

Comparison of Optic Nerve Head Parameters Measured by Kowa Three Dimensional Non-Mydriatic Retinal Camera and Heidelberg Retinal Tomograph III in Healthy Subjects

Kowa Üç Boyutlu Non-Midriyatik Retinal Kamera ve Heidelberg Retina Tomografisi III ile Ölçülen Optik Sinir Başı Parametrelerinin Sağlıklı Kişilerde Karşılaştırması

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ABSTRACT

Purpose: To compare the optic nerve head (ONH) parameters obtained by KOWA three dimensional (3D) non-mydriatic stereoscopic retinal camera (NMRC) and Heidelberg retinal tomograph III (HRT) in healthy subjects.

Materials and methods: In this study, 72 eyes of 36 healthy subjects were enrolled. Kowa 3D NMRC and HRT III examinations were performed to each subject on the same day. Nine ONH parameters, including vertical cup disc ratio, cup area, disc area, rim area, height variation contour, cup volume, rim volume, maximum cup depth, and mean cup depth values of both devices were compared and correlated.

Results: Kowa 3D NMRC and HRT revealed similar values for vertical cup disc ratio, cup volume, and rim volume ($p>0.05$). However Kowa 3D NMRC significantly overestimated the HRT determined cup area, disc area, height variation contour, and rim area ($p<0.001$). Kowa 3D NMRC significantly underestimated the HRT determined mean cup depth and maximum cup depth ($p<0.001$). A statistically significant, high degree correlation was found between the two devices for the vertical cup disc ratio, cup area, disc area, cup volume, maximum cup depth, and mean cup depth ($r=0.66-0.83$, $p<0.001$). A statistically significant but low degree correlation was found regarding height variation contour ($r=0.29$, $p=0.01$). There was no significant correlation in the measurement of rim volume and rim area ($p>0.05$).

Conclusion: Most of ONH parameters including vertical cup disc ratio are similar when measured by Kowa 3D NMRC and HRT III. Kowa 3D NMRC is a potential tool for monitoring ONH parameters.

Keywords: Heidelberg retina tomography III, KOWA non-mydriatic retinal camera, optic nerve head.

ÖZ

Amaç: Kowa üç boyutlu (3D) non-midriyatik retinal kamera (NMRK) ve Heidelberg retinal tomografi III (HRT) ile elde edilen optik sinir başı (OSB) parametrelerinin sağlıklı kişilerde karşılaştırılması.

Gereç ve yöntemler: Bu çalışmaya 36 sağlıklı bireyin 72 gözü alındı. Kowa 3D NMRK ve HRT III ölçümleri her kişiye aynı günde yapıldı. Her iki cihazın vertikal çukurluk disk oranı, çukurluk alanı, disk alanı, rim alanı, yükseklik değişkenlik kontürü, çukurluk hacmi, rim hacmi, maksimum çukurluk derinliği ve ortalama çukurluk derinliği değerlerini içeren 9 OSB parametresi kıyaslandı ve korelasyonlarına bakıldı.

Bulgular: Kowa 3D NMRK ve HRT vertikal çukurluk disk oranı, çukurluk hacmi ve rim hacmi için benzer değerler bulundu ($p>0.05$). Bununla birlikte HRT tarafından belirlenen çukurluk alanı, disk alanı, yükseklik değişkenlik kontürü ve rim alanı Kowa 3D NMRK ile daha yüksek ölçüldü. Heidelberg retina tomografisi ile belirlenen ortalama çukurluk derinliği ve maksimum çukurluk derinliği Kowa 3D NMRK ile daha düşük saptandı. İki cihaz arasında vertikal çukurluk disk oranı, çukurluk alanı, disk alanı, çukurluk hacmi, maksimum çukurluk derinliği ve ortalama çukurluk derinliği için istatistiksel olarak anlamlı, yüksek seviyeli korelasyon bulundu ($r=0.66-0.83$, $p<0.001$). Yükseklik değişkenlik kontürü ile ilgili istatistiksel olarak anlamlı, düşük seviyeli korelasyon bulundu ($r=0.29$, $p=0.01$). Rim hacmi ve rim alanı ölçümlerinde anlamlı korelasyon gözlenmedi ($p>0.05$).

Sonuç: Vertikal çukurluk disk oranını da içeren çoğu OSB parametresi Kowa 3D NMRK ve HRT III ile ölçüldüğünde benzerdir. Kowa 3D NMRK, OSB parametrelerinin monitörizasyonunda potansiyel bir cihazdır.

Anahtar kelimeler: Heidelberg retina tomografisi III, Kowa non midriyatik retinal kamera, optik sinir başı.

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INTRODUCTION

Glaucoma is a progressive optic neuropathy in which there is loss of retinal ganglion cells and corresponding nerve fiber layer.^{1,2} Glaucoma is the second most common cause of blindness worldwide.³ Early detection and prevention of glaucoma is important because the injury is irreversible.⁴ Structural changes in the optic nerve head (ONH), including thinning of the neuronal rim, enlargement of the ONH excavation, rim notch and retinal nerve fiber layer changes obtained by optical coherence tomography (OCT) occur before any detectable visual loss or visual field defects.⁵⁻⁷ Structural changes in the ONH are therefore considered as early markers of glaucoma.⁸ Morphometric ONH parameters like vertical cup disc ratio, cup and rim volume, and mean or maximum cup depth are important for detection of glaucoma.

Traditionally, evaluation of ONH morphology includes clinical examination of the disc by ophthalmoscopic examination and color fundus photographs,^{9,10} which has disadvantages such as high inter-observer variability and low reproducibility.⁶ The use of advanced equipment makes a detailed assessment of ONH morphology. For the last two decades, a confocal scanning laser ophthalmoscope, Heidelberg retina tomograph (HRT; Heidelberg Engineering GmbH, Heidelberg, Germany) is one of the most widely used device for imaging ONH damage and morphology,^{11,12} and could be used as part of a glaucoma screening.¹³ One of the limitations of the HRT is that all diagnostic analyses depend on a manually drawn contour lines to identify correct defining of the optic disc border which necessitates for a trained operator, and leads to inter-observer and intra-observer variability.¹⁴⁻¹⁶

With the advent of new imaging techniques, assessment of ONH morphology has become more objective and quantitative. Among these new methods, Kowa three dimensional (3D) non-mydratic retinal camera (NMRC) (Kowa, Tokyo, Japan) provides an objective, noninvasive, and noncontact imaging technique that does not require mydriasis during recording of the ONH.^{6,8,17} This retinal camera is able to take two photographs simultaneously at one shot and can display the quantitative results.^{17,18} The 3D analysis provides a significant advantage in terms of evaluating the depth of the optic cup and neuro retinal rim, and is expected to decrease inter-observer variability and increase reproducibility compared with standard ONH photographs.⁶ Thus a highly reproducible and real stereoscopic photo is acquired.¹⁸

The purpose of the present study was to compare and correlate the identical ONH parameters measured with the HRT III and Kowa 3D NMRC.

MATERIALS AND METHODS

Medical records of seventy-two eyes of 36 healthy subjects were enrolled retrospectively in this study. The study was conducted at Gulhane Training and Research Hospital in accordance with the tenets of the Helsinki Declaration, and approval of the institutional ethics review board was obtained. All patients were informed about the aim and procedure of the study and gave their written informed consent.

All subjects underwent complete ophthalmic examination including visual acuity, intra ocular pressure, slit lamp microscopy, and non-dilated funduscopy. Inclusion criteria were; uncorrected visual acuity $\geq 20/20$ according to Snellen chart, intra ocular pressure lower than 21 mmHg, and normal-appearing ONH. Exclusion criteria were; presence of anterior or posterior segment pathology, systemic diseases (hypertension, diabetes mellitus), hyperopia-myopia >3 dpt or astigmatisms >1 dpt, and history of intraocular surgery.

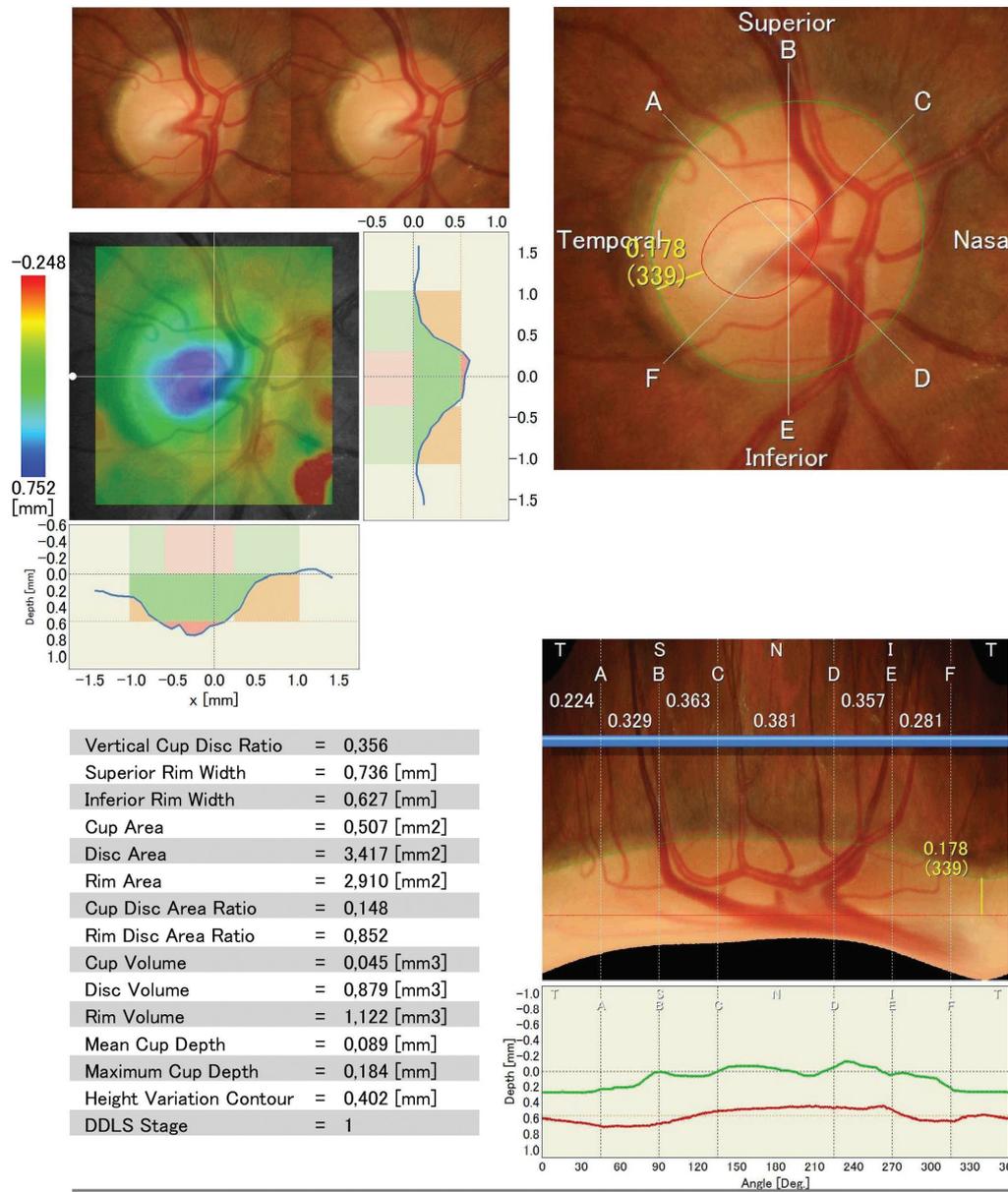
Stereometric optic disc photographs and HRT examinations were taken by the same examiner at the same visit for each subject. Nine stereometric ONH parameters, including vertical-linear cup disc ratio, cup area, disc area, rim area, height variation contour, cup volume, rim volume, maximum cup depth, and mean cup depth were obtained using both HRT and Kowa 3D NMRC. ONH images were captured from a non-dilated pupil.

Kowa 3D NMRC (Nonmyd WX; Kowa Optimed Inc.), which is the stereoscopic fundus camera were used to take nonmydratic fundus stereographs and both right and left parallax images simultaneously through a single optical system handling light paths in two directions.¹⁷ Kowa 3D NMRC can display a depth map, which shows the depth of the disc separated by color, a 3D display of the optic disc, diagnostic parameters (Figure 1). In accordance with the algorithm provided by Kowa Optimed Inc., all measurements were conducted after correcting for magnification by refractive error, axial length, and corneal curvature. After photographs were taken, two images with binocular parallax were obtained then, two images were automatically superimposed on the monitor by built-in software, and a stereoscopic 3D image was generated using polarized 3D glasses. The examiner stereoscopically observed the outline of the optic disc displayed on a monitor. The edge of disc is plotted using a computer mouse, and the cup is selected in a similar way, to determine their extent. After that, all other analysis was automatically performed by built-in software.

Images of HRT III obtained in this study were carefully reviewed for both the imaging score and overall quality score. These image-quality checks were generated by the HRT III software. Only high-quality images with an acquisition



ID: _____ Report: 06/26/2014 11:25:31
 Name: _____ Diagnosis: _____ OD
 Photo: _____



Stereo Retinal Camera - Optic Disc Analysis - (Kowa Company, LTD.)

Software: K9L-AP57B Ver.5.4.1.0

Figure 1.

sensitivity of more than 90% and a standard deviation of less than 40 were considered acceptable and used for the analyses. After scanning, an experienced investigator positioned manually six or more points in order to define the contour line around the ONH edge. The optic disc edges were defined as the inner border of the peri-papillary scleral ring (Elschnig ring).⁶ The optic cup was defined on the basis of contour and the course of the vessels on the disc.⁶ After the contour line was drawn, the software automatically

calculated all of the optic disc measurements (Figure 2). The reference plane was defined at 50 mm posterior to the mean retinal height between 350° and 356° along the contour line. The area above the reference plane was defined as the rim and the region below as the cup.

The SPSS 17.0 software package was used in data analysis. For the descriptive statistics, discontinuous variables were shown as numbers and percentages (%); continuous variables

Heidelberg Retina Tomograph
Initial Report

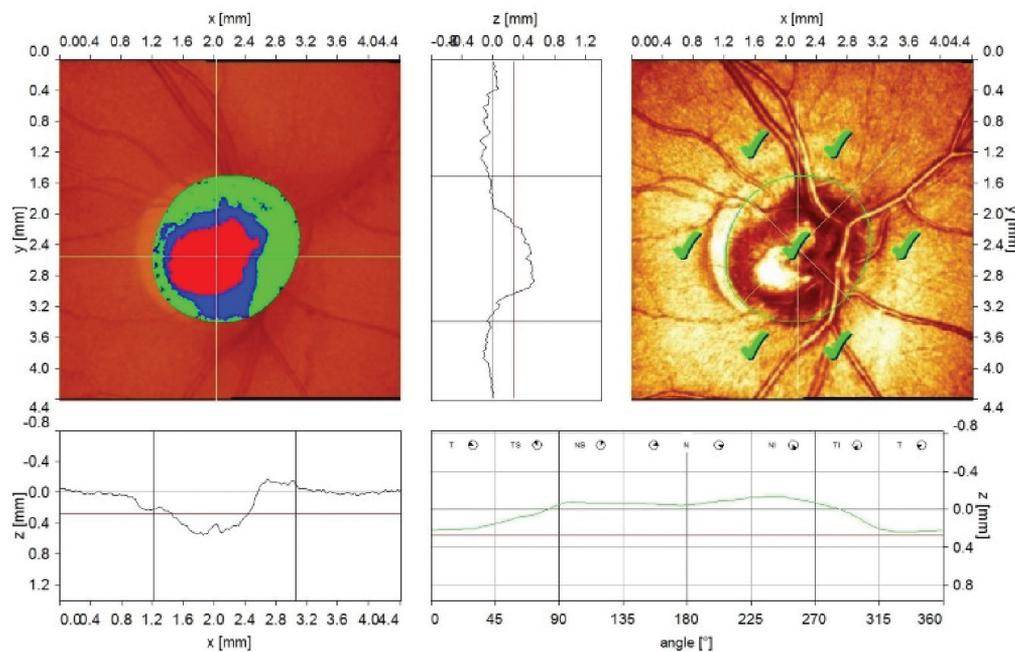


Patient:

Examination:

Scan: Focus: -1.00 dpt Depth: 2.50 mm

OD



Stereometric Analysis ONH	Normal Range	
Disc Area	2.83 mm ²	1.63 - 2.43
Cup Area	0.80 mm ²	0.11 - 0.68
Rim Area	2.02 mm ²	1.31 - 1.96
Cup Volume	0.12 mm ³	-0.01 - 0.18
Rim Volume	0.52 mm ³	0.30 - 0.61
Cup/Disc Area Ratio	0.28	0.07 - 0.30
Linear Cup/Disc Ratio	0.53	0.27 - 0.55
Mean Cup Depth	0.23 mm	0.10 - 0.27
Maximum Cup Depth	0.51 mm	0.32 - 0.76
Cup Shape Measure	-0.07	-0.28 - -0.15
Height Variation Contour	0.38 mm	0.31 - 0.49
Mean RNFL Thickness	0.25 mm	0.20 - 0.32
RNFL Cross Sectional Area	1.48 mm ²	0.99 - 1.66
Reference Height	275 μm	
Topography Std Dev.	12 μm	
FSM	0.77	
RB	1.10	

Moorfields Classification: Within normal limits (*)

(*) Moorfields regression classification (Ophthalmology 1998;105:1557-1563). Classification based on statistics. Diagnosis is physician's responsibility.

Comments:

Date: 22.Eki.2014 Signature:

Software Version: 3.2/1717

Figure 2.

were shown as mean±standard deviation. Normality of the data was evaluated with the Kolmogorov Smirnov test. For the comparison of same measurements of both devices; paired sample t-test was used for continuous variables that distributed normally and the Wilcoxon test was used for continuous variables that did not distribute normally. Pearson correlation test was used for correlations. A P value of 0.05 or less was considered significant.

RESULTS

A total of 72 eyes of 36 participants were evaluated. The mean age was 39.47±10.94 (21–67) years old. Ten (27.8%) were female, and 26 (72.2%) were male.

Kowa 3D NMRC and HRT III determined similar values for vertical cup disc ratio (p=0.17), cup volume (p=0.12), and rim volume (p=0.71). However Kowa 3D NMRC

significantly overestimated the HRT determined cup area, disc area, height variation contour, and rim area ($p < 0.001$ for all). Kowa 3D NMRC significantly underestimated the HRT determined mean cup depth and maximum cup depth ($p < 0.001$ for all) (Table 1).

A high degree and significant correlation was found between the two devices for the vertical cup disc ratio ($r = 0.66$, $p < 0.001$), cup area ($r = 0.83$, $p < 0.001$), disc area ($r = 0.63$, $p < 0.001$), cup volume ($r = 0.78$, $p < 0.001$), maximum cup depth ($r = 0.77$, $p < 0.001$), and mean cup depth ($r = 0.78$, $p < 0.001$). A significant but low degree correlation was found regarding height variation contour ($r = 0.29$, $p = 0.01$). There was no significant correlation in the measurement of rim volume ($r = 0.05$, $p = 0.67$) and rim area ($r = 0.23$, $p = 0.06$) (Table 2).

DISCUSSION

This study evaluated the comparison and correlation of ONH parameters obtained by Kowa 3D NMRC and HRT III in a cohort of healthy subjects. Pearson's correlation tests revealed significant high correlation between the two devices in evaluating most of the identical parameters including vertical cup disc ratio, cup area, disc area, height variation contour, cup volume, maximum cup depth, and mean cup depth. Only in rim area and rim volume, results showed some discrepancy compared with other parameters.

In comparisons, Kowa 3D NMRC and HRT III revealed similar values when compared for vertical cup disc ratio, cup volume, and rim volume. Kowa 3D NMRC significantly overestimated the HRT III determined cup area, disc area, rim area, and height variation contour. Kowa 3D NMRC significantly underestimated the HRT III determined mean cup depth and maximum cup depth.

These differences may have been caused by analytical differences between Kowa 3D NMRC and the HRT III and the different definitions of the neuroretinal rim and cup.¹⁹ First, a contour line of the optic disc is selected in both instruments.¹⁷ In HRT III, a reference plane 50 μm below the average contour line is automatically determined, and then, the cup is determined as a region below the reference plane, the area above the reference plane along the contour line was defined as the rim.^{17,19} Although the level of the reference plane should not affect the measurement of the disc area, its position has a direct impact on the determination of the rim and cup areas.¹⁹ In Kowa 3D NMRC, the outer border of the cup is also selected by the examiner, and then the cup size is determined.¹⁷ Therefore, the difference in the measurement principle in both instruments may cause slight differences.¹⁷ The determination of the border of the disc by analysis using HRT is difficult, and the presence of the central vessel of the retina is automatically taken to be the border of the cup, thus, HRT might have limitations in its

Table 1. Comparison of Kowa NMRC and HRT III parameters of the optic nerve head.

Optic disc Parameters	Mean	SD	Minimum	Maximum	P value
NMRC Vertical Cup Disc Ratio	0,43	0,09	0,24	0,59	0,17**
HRT Vertical Cup Disc Ratio	0,41	0,16	0,11	0,66	
NMRC Cup Area	0,50	0,26	0,12	1,11	<0,001*
HRT Cup Area	0,42	0,31	0,00	1,10	
NMRC Disc Area	2,60	0,46	1,72	3,69	<0,001*
HRT Disc Area	2,08	0,42	1,06	3,01	
NMRC Rim Area	2,10	0,33	1,51	3,08	<0,001*
HRT Rim Area	1,66	0,33	0,91	2,53	
NMRC Height Variation Contour	0,47	0,16	0,17	0,85	<0,001**
HRT Height Variation Contour	0,36	0,07	0,21	0,54	
NMRC Cup Volume	0,08	0,06	0,00	0,25	0,12
HRT Cup Volume	0,09	0,09	0,00	0,37	
NMRC Rim Volume	0,43	0,21	0,09	1,19	0,71*
HRT Rim Volume	0,42	0,13	0,17	0,72	
NMRC Maximum Cup Depth	0,35	0,15	0,04	0,67	<0,001**
HRT Maximum Cup Depth	0,54	0,22	0,09	0,97	
NMRC Mean Cup Depth	0,14	0,06	0,00	0,25	<0,001*
HRT Mean Cup Depth	0,18	0,08	0,03	0,34	

*Wilcoxon test **Paired sample t test

Table 2. Correlations of Kowa NMRC and HRT III parameters of the optic nerve head.

Optic disc parameters	Correlation coefficient (r)	P
NMRC Vertical Cup Disc Ratio	0,66	<0,001
HRT Vertical Cup Disc Ratio		
NMRC Cup Area	0,83	<0,001
HRT Cup Area		
NMRC Disc Area	0,63	<0,001
HRT Disc Area		
NMRC Rim Area	0,23	0,06
HRT Rim Area		
NMRC Height Variation Contour	0,29	0,01
HRT Height Variation Contour		
NMRC Cup Volume	0,78	<0,001
HRT Cup Volume		
NMRC Rim Volume	0,05	0,67
HRT Rim Volume		
NMRC Maximum Cup Depth	0,77	<0,001
HRT Maximum Cup Depth		
NMRC Mean Cup Depth	0,78	<0,001
HRT Mean Cup Depth		
Pearson correlation test		

capacity for determining disc and cup borders.¹⁷ In our study both Kowa 3D NMRC and HRT methods used a manual contour line alignment, which may be a major source of slight measurement variability, even though simultaneous stereoscopic viewing of the ONH photographs is known to facilitate the drawing of the contour line.

Januschowski et al.¹⁶ compared the topographic parameters of the optic disc obtained by Kowa 3D NMRC and the HRT III. The mean differences did not exceed the known interobserver or intraobserver variability.¹⁶ Similar to our study, mean differences were within a tolerable range, and there was a high or moderate degree of consistency with the cup area, cup disc ratio, and maximum cup depth.¹⁶ Likewise, Mariacher et al.¹⁸ assessed ONH parameters with HRT III and Kowa 3D NMRC and found a good agreement between those two devices. In their study, Kowa 3D NMRC exhibited the tendency to measure larger cup disc ratio values than HRT in the group with cup disc ratio < 0.5 and lower cup disc ratio values in the group with cup disc ratio ≥ 0.5 .¹⁸

HRT is an established tool for imaging and quantifying morphometric ONH parameters in patients with glaucoma or suspected glaucoma.^{18,19} This system has been used to

collect a huge amount of data on normal and glaucomatous disc topography.¹⁹ With good-quality HRT images, the 80% sensitivity for detectable rim area change requires four examinations per year, reducing the number of examinations to two per year reduces the sensitivity to 60% with simultaneous 20–30% false positive rate.¹⁸ On the other hand stereographic photography is an accepted tool for optic disc assessment in glaucoma patients but sensitivity and specificity for detecting progression of stereometric ONH parameters with ONH photography were analyzed in previous studies and seem to be limited, the best correlating ONH parameter is the cup disc rate.¹⁸

Examination of the ONH has disadvantages such as high interobserver variability and low reproducibility.⁶ The high inconsistency of disc parameters is attributed mainly to determination of the border between the rim and the cup.¹⁷ Kowa 3D NMRC provides an objective recording of the ONH, the optic disc can be visualized on a 3D display, which provides a significant advantage in terms of evaluating the depth, the cup and the neuroretinal rim.⁶ Kowa 3D NMRC is a twelve megapixel single lens reflex camera with three modes: normal, small pupil, and stereographic. In the stereographic mode, the picture is taken in the range of 34 degrees, and a 3D image can be captured in a single shot without changing the position of the camera. The 3D images can be visualized on a monitor with a 3D glasses and both automatic and manual settings of optic nerve and cup boundaries are possible. Vertical cup disc ratio measured by Kowa 3D NMRC showed good predictability for the diagnosis of glaucoma.⁶ O'Connor et al.²⁰ reported that the diagnostic accuracy of the ONH analysis was considerably higher in 3D optic disc photography than in 2D photography. The stereoscopic view is expected to decrease interobserver variability and increase reproducibility compared with standard ONH photographs.⁶ Asakawa et al.¹⁷ reported good intraexaminer reproducibility for Kowa 3D NMRC. However, the reproducibility of the volume parameters was relatively low, therefore, it is considered that the diagnostic parameters that depend on the longitudinal axis have relatively poor reproducibility, not only in Kowa 3D NMRC, but also in various other measuring instruments of the ONH.¹⁷ The stereoscopic fundus images obtained by Kowa 3D NMRC allow an additional advantages in evaluation of the optic disc regarding pallor, bleeding, and general appearance and can therefore serve as an additional assessment tool for ONH vitality.

This study has some limitations that warrant further investigation. First, glaucomatous patients were not included to the study. Other limitations of the study are the manual contour line alignment, the retrospective nature, and the relatively small sample sizes.

In conclusion, most ONH parameters including vertical cup disc ratio measured by Kowa 3D NMRC are similar with those obtained by HRT III because of statistically significant similarities in comparisons and correlations of the mean values in healthy eyes. Although a high correlation was found between Kowa 3D NMRC and HRT III ONH analysis results, further studies are needed to clarify test and retest variability. Kowa 3D NMRC is a potential tool for monitoring ONH parameters quantitatively and qualitatively, not only as an adjunct or alternative to the HRT. The combination of non-mydriatic fundus photography and optic disc analysis seems to be a very attractive and time-saving method.

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