Measurements of Optic Disk Size With HRT II, Stratus OCT, and Funduscopy Are Not Interchangeable

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• PURPOSE: To assess the interchangeability of optic disk size measurements using slit-lamp funduscopy, optical coherence tomography (OCT-3), and confocal scanning laser ophthalmoscopy (HRT-II) in clinical practice.

• DESIGN: Prospective nonrandomized clinical study.

• METHODS: Measurements of vertical disk diameter (VDD) were obtained with the three methods. Disk area was obtained from OCT and HRT printouts. True agreement between methods in measuring VDD was assessed using Bland-Altman graphs and 95% limits of agreement (LoA). Disks were classified as small, average, or large, and agreement between methods in this classification was assessed using κ statistics.

• RESULTS: Forty-eight patients were enrolled (mean age 53.4 ± 14.3 years). VDD (mean ± SD) was 1.58 ± 0.15, 1.70 ± 0.22, and 1.90 ± 0.24 mm with funduscopy, HRT, and OCT, respectively. Very large LoA were observed: −0.29 to 0.70 mm for OCT and HRT, −0.07 to 0.71 mm for OCT and funduscopy, and −0.29 to 0.53 mm for HRT and funduscopy. There was poor agreement (κ < 0.4) in classification of disk size as small, average, or large whether disk diameter or area was compared and using two definitions of disk size.

• CONCLUSIONS: We observed a large range of differences in estimating disk size with HRT, OCT, and funduscopy. This precludes interchangeable use of these measurements in clinical practice, and does not allow simple conversion formulas to be proposed. In addition, there is poor agreement between these methods in classifying disk size as small, average, or large. At present, estimation of both absolute and relative disk size can only be defined separately for each measurement modality. (Am J Ophthalmol 2006;142:375–380. © 2006 by Elsevier Inc. All rights reserved.)

EARLY DIAGNOSIS OF GLAUCOMA IS CENTERED ON evaluation of morphometric parameters of the optic nerve as changes in the optic disk often precede visual field loss.[1–5] It has become increasingly clear that to accurately assess the size of components of the optic disk such as the cup or neuroretinal rim, the size of the disk must be measured and taken into account as the disk size is a major determinant of other disk parameters.[6–11] Moreover, the discrimination between healthy and glaucomatous optic nerves is improved when disk size is taken into account.[10,12,13] Traditionally, optic disk evaluation has been performed by subjective evaluation of disk appearance during ophthalmoscopy or photography[14] and disk size can be estimated using these methods.[15–19] In recent years, imaging devices such as the Heidelberg Retinal Tomograph (HRT, Heidelberg Engineering GmBH, Dossenheim, Germany) and optical coherence tomograph (OCT, Carl Zeiss Meditec Inc, Dublin, California, USA) have been developed to provide objective and reproducible analysis of optic disk morphometric parameters.[20–23] They have higher reproducibility and lower interobserver variability compared with clinician assessment of the optic disk.[24] In addition, they allow easy documentation and archiving of disk status. For these reasons, they are increasingly being used by clinicians as diagnostic tools.

Studies that have compared measurements of disk size by HRT to those of ophthalmoscopy or disk photography, and those of HRT to OCT, have shown significant intermethod differences.[15,25–28] In the few reports in which true agreement between methods was analyzed, as proposed by Bland and Altman,[29] authors have commented that the values reported by the different techniques show poor agreement and can not be used interchangeably in clinical

Accepted for publication Mar 28, 2006.

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Supported in part by the Corinne Graber Research Fund of the New York Glaucoma Research Institute and the American Physicians Fellowship for Medicine in Israel.

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0002-9394/06/$32.00
doi:10.1016/j.ajo.2006.03.065

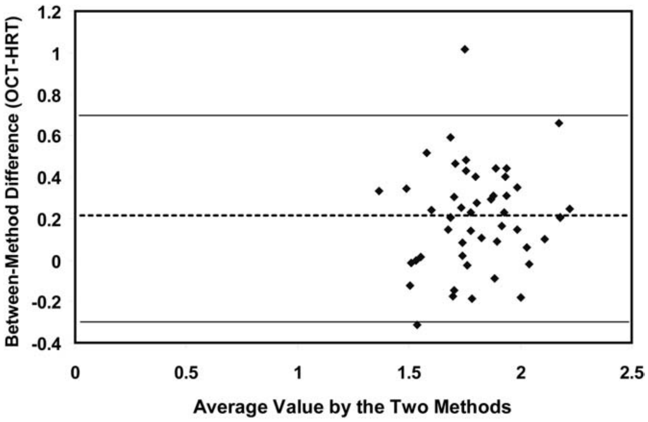

FIGURE 1. Differences in vertical disk diameter measurements between Stratus optical coherence tomography (OCT) and confocal scanning laser ophthalmoscopy (HRT-II). The mean difference is represented by the dotted line and the 95% confidence limits by the solid lines.

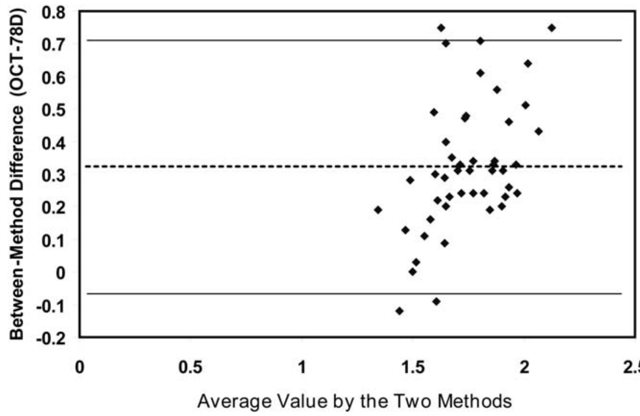

FIGURE 2. Differences in vertical disk diameter measurements between Stratus optical coherence tomography (OCT) and slit-lamp ophthalmoscopy with a 78 diopters lens. The mean difference is represented by the dotted line and the 95% confidence limits by the solid lines.

practice. In some reports, a correction factor or conversion formula were suggested, but those were based not on agreement but instead on a "best-fit" line, which does not allow appreciation of inter-method differences in individual measurements and thus clinical interchangeability.[15,26]

Jonas proposed that in routine practice, the clinician need not incorporate into his evaluation the exact numerical value of the disk size and various conversion formulae, but instead use a quick, crude estimate of whether the disk in question is average-sized (medium), smaller-than-average, or larger-than-average.[30]

In the present study, we analyzed the agreement between slit-lamp ophthalmoscopy, HRT-II, and Stratus OCT in estimating absolute disk size and in classification of the disk as small, average, or large. We hypothesized that a good agreement would be found at least in the crude classification of disk size, a finding that would allow a basis for clinical interchangeability of optic disk assessment by the three methods.

METHODS

SUBJECTS WERE ENROLLED AFTER INFORMED CONSENT WAS obtained using a consent form approved by the institutional review board (IRB) for Human Research of the New York Eye and Ear Infirmary that also approved the study protocol. All study procedures were in compliance with the IRB and Health Insurance Portability and Accountability Act (HIPAA) patient privacy requirements. Subjects were included regardless of whether they did or did not have glaucoma. Exclusion criteria were refractive error exceeding 5.0 diopters sphere and/or 3.0 diopters cylinder, any media abnormality, and atypical optic nerve head such as tilted disk. When both eyes were eligible, one eye was randomly chosen for inclusion in the study. Subjects underwent optic nerve head measurement after mydriasis with slit-lamp, HRT-II (software version 1.7.0), and Stratus OCT (software version 4.0.1) within a period of six months.

Vertical disk diameter was measured stereoscopically at the slit-lamp using a Volk 78-diopter lens by a single investigator, a glaucoma fellow (Y.B.), who was masked to the imaging results. A narrow beam was projected onto the disk. The length of the beam was adjusted to the diameter of the disk within (not including) the peripapillary scleral ring, and read on the scale of the slit-lamp in millimeters. The lens was held with the thumb and index finger while the fourth finger rested on the patient's cheek. This achieved both maintenance of a constant length between the lens and the patient's eye for all subjects and also stability of the lens, allowing more precise measurements.

HRT was performed after entering each patient's manifest refraction and average keratometry readings. Images were included if standard deviation was <40 μm and sensitivity levels were under 90%. Optic disk contour was marked within the scleral ring by an experienced operator (N.H.) while viewing a stereoscopic optic disk photograph. This investigator was masked to the clinical and OCT measurements. Disk area was read directly from the standard printout. The vertical disk diameter measurement was calculated using the interactive measurements option. A vertical line running from 12 o'clock to 6 o'clock was measured by outlining the superior and inferior margins among the inner border of the scleral ring.

Eyes were scanned with Stratus OCT after entering each patient's spherical equivalent refraction and axial length parameters. The Fast Optic Disk Scan Protocol was used. The disk margins were determined automatically by the software, without manual modification. Disk area and vertical disk size were read directly from the printout.

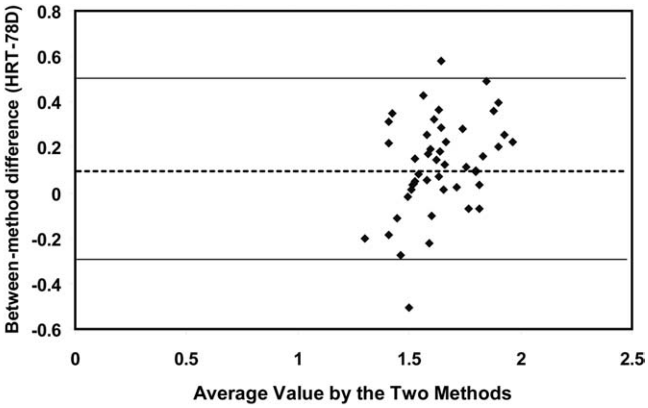

FIGURE 3. Differences in vertical disk diameter measurements between confocal scanning laser ophthalmoscopy (HRT-II) and slit-lamp ophthalmoscopy with a 78 diopters lens. The mean difference is represented by the dotted line and the 95% confidence limits by the solid lines.

TABLE 1. Agreement Between Each Pair of Methods in Classification of Optic Disk Size Into Small, Average, and Large

Pairs	Percentage of Agreement	Kappa (κ) Statistics	95% Confidence Interval
OCT and HRT disk diameter	60	.133	0–0.38
78D and OCT disk diameter	60	.193	0–0.45
78D and HRT disk diameter	60	.154	0–0.39
OCT and HRT disk area	67	.319	0.07–0.57
78D disk diameter and OCT disk area	56	.128	0–0.37
78D disk diameter and HRT disk area	56	.108	0–0.36

HRT = confocal scanning laser ophthalmoscopy; OCT = optical coherence tomography.

Average disk size was defined as mean ± standard deviation (of either diameter or area), with small and large sizes defined as less or greater than these values.

The agreement between each pair of methods in estimating the absolute value of vertical disk diameter was analyzed as proposed by Bland and Altman.[29] Graphically, the difference between each pair of measurements was plotted against their mean values. Numerically, the 95% limits of agreement (LoA) was calculated. This parameter indicates the range of difference between two measurement methods that the clinician can expect in 95% of cases, that is, in most patients, excluding atypical outliers.

Optic disks were classified as small, average, or large according to two criteria. Average size was first defined as mean ± 1 standard deviation, with small and large disks defined correspondingly outside this range. For the second criterion, optic disk sizes in the study cohort were divided into three equally-numbered tertiles; average size was defined as those sizes falling within the range of the middle tertile, and small and large disks correspondingly as those values in the other two tertiles. The agreement between each pair of methods in classifying optic disks as small, average or large was assessed with percentage agreement and κ statistics. Pair-wise agreement according to κ statistics is interpreted as follows: slight, 0.20 or less; fair, 0.21 to 0.40; moderate 0.41 to 0.60; substantial, 0.61 to 0.80; and excellent, 0.80 to 1.0.[31] We analyzed the agreement between each pair of methods in classification of disk size according to vertical disk diameter, and in addition the agreement in classification between ophthalmoscopically-measured vertical disk diameter and disk area measured with HRT and OCT.

TABLE 2. Agreement Between Each Pair of Methods in Classification of Optic Disk Size Into Small, Average, and Large

Pairs	Percentage of Agreement	Kappa (κ) Statistics	95% Confidence Interval
OCT and HRT disk diameter	50	.250	0.04–0.46
78D and OCT disk diameter	56	.344	0.14–0.55
78D and HRT disk diameter	48	.213	0.01–0.42
OCT and HRT disk area	58	.375	0.17–0.58
78D disk diameter and OCT disk area	44	.156	0–0.36
78D disk diameter and HRT disk area	56	.344	0.14–0.55

HRT = confocal scanning laser ophthalmoscopy; OCT = optical coherence tomography.

Small, average, and large disk size were defined as the lower, middle, and upper tertiles (of either diameter or area), respectively.

RESULTS

FORTY-EIGHT PATIENTS (24 MEN, 24 WOMEN), WITH A MEAN (±SD) age of 53.4 ± 14.3 years were enrolled. Vertical disk diameter was (mean ± SD) 1.58 ± 0.15, 1.70 ± 0.22, and 1.90 ± 0.24 mm with funduscopy, HRT, and OCT, respectively. Figures 1, 2, and 3 demonstrate the differences in vertical disk diameter between each pair of methods in a Bland-Altman plot of the pair difference against the mean values. Mean differences were 0.20 mm between OCT and HRT, 0.32 mm between OCT and slit-lamp funduscopy, and 0.12 mm between HRT and funduscopy. The wide range of differences between all three pairs graphically pictured in the figures is depicted by the 95% LoAs; these were −0.29 to 0.70 mm for OCT and HRT, −0.07 to 0.71 mm for OCT and slit-lamp funduscopy, and −0.29 to 0.53 mm for HRT and slit-lamp funduscopy.

Tables 1 and 2 show the agreement between each pair of methods in classification of the optic disk size as average, smaller than average, or larger than average. In Table 1, average disk size was defined as those values falling within the range of mean ± SD (of either diameter or area). In Table 2, the study population was divided to three equal tertiles, and average disk size was defined as those values within the middle tertile. Agreement was less than moderate in all comparisons.

DISCUSSION

DISK SIZE IS AN IMPORTANT PARAMETER WHEN DIFFERENTIATING normal from glaucomatous disks, because other parameters vary in direct relation to it. In healthy eyes, photographic studies showed that larger disks have a larger neuroretinal rim area, larger cup, and larger cup:disk ratio.[7–9] Similarly, confocal scanning laser ophthalmoscopy showed good correlation between disk area and both neuroretinal rim area and cup:disk area ratio.[10] When disk size was taken into account, HRT image analysis was more sensitive than expert clinical assessment of stereophotographs in distinguishing between normals and early glaucoma.[12] In another study, HRT was effective as subjective evaluation of stereophotographs in discriminating between glaucomatous and healthy optic disks.[13] Investigators in the scanning laser ophthalmoscopy ancillary study to the Ocular Hypertension Treatment Study suggested that in the diagnosis of glaucoma, optic disk size, in addition to race, must be considered.[6] Vernon and associates reported that in 918 eyes of 459 normal elderly patients, most disk topography parameters were significantly influenced by disk size.[11] Disk size has recently also been reported to be correlated to measurements of the thickness of the retinal nerve fiber layer by OCT[32] and laser scanning polarimetry.[33]

How can we best measure optic nerve head size for purposes of clinical decision making? When several methods are routinely used, clinicians must know whether they are interchangeable before they are used in diagnosis and follow-up or in research. Otherwise, investigators may reach different diagnostic conclusions regarding the same eyes only attributable to the use of different diagnostic techniques. Our results add to previously published evidence that suggests that measurements of disk size as determined by funduscopy, HRT, and OCT are not interchangeable.

The vertical disk diameter can be reliably measured at the slit lamp using contact or noncontact lenses and the length of the adjustable slit-lamp beam.[15,16,30] Lim and associates compared the values obtained with different noncontact lenses and HRT, providing magnification factors for the different lenses to correlate between the mean measurements.[15] However, individual differences between each pair of measurements with limits of agreement were not reported, and so the agreement between the methods and, consequently, their clinical interchangeability could not be determined.

We observed large mean bias and dispersal range between HRT and OCT employing automatic disk margin detection. Iliev and associates compared optic disk morphometric parameters with the Stratus OCT and HRT II in 49 eyes.[25] When the disk margin was determined automatically by OCT, the mean difference in disk area was 0.55 mm^2, and the 95% LoA 0.44 to 1.55 mm^2. When the margin was manually drawn, the mean difference was 0.16 mm^2, and the 95% LoA −0.44 to 0.76 mm^2. The authors noted that the automatic mode of OCT erroneously detected the disk margin in 53% of cases. However, both comparisons showed such a large dispersal of measurement differences that the authors concluded that optic disk morphometric parameters cannot be directly compared between OCT and HRT. A similar conclusion was reached by Hoffmann and associates, who compared several disk parameters between HRT II and Stratus OCT using automatic disk detection.[28] In their study, disk area differed by a mean of 0.18 mm^2, with 95% LoA of −0.76 to 0.39.

In another study, Schuman and associates compared optic disk measurements obtained with HRT I and OCT 2 or 3.[26] They reported a significant mean bias in disk area when automatic disk rim detection was used. HRT and OCT measurements were "highly statistically significantly correlated," however, agreement and LoA were not reported and so the clinical applicability of their findings is limited.[34]

A study comparing the estimation of vertical cup:disk ratio by ophthalmoscopy with a 66 diopters lens, stereophotographs, HRT, and a digital stereo optic disk camera (DISCAM, Marcher Enterprises, Hereford, United Kingdom) reported very large 95% LoA, that is, poor agreement between the different modalities;[35] 95% LoA were 0.61 between HRT and stereophotographs, 0.63 between HRT and ophthalmoscopy, and 0.43 between HRT and DISCAM. Others reported similar 95% LoA between these modalities for measurement of area or vertical cup:disk ratio.[27,36,37] Zangwill and associates found moderate to substantial agreement between three glaucoma experts evaluating vertical cup:disk ratio obtained by stereoscopic disk photos and HRT, with κ ranging from 0.57 to 0.72.[38]

When seeking similar measurements of disk size by different methods, optical effects such as the position of the condensing lens and refractive error must be considered. When an emmetropic eye is examined, the light rays emerging from the fundus are parallel, so the image size is independent of the position of the lens. In ametropia this is not so. We tried to minimize this optical effect by keeping the position of the lens constant as the examiner rested his hand on the subject's face rather than holding it in the air. Jonas reported that in the range of −5 diopters to +5 diopters, the same range used for inclusion in our study, ophthalmoscopic determination of disk diameter was independent of refractive error.[30] The HRT and OCT analyses in this study were performed according to the manufacturers' recommendations, supplying manifest refraction for both instruments and corneal curvature for HRT. It is plausible that the difference in proprietary method for accounting for axial length used by each instrument, in addition to the different basic differences in operating principles, partially accounts for the observed differences in disk size.

We hypothesized that, in contrast to the low intermethod agreement observed in absolute disk size measurement, there would be a better agreement in the crude classification of disks as small, average, or large. This would allow a common basis for comparing data between clinicians or in the follow-up of a single patient using the different methods. Our findings do not corroborate this hypothesis.

In this study, a single measurement of disk size was obtained by each modality by a single investigator. We assumed that a single measurement is sufficient and reliable based on extensive previous investigators' experiences and previous literature.[16,20–23] Although we believe that significant investigator-related bias is unlikely, this remains a possibility.

In conclusion, we found a large range of differences in estimating disk size with HRT, OCT, and funduscopy, despite previously reported good repeatability of all three methods. This precludes their interchangeable use in clinical practice or research, and does not allow simple conversion formulas to be proposed. In addition, there is poor agreement between these methods in classifying disks as small, average, or large. Until further technological adjustments are made, estimation of both absolute and relative disk size can only be defined separately for each measurement modality.

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