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Scanning laser polarimetry and retinal thickness analysis before and after laser in situ keratomileusis

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PURPOSE. To evaluate changes in retinal nerve fiber layer (RNFL) thickness after laser *in situ* keratomileusis (LASIK) using a scanning laser polarimeter with fixed corneal compensation (GDx) and the retinal thickness analyzer (RTA).

METHODS. Thirty-eight eyes of 19 healthy subjects (10 female and 9 male; mean age 37.0±8.8 years) underwent GDx and RTA measurements before and after LASIK. All subjects revealed mild to high myopia (mean spherical refraction: -4.0±2.75 D). Measurements using GDx were followed by RTA measurements after pupil dilation. All measurements were performed the day before LASIK and 1 week postoperatively.

RESULTS. GDx revealed a decrease in nerve fiber layer thickness measurements after LASIK, but did not reach statistical significance (p>0.05). Using RTA, mean RNFL thickness (MRNFL) and RNFL cross sectional area decreased significantly after LASIK (p=0.03 and p=0.02, respectively).

CONCLUSIONS. Scanning laser polarimetry revealed a slight decrease in RNFL thickness measurements after LASIK. MRNFL and RNFL cross section were significantly lower after LASIK using RTA. The changes might be artifacts in a small group of myopic subjects. (Eur J Ophthalmol 2005; 15: 434-40)

KEY WORDS. Retinal nerve fiber layer, Laser *in situ* keratomileusis, Scanning laser polarimeter, Retinal thickness analyzer

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INTRODUCTION

Scanning laser ophthalmoscopy is a widely used method for measuring the retinal nerve fiber layer (RNFL) and optic disk topography in glaucoma and other ocular diseases. There are different scanning laser ophthalmoscopes available, each operating on specific principles. The GDx (Laser Diagnostic Technologies, San Diego, CA) with fixed corneal compensation is a scanning laser polarimeter that measures the peripapillary nerve fiber layer thickness.

Detailed descriptions of the GDx have been published elsewhere (1-3). Briefly, the principle is as follows: a polarized laser light is sent through the birefringent RNFL. When it passes the retina the reflected light leads to optical retardation caused by the parallel retinal nerve fibers (phase shift). The amount of retardation is proportional to the thickness of the RNFL.

Earlier studies have revealed a good correlation between the measurements obtained by GDx and the histopathologic measurements of nerve fiber layer thickness in a primate model (4). The sensitivity of scanning laser polarimetry has been reported to be as high as 96%. The specificity is about 93% (5).

The Retinal Thickness Analyzer (RTA; Talia Visionary Diagnostics, Israel) is a new device developed for the early

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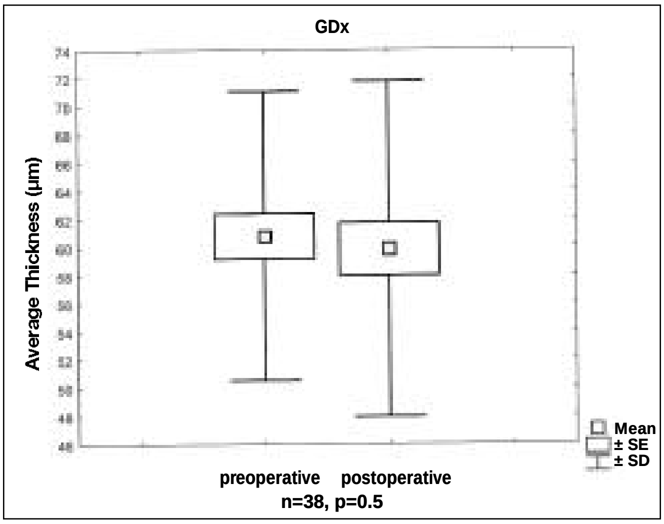

Fig. 1 - Plot showing average retinal nerve fiber layer thickness in microns (± standard deviation (SD) and standard error (SE)) measured by GDx before and after laser-assisted in situ keratomileusis. The retinal nerve fiber layer thinning was not statistically significant.

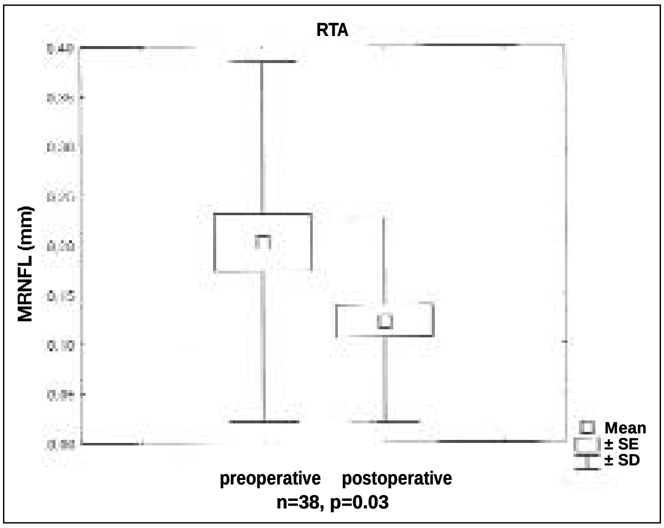

Fig. 2 - Plot showing the mean retinal nerve fiber layer thickness (± standard deviation (SD) and standard error (SE)) measured by retinal thickness analyzer (RTA) before and after laser-assisted in situ keratomileusis. The decrease in retinal nerve fiber layer thickness was statistically significant.

detection of glaucoma and diagnosis of macular pathologies. It allows measurement of the retinal thickness at the posterior pole and optic disk topography. The principle of the RTA is based on a green helium-neon laser of 540 nm, which generates cross-sections of the retinal thickness (6-8). Depth precision has been reported to be 5 to 10 µm and depth resolution 50 µm (9). RTA measurements are known to be reproducible and have a low intra- and inter-observer variability (6).

Laser in situ keratomileusis (LASIK) is a refractive surgical technique in which corneal stroma photoablation is achieved by structural and refractive changes induced by an excimer laser. The technique is used for the correction of myopia and hyperopia.

The LASIK procedure is potentially harmful to the RNFL. Reports in the literature suggest that the suction, direct irradiation, shock waves produced by each pulse, or the high intraocular pressure involved might cause damage to the retina or the optic nerve (10). Previous studies have demonstrated that the corneal changes induced by LASIK affect the measurement of the RNFL by laser scanning polarimetry (11-13). Another study has revealed unchanged RNFL thickness following LASIK surgery, measured with scanning laser tomography and optical coherence tomography (14). In this study we evaluated changes in the RNFL and retinal thickness measurements after LASIK using both the GDx and RTA.

PATIENTS AND METHODS

Thirty-eight eyes of 19 subjects (10 female, 9 male) were included in the study. The mean age was 37.0 ± 7.7 years (range 22.0 to 59.0 years). The subjects had no ocular disease or abnormality except ametropia. The GDx and RTA measurements were taken the day before and 1 week after LASIK surgery. Each patient was examined by the same investigator with experience in both devices. Written informed consent was obtained by all subjects.

Preoperatively, all patients underwent complete ophthalmologic examination including determination of uncorrected and best-corrected visual acuity (BCVA), slit lamp biomicroscopy, intraocular pressure measurement using Goldmann applanation tonometry, determination of refractive error, computerized corneal topography, ultrasonic pachymetry, and dilated fundus examination.

Preoperative mean spherical refraction was -4.0 ± 2.75 D (range -8.0 to -1.0 D). The mean cylindrical refraction was -0.75 D ± 0.7 D (range -2.5 to 0.0 D). Postoperatively, mean spherical refractive error was 0.0 D ± 0.7 D and mean cylindrical error was -0.6 D ± 0.4 D. The first measurement was always taken with GDx, because of the need to dilate the pupil prior to the RTA measurement. Each patient was measured a minimum of three times until three scans of high quality (“passed” scans) were achieved. After determining the mean image the operator

TABLE I - DESCRIPTION OF GDX PARAMETERS

Parameter	Definition	Units
The number	Predictive parameter for the presence of glaucoma	–
Symmetry	Ratio of the average of the 1500 thickest pixels in the superior quadrant to the average of the 1500 thickest pixels in the inferior quadrant	– –
Superior ratio	Ratio of the 1500 thickest pixels in the superior quadrant to the average of the 1500 median pixels in the temporal quadrant	–
Superior/nasal	Ratio of the 1500 thickest pixels in the superior quadrant to the average of the 1500 median pixels in the nasal quadrant	–
Max. modulation	The difference between the thickest and thinnest measurements within the image	–
Ellipse modulation	Indicator of the difference between the thickest and thinnest areas in the area image	–
Average thickness	Average thickness for all usable pixels in the total image area	µm
Ellipse average	Average thickness for the pixels along the measuring ellipse	µm
Superior average	Average thickness for the pixels in the superior quadrant of the measuring ellipse	µm
Inferior average	Average thickness for the pixels in the inferior quadrant of the measuring ellipse	µm
Superior integral	Total area under the curve of the nerve fiber layer along the superior portion of the measuring ellipse, corresponding to nerve fiber layer volume	mm

placed an ellipse corresponding to the rim of the optic nerve head and a measuring ellipse of 1.75 diameters disc size was generated by the software. The computer then develops the nerve fiber layer analysis and thickness values in each quadrant of the peripapillary region. The GDx parameters measured and included in the statistical analysis are listed in Table I. After GDx measurements, pupils were dilated with 10% phenylephrine and 0.5% tropicamide eye drops. Using RTA the fundus was scanned at 13 points, each 3 mm by 3 mm, including the peripapillary region and the posterior pole. After adjusting the light, the scan was performed over 0.3 seconds and the quality of the scans was determined by the RTA software. The software analyzed the retinal thickness at the posterior pole and the optic nerve head, producing two- and three-dimensional maps of the scanned regions, including different thickness values for the later results (Tab. II). Nerve fiber layer analysis and retinal thickness measurements were repeated 1 week after LASIK. All LASIK procedures were performed by the same surgeon using the Amadeus Microkeratome (AMO, Santa Ana, CA) and the Flying spot excimer laser ESIRIS (Schwind Eye-technique Solutions, Kleinostheim, Germany). The maximal suction time was 30 seconds. Statistical analysis was performed using Statistica version 6 (Statsoft Inc., Tulsa, OK). The Student t-test for paired values was used to compare preoperative and postoperative measurements.

Analysis of variance was used to investigate each parameter of the measurements preoperatively and postoperatively. Based on previous studies the statistical power was calculated to be greater than 0.8 for the sample size used in this study.

RESULTS

The LASIK procedure and the postoperative course were uncomplicated in all eyes. It was possible to perform

TABLE II - DESCRIPTION OF RTA PARAMETERS

Parameter	Definition	Units
Disc area	Whole disc area, defined by the contour line	mm^2
Cup area	Total cup area, defined by the contour line	mm^2
Cup/disc area ratio	Coefficient between cup area and disc area	–
Rim area	Total area of the rim determined by the contour line	mm^2
Cup volume	Volume of the disc	mm^3
Rim volume	Volume of the rim containing the contour line	mm^3
Mean cup depth	Average of all depths in the cup	mm
Maximum cup depth	The maximum cup depth	mm
Cup shape measure	Measure of tilting of the optic nerve head	–
Height variation contour	The distance between the lowest and highest point of the contour line	mm
Mean RNFL thickness	Average thickness along the contour line	mm
RNFL cross section area	Mean RNFL thickness multiplied with the length of the contour line	mm^2
Posterior pole minimum thickness	Minimum retinal thickness at the posterior pole	mm
Perifoveal minimum thickness	Minimal thickness at the perifoveal region	mm
Posterior pole S/I asymmetry	Ratio of the average thickness in the superior area to the average thickness in the inferior area at the posterior pole	%
Perifoveal S/I asymmetry	Ratio of the average thickness in the superior area to the average thickness of the inferior area at the perifoveal region	%
Posterior pole abnormality	Percentage of abnormal thinning of retinal thickness at the posterior pole	%
Perifoveal abnormality thin area	Percentage of abnormal thinning of retinal thickness at the perifoveal region	%
Posterior pole number of thin clusters	Number of thin clusters at the posterior pole	–
Posterior pole pattern deviation	Pattern deviation at the posterior pole	mm

RTA = Retinal thickness analyzer; RNFL = Retinal nerve fiber layer

GDx and RTA measurements in all patients postoperatively. GDx measurements were difficult to obtain in two patients with dry eye syndrome after LASIK, but after additional local therapy with artificial tears (Hylo-Comod) high quality images with both instruments were achieved. No significant changes in peripapillary RNFL thickness measurements using GDx after LASIK were found. Although a decrease was detected in the following thickness parameters, the thinning was not statistically significant ($p>0.05$): average thickness (preop: 60.8 ± SD 10.3 µm, postop: 59.9 ± SD 11.9 µm; Fig. 1), ellipse average thickness (preop: 64.0 ± SD 10.0 µm, postop: 62.0 ± SD 11.9 µm), superior average thickness (preop: 72.4 ± SD 10.7 µm, postop: 69.9 ± SD 12.6 µm), inferior average thickness (preop: 73.9 ± SD 14.0 µm, postop: 73.4 ± SD 14.5 µm), and superior integral (preop: 0.20 ± SD 0.03 µm, postop: 0.19 ± SD 0.03 µm). The parameter number increased 1 week after LASIK from 23 to 25. The number is a predictive parameter for the presence of glaucoma and therefore an indirect parameter for the loss of RNFL. The higher the number the higher the probability of glaucoma. All other parameters are listed in Table III.

RTA measurements revealed a statistically significant decrease in two thickness parameters: mean RNFL thickness (MRNFL preop: 0.2 ± SD 0.18 mm, postop: 0.12 ± SD 0.10 mm; $p=0.03$, Fig. 2) and RNFL cross section area (RNFL cross section preop: 1.28 ± SD 11.7 mm^2, postop 0.7 ± SD 0.6 mm^2, $p=0.02$). Tables III and IV summarize

TABLE III - RETINAL NERVE FIBER LAYER THICKNESS MEASUREMENTS BEFORE AND AFTER LASIK (GDX)

GDx	Inferior ratio	Average thickness (μm)	Ellipse average (μm)	Superior average (μm)	Inferior average (μm)	Superior integral (mm)
Preoperative	2.28±0.5	60.8±10.3	64.0±10	72.4±10.7	73.9±14	0.20±0.03
	2.26±0.5	59.9±11.9	62.0±11.9	69.9±12.6	73.4±14.5	0.19±0.03
Postoperative	p=0.9	p=0.5	p=0.4	p=0.1	p=0.7	p=0.1
GDx	**Symmetry**	**Superior ratio**	**Inferior ratio**	**Superior/ nasal**	**Max. modulation**	**Ellipse modulation**
Preoperative	1.0±0.13	2.19±0.48	2.27±0.5	2.04±0.3	1.44±0.45	2.4 ±0.66
	1.0±0.14	2.25±0.50	2.26±0.5	2.1 ±0.33	1.48±0.40	2.45±0.65
Postoperative	p=0.38	p=0.5	p=0.9	p=0.31	p=0.65	p=0.71
GDx	**Number**					
Preoperative	23.0±13.0					
	25.0±15.0					
Postoperative	p=0.65					

t-Test, p values below 0.05 were considered statistically significant
LASIK = Laser-assisted in situ keratomileusis

TABLE IV - RETINAL THICKNESS MEASUREMENTS BEFORE AND AFTER LASIK (RTA)

RTA	Mean RNFL thickness (mm)	RNFL cross section (mm^2)	Posterior pole minimum (mm)	Perifoveal minimum (mm)
Preoperative	0.2 ±0.18	1.28±11.7	117.3±25	126.2±26.6
	0.12±0.1	0.7 ± 0.6	107.3±19.4	113 ±20.2
Postoperative	p=0.03*	p=0.02*	p=0.4	p=0.16
RTA	**Disc area (mm^2)**	**Cup area (mm^2)**	**Cup/disc area ratio**	**Rim area (mm^2)**
Preoperative	3.23±0.9	1.2±0.9	0.37±0.22	2.07±0.9
	2.8 ±0.6	1.2±0.9	0.4 ±0.26	1.61±0.8
Postoperative	p= 0.06	p=0.9	p=0.36	p=0.06
RTA	**Cup volume (mm^3)**	**Rim volume (mm^3)**	**Mean cup depth (mm)**	**Maximum cup depth (mm)**
Preoperative	0.33±0.6	0.35±0.32	0.17±0.09	0.55±0.23
	0.25±0.33	0.28±0.22	0.14±0.08	0.46±0.22
Postoperative	p=0.43	p=0.2	p=0.07	p=0.07
RTA	**Cup shape measure (mm)**	**Height variation contour (mm)**	**Post. pole asymmetry (%)**	**Peri-foveal asymmetry (%)**
Preoperative	-0.19±0.09	0.47±0.37	-2.22± 9.37	-2.36± 8.8
	-0.21± 0.1	0.37±0.16	-2.63±11.55	-2.59±10.9
Postoperative	p=0.33	p=0.1	p=0.8	p=0.91
RTA	**Post. pole abn. thin area (%)**	**Perifoveal abn. thin area (%)**	**Post. pole number of thin clusters**	**Post. pole pattern deviation (μm)**
Preoperative	4.69±10.12	6.06±13.5	0.7±0.9	26.23±23.8
	7.95±12.28	10.16±15.6	1.1±1.3	39.2 ±32.0
Postoperative	P=0.16	P=0.18	P=0.16	P=0.08

*t-Test, p values below 0.05 were considered statistically significant.
LASIK = Laser-assisted in situ keratomileusis; RTA = Retinal thickness analyzer; RNFL = Retinal nerve fiber layer

TABLE V - CHANGES IN RNFL THICKNESS MEASUREMENTS AFTER LASIK IN PATIENTS WITH HIGH AND MILD MYOPIA

Myopia	MRNFL preoperative mm (SD)	MRNFL postoperative mm (SD)	p value*	RNFL cross section area preoperative mm^2 (SD)	RNFL cross section area postoperative mm^2 (SD)	p value*
Myopia ≥ - 3 D (n=16)	0.25 (0.23)	0.12 (0.08)	0.03	1.62 (1.44)	0.70 (0.49)	0.01
Myopia < - 3 D (n=22)	0.15 (0.11)	0.13 (0.13)	0.56	0.91 (0.66)	0.71 (0.73)	0.42

*T-test, values < 0.05 were considered statistically significant
Values are given in mean (standard deviation, SD)

the RNFL and retinal thickness measurements before and after LASIK (including standard deviations) with both instruments.

After dividing the subjects into two groups (myopia ≥3 D vs myopia <3 D), the changes in MRNFL and RNFL cross section area were no longer significant in the subjects with mild myopia. The results in the group of subjects with high myopia did not change; MRNFL and RNFL cross section area were significantly lower after LASIK. All other parameters did not change significantly after LASIK (Tab. V). The severity of myopia had no influence on the measurements with GDx.

DISCUSSION

In this study we found changes in the measurements of the RNFL thickness and RNFL cross section area using RTA after LASIK surgery. No significant RNFL changes were found with GDx. Previous studies demonstrated that the LASIK procedure may influence the measurement of RNFL thickness by scanning laser polarimetry (10, 12, 13). In effect, Hollo et al (13) demonstrated that LASIK induced a decrease of the RNFL thickness, which could be detected using polarimeters with fixed corneal compensators. After individual corneal compensation, which is implemented in the GDx VCC, the RNFL decrease was no longer found (13). The RNFL is a birefringent tissue but the cornea also has birefringent properties, so that structural changes in the corneal tissue such as after LASIK might influence the measurements of RNFL thickness. Our results with GDx reached no statistical significance, although slight changes in RNFL measurements were found. This might be explained by the small number of subjects. Overall, the subjects in our study revealed smaller mean RNFL thickness values preoperatively compared to other studies (11-13), which could be an explanation for a smaller range in the decrease of RNFL thickness values obtained by GDx.

Some authors have suggested that suction during LASIK and shockwaves from the excimer laser have a harmful effect on the RNFL (12, 15-17). Very few case reports in the literature describe visual field defects and optic neuropathy after LASIK (16, 17). In one case, a subject with previously normal visual field and healthy optic nerve heads developed an optic neuropathy, visual field defects, and increased cupping of the disc (15). Such complications may be due to barotrauma or ischemia related to the high intraocular pressure during LASIK. In contrast, Iester et al could not find any changes in the RNFL after a 45-second acute increase in intraocular pressure, such as occurs during LASIK (18).

The reason for the significant decrease in the RTA parameters after LASIK could be explained by the corneal edema that occurs after the surgery. Edema could lead to incorrect measurements, induced by optical alterations (e.g., influence on the laser beam reflexions and the backscattered light from the retina). All structural changes in the optical pathway of a scanning laser ophthalmoscope may influence its results. The technical and physical principle of the RTA (computerized slit lamp that images retinal cross sections at an angle) may predispose to a higher susceptibility of incorrect measurements using this instrument compared to scanning laser polarimetry. Postoperative alterations in the cornea and changes in the tear film might also contribute to inaccurate measurements. The reason for the inter-instrument differences is unclear, but the small study group might have influenced the results. Interestingly, after dividing the subjects into two groups (mild and high myopia), the changes in RTA measurements in subjects with mild myopia preoperatively were no longer statistically significant. Higher myopia is likely to be related to longer ablation duration, more corneal destruction, and more corneal edema, and might be one reason for measurement errors after LASIK. To our knowledge, this is the first report on the influence of LASIK on the measurement of retinal thickness using RTA. Further studies with longer follow-up and a greater number of subjects are desirable to evaluate whether the observed changes in RNFL thickness and retinal thickness after LASIK diminish after time.

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