Agreement among 3 Optical Imaging Methods for the Assessment of Optic Disc Topography

Esther M. Hoffmann, MD,[1] Christopher Bowd, PhD,[1] Felipe A. Medeiros, MD,[1] Catherine Boden, PhD,[1] Franz H. Grus, MD, PhD,[2] Rupert R. Bourne, MD,[1] Linda M. Zangwill, PhD,[1] Robert N. Weinreb, MD[1]

Purpose: To assess the agreement of disc topography measurements between the Heidelberg Retina Tomograph (HRT II), Retinal Thickness Analyzer (RTA), and Optical Coherence Tomograph (StratusOCT).

Design: Observational cross-sectional study.

Participants: Forty-two randomly chosen eyes of 42 subjects.

Methods: Each subject underwent HRT II, RTA, and StratusOCT examination. Two experienced examiners drew the contour lines for the HRT II and RTA. Bland and Altman plots were used to evaluate agreement for each topographic parameter among the instruments. The Spearman coefficient of rank correlation was evaluated for each topographic parameter.

Main Outcome Measures: Agreement in the measurement of optic disc topography among 3 imaging instruments, as evaluated by regression-based 95% limits of agreement.

Results: For optic disc area, the agreement between HRT II–RTA and StratusOCT–RTA revealed the existence of proportional bias, indicated by significant slopes of the regression lines ($P = 0.01$ and $P = 0.02$, respectively). The 95% limits of agreement between instruments varied with the actual optic disc size measurement. Heidelberg Retina Tomograph disc area measurements tended to be consistently lower than StratusOCT disc area measurements (fixed bias). The Spearman correlation coefficient between the instruments ranged from $r = 0.35$ (rim area, HRT II–StratusOCT) to $r = 0.91$ (cup area, HRT II–RTA).

Conclusions: Moderate to high correlation was found in measurements of optic disc topography among different instruments. However, the analysis of agreement indicated important discrepancies among instruments. Therefore, these instruments should not be used interchangeably to obtain measurements of the optic disc for glaucoma diagnosis. *Ophthalmology 2005;112:2149–2156 © 2005 by the American Academy of Ophthalmology.*

Assessment of the optic disc is important for diagnosis and management of glaucoma.[1–4] A number of studies have shown that morphological changes frequently are observable before functional loss can be detected using standard achromatic perimetry.[5–9] Several imaging methods are currently employed in clinical practice to obtain quantitative stereometric and volumetric information of the optic disc.[10–18] Each of these instruments can detect glaucoma with moderate to high sensitivity.[10,11,19–21] However, although these instruments measure similar characteristics of optic disc topography, their measurements may not be interchangeable.

The purpose of this study was to compare measurements of optic disc topography obtained using 3 different commercially available optical imaging instruments.

Originally received: January 20, 2005.
Accepted: July 6, 2005. Manuscript no. 2005-67.

[1] Hamilton Glaucoma Center, Department of Ophthalmology, University of California, San Diego, La Jolla, California.

[2] Department of Ophthalmology, University of Mainz, Mainz, Germany.

Research support: Deutsche Forschungsgemeinschaft, Bonn, Germany (grant no.: Ho 3277/1-1 [EMH]), and the National Institutes of Health, Bethesda, Maryland (grant no.: EY 11008 [LMZ]).

Financial disclosure: Dr Weinreb receives research support (instruments) from Carl Zeiss Meditec and Heidelberg Engineering.

Correspondence to Robert N. Weinreb, MD, Hamilton Glaucoma Center, Department of Ophthalmology, University of California of San Diego, 9500 Gilman Drive, La Jolla, CA, 92093-0946.

Materials and Methods

This observational cross-sectional study included 48 subjects who were imaged with the Heidelberg Retina Tomograph II (HRT II) (Heidelberg Engineering, Dossenheim, Germany), Retinal Thickness Analyzer (RTA) (Talia Technology Ltd., Neve Ilan, Israel), and Optical Coherence Tomograph (StratusOCT, Carl Zeiss Meditec, Dublin, CA) within 3 months between February and September 2004. One randomly selected eye of all subjects was analyzed. All subjects were evaluated at the Hamilton Glaucoma Center, University of California, San Diego as part of the Diagnostic Innovations in Glaucoma Study, a prospective longitudinal study designed to evaluate optic nerve structure and visual function in glaucoma. All patients who met the inclusion criteria described were enrolled in the current study. Patients were selected retrospectively from our research database. Informed consent was obtained from all participants. The University of California, San Diego Human Subjects Committee approved all protocols, and the

Published by Elsevier Inc.
ISSN 0161-6420/05/$–see front matter
doi:10.1016/j.ophtha.2005.07.003

methods described adhered to the tenets of the Declaration of Helsinki.

Each study participant underwent complete ophthalmologic examination, including a medical history review, best-corrected visual acuity (BCVA) measurement, slit-lamp biomicroscopy, intraocular pressure (IOP) measurement using Goldmann applanation tonometry, gonioscopy, dilated fundus examination, stereoscopic optic disc topography, and standard automated perimetry using the 24-2 Swedish Interactive Threshold Algorithm (Carl Zeiss Meditec).

Inclusion Criteria

One eye was randomly selected for the study (study eye). To be included in the study, the study eye had to have open angles, BCVA of 20/40 or better, spherical refraction within $\pm$5.0 diopters (D), and cylinder correction within $\pm$3.0 D. Eyes with parapapillary atrophy were excluded. Normal eyes had IOPs of $\leq$22 mmHg, with no history of increased IOP; normal optic discs, based on masked analysis of stereophotographs with intact rims; no hemorrhages, notches, excavation, localized pallor, or nerve fiber defects; and normal visual fields (VFs). A normal VF was defined as a mean deviation and pattern standard deviation (PSD) within 95% confidence limits and a glaucoma hemifield test result within normal limits. Family history of glaucoma was not an exclusion criterion. Eyes classified as glaucomatous had 2 consecutive (repeatable) abnormal VF test results (PSD outside the 95% confidence limits and/or glaucoma hemifield test result outside normal limits).

Instrumentation

Confocal Scanning Laser Ophthalmoscope (Heidelberg Retina Tomograph II). The HRT II, software version 2.01, is a confocal scanning laser ophthalmoscope that works by emitting a diode laser beam with a 670-nm wavelength to scan the retinal surface sequentially in horizontal and vertical directions at multiple focal planes.[22] It was designed specifically for the evaluation of the optic nerve head and provides topographic information about the disc.[20,23] A 3-dimensional topographic image consisting of 384$\times$384 (total, 147 456) pixels is constructed[15,24] to determine a wide range of optic nerve head parameters. Three topographic images are obtained in succession, which are combined and automatically aligned for a single mean topography used for analysis. The field of view is set at 15°. Before topographic disc analysis, a contour line was placed around the optic nerve head using the inner edge of Elschnig's scleral ring[25] by an experienced examiner (CB) while viewing stereophotographs of the optic disc. Contour lines were reviewed by a second examiner (EMH). All images were reviewed for quality by evaluating clarity and even illumination, nerve head centering, correction of astigmatism, standard deviation (SD) ($<$50 μm), and sensitivity score ($<$90%).

The HRT II calculates disc area as the area bounded by the drawn contour line. The other stereometric parameters used in this study (cup area, cup-to-disc [C/D] ratio area, rim area, cup volume, and rim volume) are calculated relative to the reference plane, defined as 50 μm posterior to the mean retinal height between 350° and 356° (papillomacular bundle) along the contour line. Transverse resolution of the HRT II is 10 μm per pixel, and the longitudinal resolution is 62 μm per plane.[26]

Retinal Thickness Analyzer. The RTA, software version 4.10 SP, was originally developed for the evaluation of retinal diseases throughout the posterior pole by performing cross sections of the retina.[27–30] Recently, the software has been improved to provide optic disc topography using parameters similar to those of the HRT II, including the operator-drawn contour line to determine optic disc boundaries.

The principle of the RTA is based on a helium–neon laser (543 nm), which is projected obliquely on the retina and reflected in an angle similar to slit-lamp biomicroscopy. The instrument measures retinal thickness using a beam splitter that splits light into 2 separate beams. One beam is reflected off the retinal pigment epithelium (RPE), and the other reflects off the internal limiting membrane. The difference between these 2 reflections is the measured retinal thickness.[27,29,30] Each scan (duration, 0.3 seconds) results in a 3-mm^2 image composed of 16 optical cross sections through the tissue.

More recently, software was added to measure optic disc topography. It maps out a 2- and 3-dimensional map of the optic nerve head, disc area image, and RNFL cross section curve (temporal–superior–nasal–inferior–temporal curve) divided into 6 segments. The global and predefined segmental rim areas are adjusted to the corresponding disc area using linear regression. The adjusted rim areas are compared with normative values. The measurements require a minimum pupil dilatation of 6 mm. Thirty minutes before imaging, pupils were dilated with tropicamide 0.5% (Bausch & Lomb, Tampa, FL) eyedrops.

As with the HRT II, a reference plane is placed 50 μm under the surface of the papillomacular nerve fiber bundle, and the contour line is drawn manually. Contour lines were drawn by one experienced examiner (EMH) and reviewed by another examiner (CB). Image quality was assessed by one experienced examiner (EMH). Images with incomplete scans, insufficient focus on the retina, off-centered images, and uneven illuminated images were considered poor and were not included in the analysis.

Disc area is calculated as the total area of the disc delimited by the operator-defined contour line. All other parameters analyzed in this study (cup area, C/D area ratio, rim area, cup volume, and rim volume) are calculated using the reference plane. Depth resolution of the RTA is reported to be approximately 50 μm.[27]

StratusOCT. The Optical Coherence Tomograph, software version 4.0, uses a superluminescent diode laser light that is scattered, reflected, and absorbed by retinal tissue. The technique provides in vivo cross-sectional scans of retinal structures by the use of low-coherence interferometry to resolve the distances of reflective structures in the eye. It works analogous to the ultrasound B-scan technique but uses light instead of ultrasound to acquire high-resolution images.[31]

A low-coherence beam (840 nm) is directed onto a partially reflective mirror that splits the light into 2 beams, a reference beam and a measurement beam. The measurement beam is directed into the eye and reflected from intraocular microstructures according to their reflectivity, distance, and thickness. The reference beam is reflected from the reference mirror at a known variable position. Both beams travel back to the beam splitter, recombine, and are transmitted to a detector. The pattern of interference is used to provide information about distance and thickness of retinal structures. Data are displayed as a numeric report and in a false-color topographic map. Images were automatically analyzed by the software. Quality assessment of StratusOCT scans was done by an experienced examiner (EMH). Focused images from the ocular fundus video image, an adequate strength ($>$7), and the presence of centered linear scans were requirements for acceptable quality. The optic nerve head was assessed with 6 linear scans centered on the disc. For all scans, internal fixation was used.

The StratusOCT interpolates between the scans to provide measurements throughout the optic nerve head. For optic disc topography, the automated determination of the disc margin as the end of the RPE was used for this analysis. 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, the neuroretinal rim. Resolution of the StratusOCT is $\leq$10 μm axially and 20 μm transversally.[32]

Table 1. Characteristics of the Study Population

	All Subjects (n = 42)	POAG (n = 23)	Normal (n = 19)	*P* Value*
Age (yrs) (SD)	57.9 (15.3)	65.0 (12.8)	50.0 (14.0)	<0.001
Gender (% female)	57.1	52.2	63.3	0.48
Race (% white)	73.0	78.0	69.0	0.98
Refractive error (SD)	−0.59 (1.7)	−0.79 (2.1)	−0.36 (1.2)	0.42
Mean deviation (SD)	−2.76 (4.6)	−4.35 (7.9)	−1.16 (1.6)	0.02

POAG = primary open-angle glaucoma; SD = standard deviation.
**t* test; $P<0.05$ are considered statistically significant.

Each subject was measured on all instruments within 3 months. Heidelberg Retina Tomograph II measurements were performed first before dilation (mean pupil size ranged from 3 mm to 4.5 mm), followed by RTA and StratusOCT measurements in random order after dilation. Thirty patients (71%) were examined on the same day with all 3 devices. Six patients had images that were unacceptable. Three patients had unacceptable images with all of the devices (HRT, StratusOCT, and RTA), and 3 had unacceptable images only with the RTA. Therefore, 42 eyes of 42 subjects were included in the analysis.

Statistical Analysis

Student's *t* tests were conducted to determine whether differences in age, gender, race, refractive error, and VF indexes between glaucomatous and healthy eyes were present.

Descriptive analysis, including mean values and SDs of optic disc topography measurements, was performed for each instrument. Bland and Altman plots were used to evaluate the agreement among different instruments.[33] The differences between measurements for each parameter were plotted against their mean. The comparison of means was performed by *t* tests in the agreement analysis. Bland and Altman plots allow us to investigate the existence of any systematic difference between the measurements (i.e., fixed bias). The mean difference is the estimated bias, and the SD of the differences measures the random fluctuations around this mean. If the mean value of the difference differs significantly from 0 on the basis of a 1-sample *t* test, this indicates the presence of fixed bias. We also calculated 95% limits of agreement for each comparison (mean difference $\pm$ 1.96 $\times$ SD), which tell us how far apart measurements by 2 methods were more likely to be for most individuals.

Bland and Altman plots were also used to investigate any possible relationship of the discrepancies between the measurements and the true value (i.e., proportional bias). The existence of proportional bias indicates that the methods do not agree equally through the range of measurements (i.e., the limits of agreement will depend on the actual measurement). To evaluate this relationship formally, the difference between the methods was regressed on the average of the 2 methods. When a relationship between the differences and the true value was identified (i.e., a significant slope of the regression line), regression-based 95% limits of agreement were provided.

A Spearman coefficient of rank correlation (*r*) was performed to test the strength of the relationship between topographic measurements of each instrument. Correlations were considered statistically significant if $P<0.05$. A sample size of 40 was chosen to achieve 80% power to detect differences (of at least 1 SD) between instruments.

Statistical analyses were performed with Statistica version 7 software (Statsoft Inc., Tulsa, OK) and SPSS version 11.02 (SPSS Inc., Chicago, IL).

Results

There were no statistically significant differences in gender, race, and refractive error between glaucoma patients (n = 23) and normal subjects (n = 19). Patients with glaucoma were significantly older than normal subjects (*t* test, $P<0.001$). The characteristics of the study population are summarized in Table 1.

Table 2 shows mean values of optic disc topographic parameters obtained by each instrument, and Table 3 shows the agreement between instruments. For the comparisons HRT II–RTA and StratusOCT–RTA, significant mean differences were observed for all topographic parameters, except disc area between StratusOCT and RTA. For the comparison HRT II–StratusOCT, significant differences were found for measurements of disc area, C/D ratio, cup area, and rim volume, whereas no statistically significant differences were found for rim area and cup volume. The power of this study to detect differences between the instruments was >0.8.

Table 3 also shows 95% limits of agreement obtained from Bland and Altman plots for all comparisons between instruments. The existence of fixed and proportional biases for each comparison is also indicated on the table. For some comparisons, there was evidence of proportional bias, as indicated by the significant slope of the regression line of the differences between measurements on the average of the measurements. For these parameters, equations for regression-based 95% limits of agreement were provided. Due to the large number of possible combinations, only 6 Bland and Altman plots are shown. Figure 1 shows the Bland and Altman plots for the parameter disc area. The plots for the agreement between HRT II and RTA (Fig 1A) and StratusOCT and RTA (Fig 1B) revealed the existence of proportional bias, as indicated by the significant slopes of the regression lines (*P* values of 0.01 and 0.02, respectively) of the differences between measurements on the average of the measurements. For smaller discs, RTA measurements tended to be lower than those of HRT II and StratusOCT, whereas, for larger discs, RTA measurements tended to be higher than those of HRT II and StratusOCT. As can be seen from Figure 1, the 95% limits of agreement between instruments vary with the actual optic disc size measurement. The equations for the regression lines corresponding to the 95% limits of agreement are given in Table 3.

The agreement in disc area measurements between HRT II and StratusOCT did not show proportional bias, as indicated by the nonsignificant slope of the regression line in Figure 1C ($P = 0.65$). However, the Bland and Altman plot showed the presence of fixed bias, as indicated by the significant deviation from zero of the mean difference between HRT II and StratusOCT measurements—that

Table 2. Mean Values (Standard Deviation) of Disc Parameters Measured with All 3 Instruments

	HRT II	RTA	StratusOCT
Disk area (mm^2)	2.13 (0.43)	2.26 (0.53)	2.31 (0.41)
Cup-to-disc ratio	0.34 (0.17)	0.49 (0.23)	0.38 (0.19)
Cup area (mm^2)	0.75 (0.48)	1.15 (0.73)	0.92 (0.59)
Rim area (mm^2)	1.37 (0.30)	1.11 (0.47)	1.37 (0.37)
Cup volume (mm^3)	0.19 (0.18)	0.30 (0.29)	0.18 (0.20)
Rim volume (mm^3)	0.36 (0.17)	0.20 (0.17)	0.28 (0.18)

HRT II = Heidelberg Retina Tomograph; RTA = Retinal Thickness Analyzer; StratusOCT = Optical Coherence Tomograph.

Table 3. Bland and Altman Regression-Based 95% Limits of Agreement for Heidelberg Retina Tomograph II, Retinal Thickness Analyzer and Stratus Optical Coherence Tomograph in Optic Disc Topography

Parameter	Agreement	Mean Difference	*P* Value*	Fixed Bias	R^2	*P* Value	Proportional Bias	95% Limits of Agreement†
Disk area (mm^2)	HRT II–Stratus OCT	−0.18	<0.001	Yes	0.004	0.65	No	−0.76 to 0.39
	HRT II–RTA	−0.13	0.004	Yes	0.14	0.01	Yes	−0.15–0.22× to 0.84–0.22×
	StratusOCT–RTA	0.06	0.287	No	0.13	0.02	Yes	0.06–0.28× to 1.33–0.28×
Cup/disk Ratio	HRT II–StratusOCT	−0.04	0.018	Yes	0.05	0.17	No	−0.27 to 0.18
	HRT II–RTA	−0.15	<0.001	Yes	0.24	0.0009	Yes	−0.23–0.35× to 0.23–0.35×
	StratusOCT–RTA	−0.10	<0.001	Yes	0.08	0.06	No	−0.39 to 0.18
Cup area (mm^2)	HRT II–StratusOCT	−0.17	0.001	Yes	0.15	0.01	Yes	−0.54 −0.24× to 0.58–0.24×
	HRT II–RTA	−0.39	0.009	Yes	0.17	0.01	Yes	−1.18 −0.90× to 2.14–0.90×
	StratusOCT–RTA	−0.22	<0.001	Yes	0.15	0.01	Yes	−0.54 −0.22× to 0.78–0.22×
Rim area (mm^2)	HRT II–StratusOCT	−0.01	0.931	No	0.06	0.13	No	−0.76 to +0.75
	HRT II–RTA	0.27	<0.001	Yes	0.25	0.0008	Yes	0.31–0.59× to 1.69–0.59×
	StratusOCT–RTA	0.28	<0.001	Yes	0.07	0.08	No	−0.56 to +1.11
Cup volume (mm^3)	HRT II–StratusOCT	0.01	0.786	No	0.02	0.37	No	−0.38 to +0.40
	HRT II–RTA	−0.11	<0.001	Yes	0.36	<0.0001	Yes	−0.17–0.50× to 0.41–0.50×
	StratusOCT–RTA	−0.12	0.001	Yes	0.15	0.01	Yes	−0.44–0.40× to 0.39–0.40×
Rim volume (mm^3)	HRT II–StratusOCT	0.07	0.018	Yes	0.003	0.71	No	−0.30 to +0.44
	HRT II–RTA	0.15	<0.001	Yes	0.003	0.70	No	−0.16 to +0.47
	StratusOCT–RTA	0.08	0.003	Yes	<0.0001	0.97	No	−0.26 to +0.43

HRT II = Heidelberg Retina Tomograph; RTA = Retinal Thickness Analyzer; StratusOCT = Optical Coherence Tomograph.
*One-sample *t* test.
†Equations for regression-based 95% limits of agreement are given when proportional bias was detected.

is, HRT II disc area measurements tended to be smaller than StratusOCT disc area measurements.

Figure 2 shows Bland and Altman plots for the parameter C/D ratio. The plot for the agreement between HRT II and RTA shows evidence of proportional bias (Fig 2A). For lower and higher C/D ratio values, RTA measured higher values than HRT with increasing trend, indicated by the significant slope of the regression line ($P<0.001$). Although the same trend was observed for the comparison StratusOCT–RTA (Fig 2B), the slope of the regression line was not statistically significant ($P = 0.06$).

The Spearman rank correlation coefficients (*r*s) ranged from $r = 0.35$ (rim area, HRT II vs. StratusOCT) to $r = 0.91$ (cup area, HRT II vs. RTA). Both rim parameters (rim area and rim volume) showed moderate correlations among the instruments (range, $r = 0.35$ to $r = 0.64$). All correlations were statistically significant ($P<0.05$). Table 4 shows the Spearman rank correlation coefficients for each parameter.

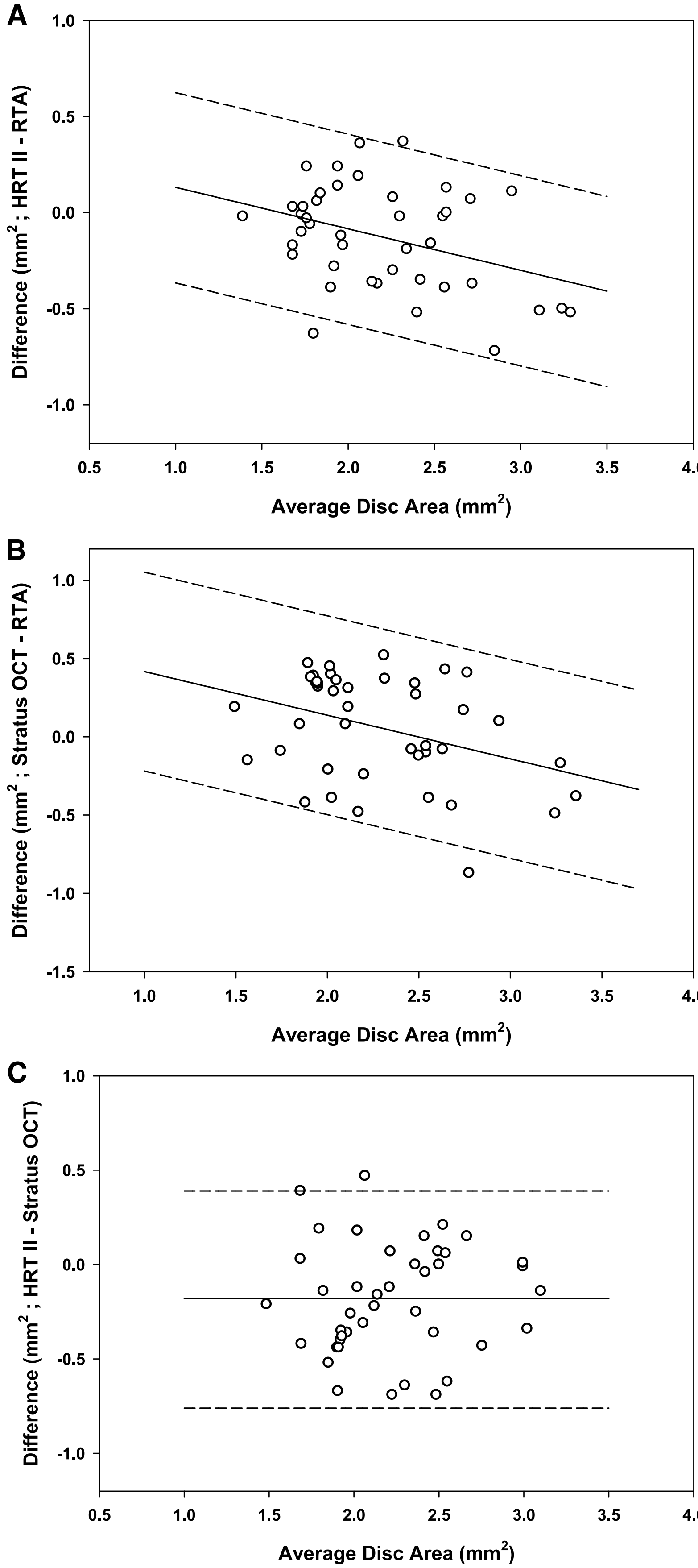
Discussion

This study compares optic disc topographic measurements obtained with the HRT II, RTA, and StratusOCT. These instruments use different techniques to provide these measurements. Important differences in the measurements of all topographic parameters were identified among the instruments.

Previous studies have compared topographic measurements obtained with the HRT and other instruments[11,34] (Invest Ophthalmol Vis Sci 44[Suppl]:e-abstract 3385, 2003).

Evaluating a group of glaucoma patients, glaucoma suspects, and normal subjects, Schuman et al[11] found that optic disc area measurements obtained by the HRT and Stratus OCT were highly correlated, although HRT measurements were significantly smaller than those obtained by either OCT2 or StratusOCT. In our study, we also found a high correlation between the 2 instruments, and the mean disc area values obtained with the HRT II were also significantly lower than those obtained with StratusOCT (mean difference HRT II–StratusOCT, -0.18 mm^2; $P<0.001$). However, close observation of Figure 1C shows that, for several patients, StratusOCT disc area measurements were actually lower than HRT II measurements. Further, although the measurements were highly correlated, important discrepancies were identified in the Bland and Altman plots. In fact, the 95% limits of agreement ranged from -0.76 mm^2 to 0.39 mm^2 (i.e., HRT II disc area measurements could be as much as 0.76 mm^2 lower than StratusOCT or as much as 0.39 mm^2 higher than StratusOCT measurements). Considering an average optic disc size of 2.00 mm^2, these discrepancies would be on the order of approximately 20% to 40%. These findings emphasize the low utility of correlation coefficients to assess agreement between instru-

Figure 1. Regression-based Bland and Altman plots for the parameter disc area. The plots for agreements between the Heidelberg Retina Tomograph (HRT II) and Retinal Thickness Analyzer (RTA) (**A**) and Optical Coherence Tomograph (StratusOCT) and RTA (**B**) revealed the existence of proportional bias, as indicated by the significant slopes of the regression lines (*P* values of 0.01 and 0.02, respectively) of the differences between measurements on the average of the measurements. Regression-based 95% limits of agreement are shown by the 2 lines parallel to the regression line. (**C**), The plot for the agreement between the HRT II and StratusOCT did not show proportional bias (nonsignificant slope of the regression line, $P = 0.65$), but fixed bias, indicated by the significant deviation from zero of the mean differences. The HRT II disc area measurements were smaller than StratusOCT values.


A
Difference (mm^2 ; HRT II - RTA)
Average Disc Area (mm^2)
B
Difference (mm^2 ; Stratus OCT - RTA)
Average Disc Area (mm^2)
C
Difference (mm^2 ; HRT II - Stratus OCT)
Average Disc Area (mm^2)

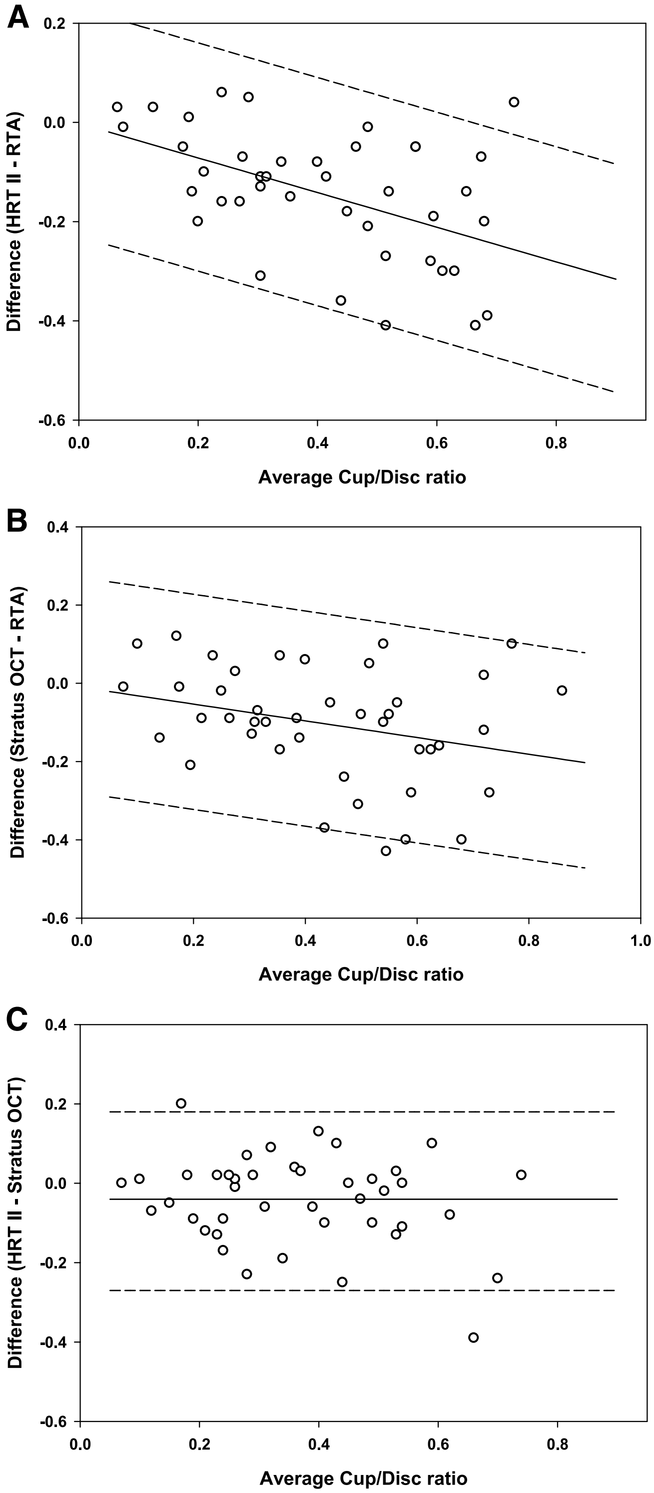


Figure 2. Regression-based Bland and Altman plots for the parameter cup-to-disc (C/D) ratio. **A,** The plot for the Heidelberg Retina Tomograph (HRT II)– Retinal Thickness Analyzer (RTA) agreement shows evidence of proportional bias. For lower and higher C/D ratio values, the RTA measured higher values than the HRT II with increasing trend, indicated by the significant slope of the regression line ($P<0.001$). **B, C,** For the comparisons Optical Coherence Tomograph (StratusOCT)–RTA and StratusOCT–HRT II, the slopes of the regression lines were not statistically significant ($P = 0.06$ and $P = 0.17$, respectively).

ments, an issue that has already been extensively demonstrated in the literature.[35–37] Although some lack of agreement between different methods is inevitable, what matters is the amount by which the methods disagree. This will indicate whether or not the measurements can be used interchangeably. For the comparison in disc area measurement between the HRT II and StratusOCT, the wide 95% limits of agreement indicate that, although highly correlated, measurements performed by these 2 instruments cannot be used interchangeably.

For the other topographic parameters, important discrepancies were also identified between the HRT II and StratusOCT. For example, for the parameter rim area, although no fixed bias was detected, the 95% limits of agreement were wide, ranging from -0.76 mm^2 to 0.75 mm^2.

Two earlier studies compared optic disc topographic measurements obtained by the RTA and HRT.[16,17] Neither study addressed the agreement between the instruments, but only the correlation in optic disc topographic measurements. Itai et al[16] measured the reproducibility of the RTA and HRT II using coefficients of variation without detecting statistically significant differences between the instruments in disc topography measures. Martinez de la Casa et al[17] also reported correlation coefficients between the RTA and HRT, with the highest correlation coefficients found for cup parameters (ranging from 0.67 for cup shape measure to 0.92 for maximum cup depth). Although the mean disc area reported for the HRT (2.17 ± 0.25 mm^2) was smaller than that for the RTA (2.86 ± 0.31 mm^2), no formal analysis was provided to evaluate whether a statistically significant difference existed between these measurements. In our study, topographic measurements obtained by the RTA were also significantly correlated with those obtained by the HRT II and StratusOCT. However, the analysis of agreement identified important discrepancies between these instruments. Interestingly, a proportional bias was identified for most of the comparisons involving the RTA. The existence of proportional bias indicates that the amount of disagreement between 2 instruments is not constant throughout the range of measurements, but instead varies with the actual measurement. Therefore, the estimation of the 95% limits of agreement between 2 instruments depends on the actual measurement. When proportional bias was identified, the regression equations provided in Table 3 could be used to assess the agreement according to the range of measure-

Table 4. Rank Correlation Coefficients* of Topographic Measurements Obtained by the Heidelberg Retina Tomograph II (HRT II), Retinal Thickness Analyzer (RTA), and Optical Coherence Tomograph (OCT)

	HRT II–RTA	HRT II–OCT	RTA–OCT
Disk area	0.84	0.73	0.73
Cup-to-disc ratio	0.84	0.81	0.8
Cup area	0.91	0.88	0.88
Rim area	0.51	0.35	0.55
Cup volume	0.87	0.85	0.87
Rim volume	0.61	0.51	0.64

*Spearman coefficients of rank correlation (r). All correlations were significant, $P<0.05$.

ments. For optic disc area, RTA measurements tended to be higher than HRT II and StratusOCT measurements in patients with larger discs, with an inverse relationship occurring in patients with smaller discs (Fig 1A, B). This relationship was observed for both comparisons involving the RTA, but not for the comparison between the HRT II and StratusOCT. The reason for this is unclear.

It should be noted that our study was restricted to the analysis of agreement between instruments. Other relevant issues such as diagnostic performance and repeatability were not evaluated. The evaluation of the repeatability of each method is relevant, as the repeatability of 2 methods of measurement limit the amount of agreement that is possible. Lack of agreement between 2 methods of measurement can also be caused by lack of repeatability of one of the methods. Several studies have demonstrated that optic disc topographic measurements obtained by the HRT are reproducible.[38] Recent studies found reproducible optic disc measurements with StratusOCT.[39] For the RTA, Hoffmann et al[40] assessed repeatability and reproducibility of optic disc topographic parameters and found a large overall variation in optic nerve head measurements, indicating low reproducibility and repeatability.

In conclusion, when measuring optic disc topography, examiners should be aware that results are likely to be influenced by the method of measurement used and that each of the instruments may provide different results when tested on the same individual. Our results indicate that, although significantly correlated, measurements provided by the HRT II, StratusOCT, and RTA should not be used interchangeably for the assessment of optic disc topography in glaucoma.

References

1. Caprioli J, Miller JM. Optic disc rim area is related to disc size in normal subjects. Arch Ophthalmol 1987;105:1683–5.
2. Jonas JB, Bergua A, Schmitz-Valckenberg P, et al. Ranking of optic disc variables for detection of glaucomatous optic nerve damage. Invest Ophthalmol Vis Sci 2000;41:1764–73.
3. Garway-Heath DF, Hitchings RA. Quantitative evaluation of the optic nerve head in early glaucoma. Br J Ophthalmol 1998;82:352–61.
4. Iester M, Mikelberg FS. Optic nerve head morphologic characteristics in high-tension and normal-tension glaucoma. Arch Ophthalmol 1999;117:1010–3.
5. Motolko M, Drance SM. Features of the optic disc in preglaucomatous eyes. Arch Ophthalmol 1981;99:1992–4.
6. Caprioli J, Miller JM, Sears M. Quantitative evaluation of the optic nerve head in patients with unilateral visual field loss from primary open-angle glaucoma. Ophthalmology 1987;94: 1484–7.
7. Quigley HA, Addicks EM, Green WR. Optic nerve damage in human glaucoma. III. Quantitative correlation of nerve fiber loss and visual field defect in glaucoma, ischemic neuropathy, papilledema, and toxic neuropathy. Arch Ophthalmol 1982; 100:135–46.
8. Sommer A, Katz J, Quigley HA, et al. Clinically detectable nerve fiber atrophy precedes the onset of glaucomatous field loss. Arch Ophthalmol 1991;109:77–83.
9. Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol 2002;120:701–13, discussion 829–30.
10. Schuman JS, Hee MR, Arya AV, et al. Optical coherence tomography: a new tool for glaucoma diagnosis. Curr Opin Ophthalmol 1995;6:89–95.
11. Schuman JS, Wollstein G, Farra T, et al. Comparison of optic nerve head measurements obtained by optical coherence tomography and confocal scanning laser ophthalmoscopy. Am J Ophthalmol 2003;135:504–12.
12. Weinreb RN. Assessment of optic disc topography for diagnosing and monitoring glaucoma. Arch Ophthalmol 1998;116: 1229–31.
13. Kiriyama N, Ando A, Fukui C, et al. A comparison of optic disc topographic parameters in patients with primary open angle glaucoma, normal tension glaucoma, and ocular hypertension. Graefes Arch Clin Exp Ophthalmol 2003;241: 541–5.
14. Bass SJ, Sherman J. Optic disk evaluation and utility of high-tech devices in the assessment of glaucoma. Optometry 2004;75:277–96.
15. Bathija R, Zangwill L, Berry CC, et al. Detection of early glaucomatous structural damage with confocal scanning laser tomography. J Glaucoma 1998;7:121–7.
16. Itai N, Tanito M, Chihara E. Comparison of optic disc topography measured by Retinal Thickness Analyzer with measurement by Heidelberg Retina Tomograph II. Jpn J Ophthalmol 2003;47:214–20.
17. Martinez de la Casa JM, Garcia Feijoo J, Castillo Gomez A, Garcia Sanchez J. Correlations between retinal thickness analyzer (RTA) and confocal scanning laser tomography (HRT) in optic disc analysis [in Spanish]. Arch Soc Esp Oftalmol 2004;79:21–5.
18. Weinreb RN, Zangwill LM. Imaging technologies for assessing neuroprotection in glaucomatous optic neuropathy. Eur J Ophthalmol 1999;(suppl):S40–3.
19. Medeiros FA, Zangwill LM, Bowd C, Weinreb RN. Comparison of the GDx VCC scanning laser polarimeter, HRT II confocal scanning laser ophthalmoscope, and Stratus OCT optical coherence tomograph for the detection of glaucoma. Arch Ophthalmol 2004;122:827–37.
20. Miglior S, Guareschi M, Albe E, et al. Detection of glaucomatous visual field changes using the Moorfields regression analysis of the Heidelberg retina tomograph. Am J Ophthalmol 2003;136:26–33.
21. Kruse FE, Burk RO, Volcker HE, et al. Reproducibility of topographic measurements of the optic nerve head with laser tomographic scanning. Ophthalmology 1989;96:1320–4.
22. Bartz-Schmidt KU, Weber J, Heimann K. Validity of two-dimensional data obtained with the Heidelberg Retina Tomograph as verified by direct measurements in normal optic nerve heads. Ger J Ophthalmol 1994;3:400–5.
23. Wollstein G, Garway-Heath DF, Fontana L, Hitchings RA. Identifying early glaucomatous changes. Comparison between expert clinical assessment of optic disc photographs and confocal scanning ophthalmoscopy. Ophthalmology 2000;107: 2272–7.
24. Weinreb RN. Laser scanning tomography to diagnose and monitor glaucoma. Curr Opin Ophthalmol 1993;4(2):3–6.
25. Jonas JB, Budde WM, Panda-Jonas S. Ophthalmoscopic evaluation of the optic nerve head. Surv Ophthalmol 1999;43:293–320.
26. The Heidelberg Retina Tomograph II. Information Folder. Dossenheim, Germany: Heidelberg Engineering; 2004.
27. Zeimer R, Shahidi M, Mori M, et al. A new method for rapid

mapping of the retinal thickness at the posterior pole. Invest Ophthalmol Vis Sci 1996;37:1994–2001.
28. Tanito M, Itai N, Ohira A, Chihara E. Reduction of posterior pole retinal thickness in glaucoma detected using the Retinal Thickness Analyzer. Ophthalmology 2004;111:265–75.
29. Asrani S, Zeimer R, Goldberg MF, Zou S. Application of rapid scanning retinal thickness analysis in retinal diseases. Ophthalmology 1997;104:1145–51.
30. Asrani S, Zou S, d'Anna S, et al. Noninvasive mapping of the normal retinal thickness at the posterior pole. Ophthalmology 1999;106:269–73.
31. Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. Science 1991;254:1178–81.
32. STRATUSOCT User Manual. Jena, Germany: Carl Zeiss Meditec; 2004.
33. Bland JM, Altman DG. Measuring agreement in method comparison studies. Stat Methods Med Res 1999;8:135–60.
34. Spencer AF, Sadiq SA, Pawson P, Vernon SA. Vertical optic disk diameter: discrepancy between planimetric and SLO measurements. Invest Ophthalmol Vis Sci 1995;36:796–803.
35. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307–10.
36. Medeiros FA, Zangwill LM, Bowd C, et al. Evaluation of retinal nerve fiber layer, optic nerve head, and macular thickness measurements for glaucoma detection using optical coherence tomography. Am J Ophthalmol 2005;139:44–55.
37. Ludbrook J. Statistical techniques for comparing measurers and methods of measurement: a critical review. Clin Exp Pharmacol Physiol 2002;29:527–36.
38. Zangwill LM, Medeiros FA, Bowd C, Weinreb RN. Optic nerve imaging devices: recent advances. In: Grehn SA, Stamper R, eds. Glaucoma. Berlin: Springer-Verlag; 2004:63-91. Essentials in Ophthalmology 1612–3212.
39. Paunescu LA, Schuman JS, Price LL, et al. Reproducibility of nerve fiber thickness, macular thickness, and optic nerve head measurements using StratusOCT. Invest Ophthalmol Vis Sci 2004;45:1716–24.
40. Hoffmann EM, Medeiros FA, Kramann C, et al. Repeatability and reproducibility of optic nerve head topography using the Retinal Thickness Analyzer. Graefes Arch Clin Exp Ophthalmol. In press.