SHORT-TERM INTRA-INDIVIDUAL VARIABILITY IN HEIDELBERG RETINA TOMOGRAPH II

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SUMMARY

We determined the short-term intra-individual variability for each parameter of the Heidelberg Retina Tomograph II (HRT II). Therefore we examined prospectively 20 healthy volunteers 3 times within 2 weeks. The variability was expressed as the coefficient of variation for each parameter. The short-term intra-individual variability in normal subjects was ≤ 12% in all but 3 parameters. Rim Area was the least variable parameter(2±1%). Cup Volume had the highest variability(25±38%).

SAMENVATTING

We hebben de korte termijn intra-individuele variabiliteit onderzocht van elke parameter van de Heidelberg Retina Tomograph II (HRT II). Hiervoor hebben we,op prospectieve wijze, 20 gezonde vrijwilligers 3 maal onderzocht in een tijdspanne van 2 weken. De variabiliteit hebben we uitgedrukt in de variatiecoëfficiënt van elke parameter. De korte termijn intra-individuele variabiliteit was ⩽ 12% voor alle parameters, behalve 3. Rim area was de minst variabele parameter(2±1%). Cup volume vertoonde de grootste variabiliteit(25±38%).

RÉSUMÉ

Nous avons mesuré la variabilité intra-individuelle à court terme de chaque paramètre du Heidelberg Retina Tomograph II (HRT II). Pour cela 20 volontaires sains ont été examinés de manière prospective 3 fois sur une période de 2 semaines. Nous avons exprimé la variabilité par le coefficient de variation de chaque paramètre. La variabilité intra-individuelle à court terme était ⩽ 12% pour tous les paramètres, sauf 3. Rim area montrait la variabilité la plus basse (2±1%). Cup volume était le paramètre le plus variable (25±38%).

KEY-WORDS

HRT II- variability - coefficient of variation - reproducibility

MOTS-CLÉS

HRT II- variabilité - coefficient de variation - reproductibilité

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INTRODUCTION

In glaucoma optic disc changes usually precede visual field defects(14). A change in the appearance of the optic nerve head is an important objective sign for diagnosing and managing glaucoma.

The optic nerve head can be evaluated in different ways. Widely used methods include direct ophthalmoscopy, stereoscopic biomicroscopy and disc photography. These methods are subjective and are associated with a considerable intra observer and inter observer variability (7). Automated instruments have been developed to quantitatively and more objectively assess optic nerve topography using confocal laser scanning tomography. Heidelberg Engineering used the research results obtained with the HRT I during the last 10 years to develop a new instrument, the HRT II. In comparison to the HRT I, the HRT II has a greater resolution (384 x 384 pixels to 256 x 256 pixels), a shorter acquisition time (0.025 sec to 0.032 sec), is more user friendly, and is less costly.

To be applied clinically for the follow-up of glaucoma patients, the generated data need to be reproducible. The present work investigates the short-term variability of morphometric parameters calculated by the HRT II on normal subjects.

MATERIAL AND METHODS

Instrumentation

The HRT II is a confocal scanning laser tomograph and therefore does not require dilation. The imaging system of the HRT II uses a diode laser beam at a wavelength of 670 nm that is scanned across the retina in x and y directions. The confocal imaging technique uses the principle of pinhole focusing for both the incoming laser beam and the beam that returns to the imaging detector. Thus, only light reflected at or near the adjusted focal plane is detected and contributes to the image (3). By changing the focal plane of the scanning beam, a series of images at different depths along the optic nerve can be recorded. The software computes and automatically sets the correct location of the focal plane and the required scan depth for that eye. The number of image planes acquired depends on the required scan depth; 16 images per mm scan are acquired. The device uses a fixed 15-degree field of view with 384x384 pixels per image plane, providing a resolution in the xy plane of about 10 microns per pixel. At each image plane a software algorithm calculates the height of the structure at each pixel. All this measurements are put together to form a 3-dimensional image of the entire optic nerve. By colour coding the area of elevation and depression, the HRT II provides a 2-dimensional representation. After definition of the optic disc contour line (this is the only subjective step) the 14 stereometric parameters, a comparison to previous examinations and to a normative database are presented (5).

All parameters were corrected for refractive error and actual radius of corneal curvature.

The following parameters were calculated:

1=disc area= total area enclosed by the contour line.

2=cup area= total area enclosed by the contour line and located beneath the reference plane.

3=rim area= total area enclosed by the contour line and located above the reference plane.

4=cup volume= 2 volume

5=rim volume= 3 volume

6=cup/disc ratio= 2/1

7=horizontal cup/disc ratio

8=vertical cup/disc ratio

9=mean cup depth= average of all height values within the cup

10=maximum cup depth= mean cup depth of the highest 5% of all depth values

11=cup shape measure= skewness of the frequency distribution of depth values within the cup

12=heigth variation contour= max height-min height at the contour line

13=mean retinal nerve fibre layer thickness (RNFLt) = mean height at the contour line

14=RNFL cross sectional area= mean RNFLt x length of the contour line

reference plane= plane parallel to the retinal surface and located 50μm posteriorly to the retinal surface at the papillo-macular bundle.

Patients

Twenty eyes of 20 normal volunteers were enrolled in this study. There was no history of glaucoma, ocular hypertension, trauma or chronic ocular disease. One patient had undergone a radial keratotomy in the past. The intraocular pressure was measured whenever possible.

Study design

The following protocol was followed for each patient in the study. All images were obtained by the same operator. One eye per patient was included; the eye examined was randomly selected. Three measurements were performed within a time interval of 2 weeks, each measurement comprising a set of 3 sequential images. The images were taken trough non dilated pupils. The contour line was defined by the same operator for the first stored scanning series only. Later on, this definition was automatically transposed by the computer onto the 2 following scanning series.

Examinations with a standard deviation (SD)>30μm were excluded. This is an image quality control advised by HRT. Images whose overall "Topography Std.Dev." >30μm should be considered as "non-acceptable" and thus discarded. Every patient had three sequential images whose overall "Topography Std. Dev."<30μm. Therefore only images of good quality were compared; this should not affect the coefficient of variation.

Statistics

Mean, standard deviation (SD) and coefficient of variation (CV) were computed for each parameter of each disc. CV is defined as the standard deviation divided by the mean. The mean coefficient of variation ± SD of each parameter was calculated.

RESULTS

Patients' characteristics: the intraocular pressure was measured whenever possible and did not exceed 21 mm Hg. Best corrected visual acuity was 0.7 or better. The mean refraction was -2.6 D (range from -7.75D to +0.5D). Javal keratometry varied from 0 to 0.3 mm with the rule astigmatism. There were 3 men and 17 women. Their mean age was 32.7 years (range from 24 years to 52 years).

The mean of 3 measurements for each parameter per patient is shown in table 1.

The mean coefficient of variation ± SD for each parameter (figure 1) was:

Cup Area=15±19%; Rim Area=2±1%; Cup Volume=25±38%; Rim volume=7±4%;

C/D Area Ratio=15±19%; Horizontal C/D Ratio=12±20%;Vertical C/D Ratio=10±27%;

Mean Cup Depth=6±4%; Max.Cup Depth=5±4%; Cup Shape Meas.=12±7%;

Height Var.Contour=6±3%; Mean RNFL Thickness=7±4%;

RNFL Cross Sect.Area=6±4%.

The mean coefficient of variation of all parameters was 10 ± 12%.

DISCUSSION

The HRT II has a very good reproducibility. This can be explained by many factors.

First there are the machine-related factors: the method is largely independent of operator judgement. The HRT II updated software makes it easier to draw the contour line. By looking at the surface height variation along the position marker, it is easier to find the proper location of the disc margin. Drawing the contour line is the only subjective step of the examination. This source of variability is limited by the automatic transposition of the contour line of the first measurement to the next measurements. Though Hatch et al.(4) showed an almost perfect interobserver agreement for the HRT parameters, we preferred the contour line to be traced by always the same operator to obtain a variability as low as possible. The confocal principle with its minimal depth of focus renders an improvement of accuracy in depth estimations and 3-dimensional measurements. It is a completely birefringent-free technology unaffected by corneal artefacts. Pulsatile changes of the eye, which lead to difficulties in corneal measurements, do not influence the actual focal plane at the posterior pole (13). The HRT II has a shorter scanning time and a greater resolution compared to the HRT I. An immediate control of the examination quality during the recording session is possible, to facilitate the selection and storing of the best series of the ex-

Table 1: *Mean of 3 measurements for each parameter per patient*

patient	Disc area	cup area	rim area	cup vol	rim vol	c/d area ratio	horiz c/d ratio	vertic c/d ratio	mean cup depth
1	1,91	0,241333	1,668667	0,029	0,484667	0,126333	0,340667	0,041	0,163
2	2,455	0,431333	2,024	0,064333	0,552333	0,175667	0,438333	0,341667	0,19
3	2,31	0,116	2,179333	0,005333	0,515667	0,05	0,170667	0,099333	0,080667
4	2,189	0,548667	1,640333	0,113667	0,449333	0,251	0,560667	0,416667	0,272
5	2,465	0,640667	1,824333	0,186333	0,657	0,26	0,591	0,393	0,327333
6	2,577	0,842333	1,734333	0,174333	0,687333	0,327	0,632667	0,51	0,320333
7	2,199	0,379667	1,819333	0,056333	0,468	0,172667	0,52	0,263667	0,158333
8	2,934	0,941667	1,993333	0,327667	0,552	0,320667	0,657	0,528333	0,357333
9	2,277	0,060667	2,216333	0,001333	0,645333	0,026333	0,352333	0	0,081333
10	2,534	0,970667	1,563333	0,257333	0,469333	0,382667	0,633	0,438	0,330333
11	3,441	1,033667	2,407333	0,262	0,688667	0,300667	0,628333	0,471	0,308
12	2,621	0,357	2,264667	0,025333	0,758333	0,136	0,310667	0,275333	0,178333
13	1,711	0,277333	1,434333	0,040333	0,477333	0,162	0,331333	0,195	0,210333
14	2,979	0,067667	2,911333	0,001667	0,688333	0,022667	0,034667	0	0,064667
15	1,989	0,017667	1,971333	0,000667	0,749667	0,009	0,031	0	0,086
16	2,161	0,571333	1,589667	0,101667	0,363	0,264333	0,471	0,370333	0,185333
17	2,003	0,191	1,812	0,038333	0,680333	0,095	0,320333	0,243	0,181
18	2,409	0,671333	1,737667	0,075333	0,561333	0,278667	0,492	0,541667	0,236667
19	2,415	0,115333	2,299333	0,005667	0,714667	0,048	0,285667	0	0,093333
20	1,825	0,203333	1,622333	0,012667	0,452667	0,111333	0,246333	0	0,116667

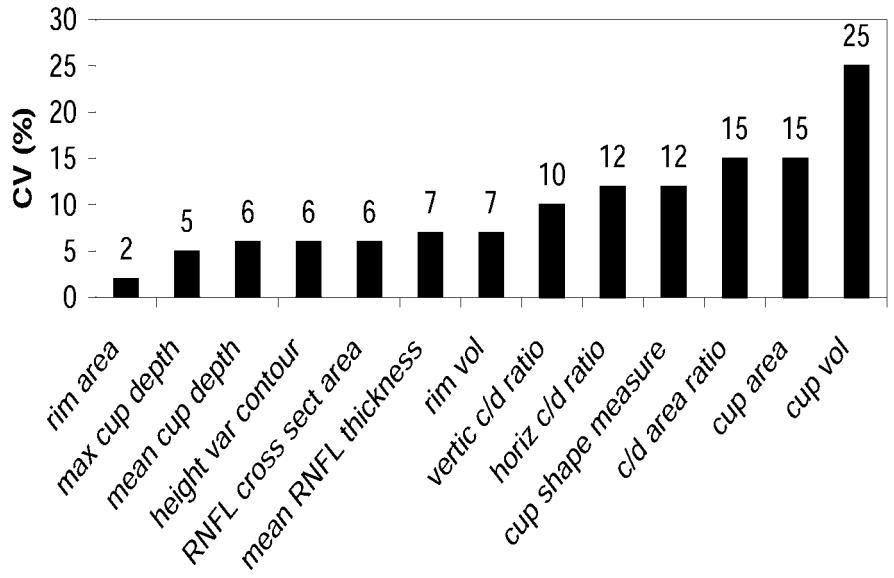
horiz=horizontal; vertic=vertical; c/d ratio=cup/disc ratio

Table 1 (continuation)

patient	max cup depth	cup shape measure	height var contour	mean RNFL thickness	RNFL cross sect area	reference height	topo
1	0,443333	-0,177	0,334	0,254333	1,247667	0,133	19
2	0,533667	-0,20433	0,334333	0,241333	1,343333	0,273	24
3	0,252667	-0,24967	0,267333	0,15	0,808333	0,079	13,33333
4	0,629667	-0,101	0,349667	0,244333	1,282	0,33	16
5	0,887	-0,18667	0,518	0,354333	1,972333	0,586333	24,66667
6	0,915333	-0,18033	0,572333	0,383667	2,182667	0,55	7,485
7	0,574	-0,29867	0,278333	0,223667	1,178	0,185333	20
8	0,909667	-0,18233	0,344	0,272	1,653667	0,228667	27,66667
9	0,215	-0,14833	0,337	0,238667	1,244	0,272333	19
10	0,824	-0,13733	0,467667	0,277667	1,569667	0,385667	19,33333
11	0,770333	-0,153	0,393667	0,285333	1,876333	0,287667	22
12	0,476333	-0,16267	0,456	0,332333	1,909333	0,368	14
13	0,571667	-0,163	0,396	0,304667	1,415333	0,303	21,33333
14	0,198	-0,18133	0,34	0,19	1,161333	0,140333	16,33333
15	0,292	-0,23367	0,431	0,3	1,500333	0,375333	16,66667
16	0,575667	-0,21033	0,383667	0,239	1,245	0,315333	18,66667
17	0,762333	-0,36667	0,612333	0,376333	1,887333	0,384667	18,33333
18	0,560333	-0,10233	0,539333	0,356333	1,963667	0,443	12
19	0,291667	-0,21867	0,373333	0,258667	1,426333	0,167	16
20	0.332	-0.169	0.350333	0.249333	1.195333	0.181667	24

max=maximal; var=variation; RNFL=retinal nerve fibre layer; sect=sectional

Figure 1: mean coefficient of variation (CV) of each parameter



amination. Each measurement comprises 3 image series. The investigation parameters of each series are recorded by the laser tomographic scanner. The intensity of the laser light, the level (focal plane) of the first and the last section image, and the position of the laser source and the patient's eye (chin/head rests) are documented in a numeric code. Therefore, the next recordings of the same patient can be made with the same parameters (6). There is no learning effect produced by the patients.

Other factors contributing to the good reproducibility are related to the patient population and study design: our patient population has a relative low mean age and consequently shows clear optic media and a good fixation. All measurements were made within a time-interval of 2 weeks. The short-term variability is usually better than the long-term variability.

We can't exclude some factors that will influence the variability negatively: our patient population is small (20 eyes) and all discs are non-glaucomatous. Garway et al.(2) showed a greater magnitude of difference between the observers for normal than for glaucomatous optic discs. This is likely to result from difficulty in identifying Elschnig's ring in parts of the optic disc when the nerve fibre layer is thicker, at the poles and nasal part of the disc. In glaucoma, as the nerve fibre layer thins, Elschnig's ring becomes progressively more visible. Yamazaki et al.(12) found a negative influence of myopic disc shape on the diagnostic precision of the Heidelberg Retina Tomograph. Rim volume, height variation contour, mean RNFLthickness and RNFL cross-section area were significantly larger in eyes with myopic disc shapes. Our patient population shows a myopic shift. There was no exclusion criterion based on refractive error in our study. The myopic crescent makes the accuracy of drawing the contour line more difficult. Myopic discs are bigger and might consequently show a greater variability.

There has been considerable previous work on the subject of the reproducibility of computerised methods of measuring optic nerve head topography. Some of these works focused on the repeatability of signals at the pixel level, and other technical reproducibility issues. A different approach is taken in this work namely, we evaluated the instrument as it would be used in a clinical setting and examined the output

Table 2: *Study of literature*

Ref	hrt	Number of normals	Number of measurements	time	dilatation	Refraction error criteria	Mean age	Mean refraction error
1	I	10	10	1 d	no	yes	29±7.3	-1.3±1.2
10	I	13	3	1 d	no	yes	37±11	
11	I	10	5-10	1 d	no	no	26.4 (24-32)	-4±3.2
2	I	15-15 glaucoma pts	15-15	1 w	yes	yes	56±12.8	
8	I	5	5	1 d		no		
Our study	II	20	3	2 w	no	no	32.7 (24-52)	-2.6 (-7.75-+0.5)

Ref	Mean cup vol	Mean CV of cup area	Mean CV of rim area	Mean CV of cup vol	Mean CV of mean cup depth	Mean CV of maximal cup depth
1		8.1		11.2	4.6	4.3
10	0.342±0.013	3.4	4.8	4.6	3.3	4.0
11	0.228±0.117			7.28±4.67	7.33±4.61	
2			4.5			
8		4.1		8		8.2
Our study	0.085±0.099	15±19	2.1	25±38	6±4	5±4

Ref=reference; hrt=heidelberg retina tomograph; pts=patients; d=day; w=week; vol=volume; CV=coefficient of variation

variables that the instrument has intended for clinical assessment of the optic disc (9).
No other paper written in English described the reproducibility of the HRT II by our knowledge. We compared our results with HRT I variability measurements in literature (1, 2, 8, 10, 11) (table 2). These are all short-term studies (from 1 day to 2 weeks). The number of patients varies from 5 to 20. All data concerned normal patients, except for study 10 where 15 glaucoma patients were included. We made three measurements on each patient, the other studies made 3 or more measurements. We did not use dilation as in most studies. The majority of the studies used exclusion criteria based on refraction error measurements, we didn't. The mean age of the patients is comparable from study to study, except for study 8 where the mean age is higher because of inclusion of glaucoma patients.
We obtained good reproducibility results especially for rim area which has the lowest variability (2±1%). The coefficients of variation of cup area and cup volume were higher in our study compared to the other studies. We couldn't find any significant difference in population characteristics between the studies to explain this difference.

CONCLUSIONS:

Short-term intra-individual variability for HRT II measurements in normal subjects was ≤12% in all but 3 parameters. Cup Volume had the highest variability(25±38%). Rim Area was the least variable parameter(2±1%).

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