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Comparison of Spectral-Domain Optical Coherence Tomography and Heidelberg Retina Tomograph III Optic Nerve Head Parameters in Glaucoma

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Key Words
Spectral-domain optical coherence tomography · Heidelberg retina tomograph III · Optic nerve head · Glaucoma

Abstract
Background: To evaluate the agreement between the optic nerve head (ONH) measurements obtained by spectral-domain optical coherence tomography/scanning laser ophthalmoscope (SD-OCT/SLO) and the Heidelberg retinal tomograph III (HRT-III), and to compare the ONH measurements of both devices in different glaucoma types. ***Methods:*** In a prospective study, 30 patients with primary open-angle glaucoma (POAG) and 30 patients with pseudoexfoliation glaucoma (PXG) were enrolled. All patients underwent SD-OCT/SLO and HRT-III evaluation of the ONH during the same visit. Agreement between measurements of SD-OCT/SLO and HRT-III were evaluated by determination of intraclass correlation coeficients. In addition, mean ONH measurements obtained with both devices were compared between POAG and PXG patient groups. ***Results:*** Mean SD-OCT/SLO measurements were greater than those of HRT-III, except for mean and maximum cup depth. Intraclass correlation coefficient values for disc area, rim area, cup area, cup/disc area ratio, mean cup depth and maximum cup depth were 0.367, 0.213, 0.632, 0.681, 0.775 and 0.661, respectively. No significant differences were found between ONH parameters of POAG and PXG patients as measured with both devices ($p > 0.01$). ***Conclusion:*** ONH measurements with SD-OCT/SLO and HRT-III did not show clinically acceptable agreement in glaucoma patients. This precludes interchangeable use of these measurements in clinical practice. PXG and POAG patient groups displayed similar ONH measurements with both devices.

Introduction

Optic nerve head (ONH) evaluation is essential in the diagnosis and management of glaucoma. Morphological analysis of the ONH lies at the cornerstone of early glaucoma detection. Clinical assessment of the ONH can be subjective and fraught with high intraobserver and interobserver variability [1, 2]. With the emergence of newer optical imaging techniques, assessment of optic disc morphology has become more objective and quantitative even in the hands of nonexpert operators [3]. The most widely used devices for ONH assessment are optical coherence tomography (OCT) and the Heidelberg retina tomograph (HRT).

OCT is a noninvasive, noncontact, transpupillary imaging technique which provides in vivo, high-resolution,

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cross-sectional images to visualize and measure anatomical layers of the retina and ONH. It measures echo time delay and intensity of backscattered light from various retinal layers using an optical correlation technique known as Michelson low-coherence interferometry. In the new-generation spectral domain (SD) OCT/scanning laser ophthalmoscope (SLO), reflectance interference between the reference arm and retina at each A scan location is Fourier transformed to simultaneously acquire all points along the depth of the A scan without reference arm movement. As each A scan is acquired all at once, the acquisition rate is much higher as opposed to the time domain OCT rate. The fast acquisition rate allows for much faster scanning time, reducing motion artifacts and enabling denser patterns across the ONH when compared to Stratus OCT [4].

The HRT is a confocal scanning laser ophthalmoscope that acquires 3-dimensional topographic images of the optic disc and surrounding retina. The HRT was developed to provide objective and reproducible analysis of optic disc morphometric parameters [5, 6]. The new generation of the HRT-III (software version 3.0) uses an enlarged race-specific database improving the ability to detect glaucoma [7].

In clinical practice, some ophthalmologists rely on HRT measurements for assessing ONH and some on OCT measurements. We have been wondering whether ONH measurements of HRT and OCT machines are interchangeable and consistent. The purpose of this study was to evaluate the agreement of ONH measurements obtained by SD-OCT/SLO and HRT-III and to compare the ONH parameters with regard to glaucoma type.

Materials and Methods

Sixty eyes of 60 consecutive subjects (30 patients with primary open-angle glaucoma, POAG, and 30 patients with pseudoexfoliative glaucoma, PXG) were included in this study. The study was approved by our institutional review board and complied with the tenets of the Declaration of Helsinki. All subjects enrolled in this study provided informed consent. All subjects were 45 years of age or older, having a best-corrected visual acuity of ≥20/40 and a refractive error within ±6.0 dpt (spherical equivalent).

All subjects underwent a complete ophthalmic evaluation, including medical history, intraocular pressure measurement using Goldmann applanation tonometry, gonioscopy, manifest refraction, visual field testing and dilated biomicroscopy. The subjects also underwent SD-OCT/SLO and HRT-III ONH scanning within 1 week of the baseline examinations.

We grouped the eyes into the following 2 diagnostic groups: POAG and PXG. One eye of 60 subjects was randomly selected for inclusion in the study. Exclusion criteria were any other ocular comorbidity including high myopia, visually significant cataracts, pseudophakia and diabetic retinopathy that may interfere with the results. A history of any central nervous system disease that could influence ONH morphology also warranted exclusion.

All HRT scans were done with software version 3.0 (Heidelberg engineering GmbH, Dossenheim, Germany). The HRT scanned a continuous grid of 256 × 256 measuring points with an image field of 15° × 15° along the ONH region, and the operator was required to draw a contour line, along the disc margin. Based on the mean height along 6° of the contour line in the temporal inferior (350–356°) sector, the machine automatically calculated the reference plane that was located 50 μm posterior to the retinal surface in this area. Structures underneath the reference plane and within the contour line were defined as the disc cup. Structures above the reference plane and within the contour line were defined as the neuroretinal rim. Good image quality was defined as follows: acquisition sensitivity <80%, topography standard deviation <30 mm, minimal movement during the acquisition movie, no floaters over the disc and good imaging clarity and exposure. In all subjects the ONH border was drawn just inside the inner boundary of the scleral ring of Elschnig by a single experienced ophthalmologist. If determining the disc margin was impossible, the case was excluded. The following parameters were analyzed: optic disc area, cup area, cup/disc area ratio, rim area, mean cup depth, maximum cup depth.

The images of ONH were acquired with SD-OCT/SLO (OPKO/OTI, V2.26, Miami, Fla., USA) using the optic nerve topography scan mode by a single experienced technician. While scanning, the location of the ONH was observed on the SLO image to ensure proper positioning of the scan. The topography stack covers an area of 5.5 × 5.5 mm with a depth of 2 mm. The device automatically determines the disc margin as the end of the retinal pigment epithelium (RPE) and a straight red line connects the edge of the RPE. A parallel yellow line is constructed at a fixed offset of 150 μm anterior to the plane of the RPE reflection. Measurements below this line are defined as the cup and measurements above are considered the neuroretinal rim. Optic disc area, cup area, cup/disc area ratio, rim area, mean cup depth and maximum cup depth were acquired and used for the analysis. Only images with a focused SLO image of the ONH, with signal strength ≥7, were considered to be of acceptable quality.

Data were evaluated using the SPSS program (version 13.1). To assess agreement between the devices, intraclass correlation coefficients (ICC) were calculated. ICC were interpreted as follows: 0–0.2 indicates poor agreement; 0.3–0.4 indicates fair agreement, 0.5–0.6 indicates moderate agreement; 0.7–0.8 indicates good agreement, and >0.8 indicates almost perfect agreement. This study also compared ONH measurements between POAG and PXG groups by using the Mann-Whitney test; significance was set at $p < 0.01$.

Results

A total of 60 glaucoma patients (27 male, 33 female) were enrolled in the study. The mean age of patients was 65.6 ± 9.8 years. Demographic characteristics of the study population are summarized in table 1.

Table 1. Patient demographics and mean values ± SD

	POAG (n = 30)	PXG (n = 30)	p value
Age, years	66.8 ± 13.2	64.2 ± 15.4	0.92
Gender (male:female), n	13:17	14:16	0.45
Refractive error, dpt	–1.3 ± 1.6	–1.5 ± 1.4	0.24

n = Number of eyes; SD= standard deviation. p values obtained by the χ^2 test.

Table 2. Mean ONH results ± SD from HRT-III and SD-OCT/SLO and ICC (n = 60)

ONH parameter	HRT	OCT	ICC	p value
Disc area, mm^2	1.99 ± 0.41	3.42 ± 0.82	0.367	0.006
Cup area, mm^2	0.73 ± 0.48	1.78 ± 1.09	0.632	<0.0001
Rim area, mm^2	1.25 ± 0.34	1.61 ± 0.95	0.213	0.078
Cup/disc area ratio	0.35 ± 0.17	0.51 ± 0.24	0.681	<0.0001
Mean cup depth, mm	0.27 ± 0.11	0.21 ± 0.11	0.775	<0.0001
Max. cup depth, mm	0.67 ± 0.22	0.50 ± 0.21	0.661	<0.0001

SD = Standard deviation; max. = maximum.

Table 3. ICC between SD-OCT/SLO and HRT-III separately in the two diagnostic groups and comparison of ONH measurements between clinical diagnostic groups

ONH parameter	POAG (n = 30)			PXG (n = 30)			p value 1	p value 2
	SD-OCT/SLO	HRT-III	ICC	SD-OCT/SLO	HRT-III	ICC		
Disc area, mm^2	3.70 ± 0.82	2.09 ± 0.43	0.432 (0.018)	3.12 ± 0.74	1.88 ± 0.37	0.203 (0.177)	0.02	0.17
Cup area, mm^2	1.97 ± 1.14	0.83 ± 0.56	0.705 (0.000)	1.57 ± 1.03	0.63 ± 0.36	0.515 (0.006)	0.18	0.29
Rim area, mm^2	1.64 ± 1.02	1.26 ± 0.33	0.300 (0.077)	1.58 ± 0.91	1.24 ± 0.36	0.103 (0.320)	0.93	0.93
Cup/disc area ratio	0.53 ± 0.24	0.37 ± 0.19	0.801 (0.000)	0.49 ± 0.25	0.32 ± 0.15	0.538 (0.004)	0.44	0.45
Mean cup depth, mm	0.25 ± 0.12	0.29 ± 0.12	0.823 (0.000)	0.17 ± 0.17	0.24 ± 0.19	0.616 (0.001)	0.02	0.22
Maximum cup depth, mm	0.58 ± 0.22	0.70 ± 0.22	0.756 (0.000)	0.42 ± 0.20	0.64 ± 0.23	0.558 (0.003)	0.04	0.50

n = Number of eyes. Figures in parentheses indicate within-group p values. p value 1: comparison of ONH measurements between POAG and PXG groups obtained by SD-OCT/SLO (Mann-Whitney test). p value 2: comparison of ONH measurements between POAG and PXG groups obtained by HRT-III (Mann-Whitney test).

Mean ONH results from the SD-OCT/SLO and HRT-III measurements are presented in table 2. ICC showed fair agreement for disc area, poor agreement for rim area, moderate agreements for cup area, cup/disc area ratio and maximum cup depth, and good agreement for mean cup depth. Overall, the SD-OCT/SLO results tended to be greater than the HRT-III results except for mean and maximum cup depth.

The mean ONH results from SD-OCT/SLO and HRT-III and ICC values separately in POAG patients and PXG patients are displayed in table 3. ICC showed fair to poor agreement for disc and rim area and moderate to good agreement for other ONH parameters. Comparison of HRT-III measurements between the two diagnosis groups showed that ONH parameters were not different between POAG and PXG groups ($p > 0.01$ for all; table 3).

Discussion

This study evaluated the agreement between measurements obtained by HRT-III and SD-OCT/SLO in glaucoma patients and also compared the ONH measurements of both devices with regard to glaucoma type. A number of studies have been conducted to evaluate the role of time domain OCT compared with the previous versions of HRT in the detection of glaucoma [8, 9]. The fast acquisition rate of SD-OCT allows for much faster scanning time, and thus enables denser patterns across the ONH with improved axial resolution when compared to time domain Stratus OCT [4]. The SD-OCT has been shown to obtain accurate and reproducible measurements in the diagnosis and management of glaucoma [10].

Previous histological studies have measured the optic disc area to range between 2.48 and 2.75 mm^2 [11–13]. However, the ONH size as measured with the SD-OCT/

SLO, is larger than the histological ONH area measurement, and the ONH size as measured with the HRT-III is smaller than the histological ONH area measurement than that obtained by the histological studies. Previous studies have found a moderate to high correlation between HRT ONH results and computer-assisted planimetry [14–17], whereas Barkana et al. [9] have reported that measurements of optic disc size with HRT-II, Stratus OCT and funduscopy were not interchangeable.

The method of scanning and analysis of the ONH are substantially different between HRT and OCT. This, along with different reference plane-to-cup offset settings and evaluation protocols inbuilt in the respective machines causes a difference in the measured values of the various parameters evaluated by the two modalities. It was therefore important to evaluate the relationship between measurements obtained with both devices.

In this study, SD-OCT/SLO results tended to be larger than the HRT-III results, except for mean and maximum cup depth. Overall, ICC values showed fair agreement for disc area, poor agreement for rim area, moderate agreements for cup area, cup/disc area ratio and maximum cup depth, and good agreement only for mean cup depth. None of the parameters displayed near perfect or perfect clinical agreement (i.e. ICC values above 0.8). When we looked for agreement between devices separately in the two diagnosis groups, ICC showed fair to poor agreement for disc and rim area and moderate to good agreement for other cup-related ONH parameters. Again, none of the ONH parameters in POAG and PXG diagnosis groups displayed strong or perfect clinical agreement between the two devices. Thus, measurements of HRT-III and SD-OCT/SLO do not seem to be clinically interchangeable.

In a similar study by Schuman et al. [18], the authors found that disc area, cup/disc area ratio and cup area were greater with OCT compared to HRT, while the reverse was found for the rim volume. While it is difficult to compare our results with those of Schuman et al. because of different population characteristics, cup-related parameters displayed higher agreement between HRT-III and SD-OCT/SLO devices in both studies.

Another relevant study by Naithani et al. [8] reported that there were no significant differences in the disc area as measured by the HRT-II and OCT-3. On the other hand, similar to ours and the study of Schuman et al. [18], they found that the cup area and related parameters were measured to be larger by the OCT than by the HRT [8]. Schuman et al. [18] partly attributed this increase in cup area and related parameters to the significantly larger disc size measured by the OCT.

The discrepancies between HRT and SD-OCT/SLO measurements possibly rely on the fact that HRT-derived disc size depends on drawing a contour line, while SD-OCT is operator independent in this respect. The OCT machine automatically determines the edge of the ONH as the end of the RPE/choriocapillaris layer. A straight line connects the edges of the RPE/choriocapillaris, and a parallel line is constructed 150 μm anteriorly. Structures below this line are defined as the disc cup and above this line as the neuroretinal rim [18]. On the other hand, the HRT machine automatically calculates a reference plane that is located 50 μm posterior to the retinal surface, based on the mean height along 6° of the contour line in the temporal inferior sector. Structures underneath the reference plane and within the contour line are defined as the disc cup. Structures above the reference plane and within the contour line are defined as the neuroretinal rim.

The reason for the difference in the measurements between the two devices may be the different definition used for locating the plane separating the neuroretinal rim and the cup. It may be that the plane used for this purpose by OCT tended to be located more anteriorly than the HRT; therefore, the cup/disc area ratio, disc area and cup area were larger by OCT, while the OCT-measured mean and maximum cup depth was smaller.

In this study we also attempted to compare HRT-III and SD-OCT/SLO parameters in patients with POAG and PXG. A comparison between common parameters acquired by SD-OCT and HRT-III has, to the best of our knowledge, not been conducted in the literature between POAG patients and PXG patients. Iester et al. [19] compared 132 high-tension glaucoma patients with 50 normal-tension glaucoma patients and found no significant difference in any of the HRT parameters between the two groups. In our study ONH parameters as measured with the HRT-III were smaller in PXG patients than in POAG patients; however, these minor differences did not reach statistical significance.

When we compared SD-OCT/SLO parameters between POAG and PXG groups, we again found that ONH parameters in PXG patients were smaller than those in POAG patients; however, none of these differences were statistically significant. These results are in agreement with previous literature. The mean disc area has been reported to be smaller in eyes with exfoliation syndrome, with or without glaucoma [20, 21]. In addition, Tezel and Tezel [22] have reported that cupping in PXG tends to be diffuse compared to POAG. This subject needs to be evaluated further in larger study populations.

In conclusion, SD-OCT/SLO and HRT-III ONH measurements do not show strong and acceptable clinical agreement in glaucoma patients. Since the SD-OCT/SLO results tend to be greater than those of the HRT-III, this precludes interchangeable use of these measurements in clinical practice. Results of this study also suggest that PXG and POAG groups displayed similar ONH paremeters with both devices.

Disclosure Statement

The authors have no proprietary or financial interest in any materials discussed in this article.

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