Haag-Streit 900, Haag-Streit, Koeniz, Switzerland) with a 78 D lens (Volk Optical Inc., Mentor, OH) and under pharmacologic mydriasis. The procedure consisted of directing a narrow slit beam onto the surface of the neuroretinal rim. The length of the slit was then successively adjusted to the horizontal (CHD) and vertical (CVD) cup diameters, recording their measures using the slit lamp's millimeter scale. Next, the optic disc horizontal (ODHD) and vertical (ODVD) diameters were measured in the same way. For analysis purposes, these measurements were expressed as the coefficients H-CDR (CHD/ODHD) and V-CDR (CVD/ODVD). Finally, each examiner was requested to provide a subjective estimate of the cup/disc ratio (A-CDR) for each eye.
The order in which the observers performed these examinations was pre-established using a randomization list obtained from www.randomization.com. In no case was the second examiner aware of the measurements obtained by the first examiner. Examiner 3 (F.S.F.), who was also blind to the results obtained by the remaining examiners, determined the same three optic nerve head variables using the fast optic disc protocol of the OCT. This procedure consists of six radial scans centered on the optic nerve head. In each scan, the instrument automatically detects the margins of the retinal pigment epithelium (RPE). A straight line connects the edges of the RPE, and a parallel line is constructed 150 μm anteriorly. Structures below this line are defined as the disc cup, and structures above this line as the neuroretinal rim. Examiner 4 (J.G.F.) was responsible for checking fulfillment of the inclusion/exclusion criteria at the time of patient recruitment.
All statistical tests were performed using SPSS 12.0 software for Windows (SPSS Inc.). The Kolmogorov-Smirnov test was used to check for a normal distribution of quantitative data, provided as means and their SD. Differences between the OCT and slit lamp measurements were evaluated using the Student paired *t* test, while inter-method reliability was established by calculating intraclass correlation coefficients. A Bland-Altman plot (15) of the difference between slit lamp measurements made by Examiners 1 and 2 and the OCT measurements against the average of the two was drawn to assess agreement between the two methods. Bland Altmann plots serve to identify a systematic difference between the two sets of measurements. The mean difference is the observed bias. If the mean value of the difference differs significantly from 0 on the basis of a single sample *t* test, this indicates

a fixed bias. This method also explores the possibility of proportional bias, that is, the relationship between possible discrepancies between the measurements obtained and the true value. The existence of proportional bias indicates that the methods show dissimilar disagreement within the range of measurements recorded.

The level of significance for each contrast was set at p<0.05. An a posteriori Bonferroni test was used to correct for the effect of multiple comparisons.

RESULTS

For the three variables determined (A-CDR, H-CDR, V-CDR), agreement between the slit lamp (SL) measurements made by Examiners 1 and 2 was high for both the patients and control subjects (Tabs. I and II). In 46 out of 47 normal eyes (97.9%) and 43 out of 47 glaucomatous eyes (91.5%), the difference in A-CDR was equal or less than 0.2.

Correlation between the results obtained by OCT and the examiners' estimates was significantly higher for the glaucoma group (ICC between 0.85 and 0.93) than for the control group (ICC between 0.44 and 0.67) (Tabs. III and IV).

Table IV shows the agreement recorded between the OCT measurements and the two sets of slit lamp measurements in the glaucoma group. The OCT tended to underestimate the A-CDR compared to the slit lamp (OCT: 0.49±0.25; SL Examiner 1: 0.59±0.24, p<0.001; SL Examiner 2: 0.62±0.22, p<0.001). When we compared the OCT results with measurements made by SL Examiners 1 and 2, the differences observed were clinically significant, defined as a difference greater than 0.2, for 9 (19.1%) and 11 (23.4%) of the eyes respectively. The Bland-Altmann plots revealed a fixed bias, such that the OCT underestimated the cup-disc ratio compared to the two sets of slit lamp measurements. The lack of a proportional bias indicates that the differences observed remained constant over the range of cup-disc ratios tested.

When estimating H-CDR, the OCT cup-disc ratio was overestimated compared to the slit lamp measurements obtained by Examiners 1 and 2 (OCT: 0.70±0.21; SL Examiner 1: 0.59±0.23, p<0.001; SL Examiner 2: 0.62±0.22, p<0.001). As for the A-CDR, the Bland-Altmann plots revealed a fixed bias rendering the significant differences detected. Once again, the lack of a proportional bias means that the horizontal diameter differences observed persisted over the range of cup-disc ratios tested.

For the V-CDR, our results indicated no significant differ-

TABLE I - DEMOGRAPHIC CHARACTERISTICS OF NORMAL AND GLAUCOMA GROUPS: MEAN ± SD (range)

	Normal	Glaucoma	p
No. of subjects	47	47	
Age, yr	63.7±15.2 (34–89)	68.2±14.2 (40–90)	0.145
Male/female	21/26	19/28	
Mean defect (dB)	0.2±1.2 (–0.9–3.2)	10.3±3.7 (5.1–17.2)	p<0.001
Loss variance (dB)	3.2±2.9 (0.5–9)	46.5±21.4 (23–59)	p<0.001

TABLE II - BLAND-ALTMANN ANALYSIS OF DIFFERENCES IN SLIT LAMP MEASUREMENTS MADE BY EXAMINERS 1 AND 2, NORMAL SUBJECTS: MEAN ± SD (range)

	Examiner 1	Examiner 2	ICC	Mean difference	p*	Fixed bias	Proportional bias
A-CDR	0.28±0.14 (0.10–0.60)	0.25±0.14 (0.10–0.60)	0.89	0.029±0.013 (–0.20–0.30)	0.025	Yes	No
H-CDR	0.28±0.15 (0.10–0.68)	0.24±0.13 (0.10–0.60)	0.90	0.036±0.012 (–0.10–0.20)	0.005	Yes	No
V-CDR	0.28±0.15 (0.10–0.58)	0.24±0.14 (0.10–0.62)	0.91	0.023±0.012 (–0.20–0.30)	0.004	Yes	No

*One-sample t test.
ICC = Intraclass correlation coefficients; A-CDR = Cup-disc area ratio; H-CDR = Horizontal cup-disc ratio; V-CDR = Vertical cup-disc-ratio

TABLE III - BLAND-ALTMANN ANALYSIS OF DIFFERENCES IN SLIT LAMP MEASUREMENTS MADE BY EXAMINERS 1 AND 2, GLAUCOMA PATIENTS: MEAN ± SD (range)

	Examiner 1	Examiner 2	ICC	Mean difference (1–2)	p*	Fixed bias	Proportional bias
A-CDR	0.59±0.24 (0.10–1)	0.61±0.22 (0.20–1)	0.91	–0.027±0.019 (–0.30–0.20)	0.156	No	No
H-CDR	0.59±0.23 (0.10–1)	0.62±0.22 (0.20–1)	0.88	–0.046±0.021 (–0.30–0.30)	0.153	No	No
V-CDR	0.63±0.25 (0.10–1)	0.63±0.24 (0.23–1)	0.95	0.004±0.193 (–0.40–0.20)	0.231	No	No

*One-sample t test.
ICC = Intraclass correlation coefficients; A-CDR = Cup-disc area ratio; H-CDR = Horizontal cup-disc ratio; V-CDR = Vertical cup-disc-ratio

TABLE IV - BLAND-ALTMANN ANALYSIS OF DIFFERENCES BETWEEN THE SLIT LAMP (SL) MEASUREMENTS MADE BY EXAMINERS 1 OR 2 AND THE OCT MEASUREMENTS, NORMAL SUBJECTS

Variable	Agreement	ICC	Mean difference	p* value	Fixed bias	Proportional bias
A-CDR	SL(1) – OCT	0.44	–0.04±0.21	0.217	No	Yes
	SL(2) – OCT	0.53	–0.07±0.19	0.021	Yes	Yes
H-CDR	SL(1) – OCT	0.66	–0.26±0.18	<0.001	Yes	No
	SL(2) – OCT	0.67	–0.30±0.17	<0.001	Yes	Yes
V-CDR	SL(1) – OCT	0.53	–0.20±0.19	<0.001	Yes	No
	SL(2) – OCT	0.54	–0.23±0.18	<0.001	Yes	Yes

*One sample t test.
ICC = Intraclass correlation coefficients; A-CDR = Cup-disc area ratio; H-CDR = Horizontal cup-disc ratio; V-CDR = Vertical cup-disc-ratio

TABLE V - BLAND-ALTMANN ANALYSIS OF DIFFERENCES BETWEEN THE SLIT LAMP (SL) MEASUREMENTS MADE BY EXAMINERS 1 OR 2 AND THE OCT MEASUREMENTS, GLAUCOMA PATIENTS

Variable	Agreement	ICC	Mean difference	p* value	Fixed bias	Proportional bias
A-CDR	SL(1) – OCT	0.91	0.09±0.14	<0.001	Yes	No
	SL(2) – OCT	0.92	0.13±0.13	<0.001	Yes	No
H-CDR	SL(1) – OCT	0.85	–0.13±0.16	<0.001	Yes	No
	SL(2) – OCT	0.92	–0.08±0.12	<0.001	Yes	No
V-CDR	SL(1) – OCT	0.90	–0.02±0.14	0.153	No	Yes
	SL(2) – OCT	0.93	–0.02±0.11	0.151	No	Yes

*One sample t test.
ICC = Intraclass correlation coefficients; A-CDR = Cup-disc area ratio; H-CDR = Horizontal cup-disc ratio; V-CDR = Vertical cup-disc-ratio

ences between the mean slit lamp measurements obtained by Examiners 1 and 2 and the data provided by the OCT (OCT: 0.65±0.19; SL Examiner 1: 0.63±0.25, p=0.153; SL Examiner 2: 0.63±0.24, p=0.151). A proportional bias emerged, however, when the OCT measurements were compared to the measurements obtained by SL Examiners 1 and 2, since the OCT overestimated small diameters and underestimated large diameters.

DISCUSSION

Assessment of the optic nerve head is of paramount importance when evaluating a glaucoma patient or glaucoma suspect and, in most cases, structural damage to the nerve head can be detected before any defects in the visual field appear (16, 17). The development of new automatic diagnostic instruments based on the structural analysis of the optic nerve head and nerve fibre layer has therefore had a huge impact on managing the patient with glaucoma since these instruments provide objective morphometric data.

In current clinical practice, HRT, OCT, and RTA procedures enable a complete analysis of papillary morphology and provide easily understandable quantitative data that can be compared with normality measurements from databases. In some cases, the examiner may need to manually define the contour of the papilla or correct possible errors when the instrument tries to fix the edge of the retinal pigment epithelium. Although interventions such as these can diminish the objectivity of these techniques to a certain extent, their measurements can still be considered highly reproducible (13, 18-20). In a comparison of these three instruments performed by Hoffmann et al (21), measurements obtained in an analysis of papillary topography varied significantly such that results could not be considered interchangeable among the three instruments.

To our knowledge, no previous study has evaluated the relationship between standard optic nerve head measurements determined using the slit lamp and those automatically provided by the OCT in control subjects and patients with glaucoma. Despite being considered the gold standard, we decided not to use stereoscopic photographs as a reference, so that we could determine whether OCT results could be interchanged with measurements obtained in daily clinical practice.

Our results indicate greater agreement between OCT and fundus examination measurements in the glaucoma group than the control group. In the glaucoma group, agreement between both methods was high for the variables A-CDR, V-CDR, and H-CDR. In this patient group, high intraclass correlation coefficients and no significant differences between means were observed. In contrast, differences between the methods emerged when the three variables were determined in the control subjects, perhaps because of their shallower optic disc cups.

In the patients with glaucoma, the OCT underestimated the A-CDR and overestimated the H-CDR. Using planimetry, Neubauer et al (12) compared horizontal and vertical cup-disc ratios obtained with the OCT to those obtained through stereophotographs in healthy subjects. Contrary to our findings, the OCT underestimated the H-CDR although their measurement method (pixels converted into absolute distances) differed from ours (ratios), and only 6 of the 25 eyes included in their study were examined using the Stratus OCT. For the V-CDR, we observed no overall differences between slit lamp and OCT measurements. However, the Bland-Altmann plot revealed that differences did indeed exist. Thus, the proportional bias detected indicates that differences between the two methods were related to disc size, such that discs with small vertical diameters, which could pose more problems for an examiner, are overestimated by the OCT compared to subjective measurements. In the case of papillae of larger vertical diameter, the reverse occurs, offsetting the differences detected, and the mean difference is not significantly different to zero. In a previous study, V-CDR measurements obtained by HRT were compared to direct slit lamp measurements made in healthy subjects (14). The authors noted excellent correlation and a lack of significant differences between measurements made using both instruments. These discrepancies with our findings could be attributed to the different approaches used by the HRT and OCT to measure the vertical cup-disc ratio or to the different study populations, since in their study, Watkins et al (14) only included healthy subjects with cup-disc ratios that were possibly smaller than those we would expect to find in a series of patients with glaucoma. In a study by Arnalich-Montiel et al (22), in which agreement was determined between three observers and the OCT in estimating cup to disc ratios in glaucomatous and ocular-hypertensive patients, the OCT was found to overestimate ratios and these overestimates were greater for smaller disc sizes.

In conclusion, our findings indicate that the OCT is a useful tool for evaluating the optic nerve head, but when its measurements are compared with those determined by experienced clinicians we should expect some level of disagreement to the extent that these automatic measurements cannot be interchanged with data subjectively determined using the slit lamp.

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Reprint requests to:
Federico Sáenz-Francés San Baldomero, MD
c/. Julián Romea 7 2
28003 Madrid, Spain
federicosaenzfrancessb@mail.com

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