Retinal Nerve Fiber Layer Measurements Before and After Photorefractive Keratectomy

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ABSTRACT
PURPOSE: To determine whether the nerve fiber analyzer GDx with the new variable corneal compensation (VCC) device allows measurements of retinal nerve fiber layer parameters independent from birefringence changes of the cornea after photorefractive keratectomy (PRK).

METHODS: Retinal nerve fiber layers of 32 eyes in 32 myopic patients undergoing PRK were analyzed using the GDx-VCC. Photorefractive keratectomy was performed using a NIDEK EC-5000 excimer laser. Measurements were obtained before and after PRK without dilating the pupil. To evaluate birefringence changes, GDx-VCC macular images also were taken before and after PRK.

RESULTS: After PRK, superior and inferior ratios, superior/nasal max modulation, and temporal-superior-nasal-inferior-temporal average changed significantly (P < .001) when corneal birefringence correction was not applied. When corneal birefringence correction was applied, only temporal-superior-nasal-inferior-temporal average and superior maximum improved significantly. Furthermore, a comparison of the postoperative data without polarization correction to the data with corrected corneal polarization demonstrated significant changes in superior ratio (P = .004), superior/nasal (P < .001), ellipse modulation (P = .007), and temporal-superior-nasal-inferior-temporal standard deviation (P = .009).

CONCLUSIONS: Our results show the VCC algorithm is able to compensate for most of the changes in corneal birefringence induced by corneal refractive surgery if the polarization has been re-calculated. Because mild changes in GDx parameters could affect the interpretation of the results in some patients, a new postoperative baseline macular image should be acquired. [J Refract Surg. 2008;24:639-644.]

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canning laser polarimetry (GDx; Carl Zeiss Meditec, Jena, Germany) assesses the phase shift or retardation that occurs when polarized light passes through a birefringent structure such as the retinal nerve fiber layer.1-3 Because a correlation exists between retinal nerve fiber layer thinning and ganglion cell loss in glaucoma,2 this technology has been proposed for the diagnosis and follow-up of glaucoma.4 The amount of retardation that occurs is proportional to the thickness of the retinal nerve fiber layer.2 Because a birefringence effect has been shown in the human cornea, a fixed corneal compensator (FCC) was added to the system to compensate for the birefringency of the cornea of all patients. However, because 20% of the population do not have a standard corneal polarization, in those cases, the GDx-FCC is not able to compensate.5 To avoid this possible error, a new polarimeter with a variable corneal compensator (VCC) was introduced.6,7 Using this new technology (GDx-VCC), it should be possible to correctly assess the retinal nerve fiber layer thickness regardless of corneal changes.8

Conical refractive surgery changes the corneal thickness, curvature, and refraction. The retinal nerve fiber layer thickness should be unaffected by this type of surgery. Several studies have shown controversial results after refractive corneal surgery with both photorefractive keratectomy (PRK) and LASIK.9-24 Because corneal refractive surgery is performed in a large number of patients, it is important to understand whether any change in the retinal nerve fiber layer is caused by the loss of ganglion cells or by an artifactual surgical change in corneal birefringence.

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This study examined whether the GDx-VCC allows measurement of retinal nerve fiber layer parameters independent from birefringence changes of the cornea after PRK.

PATIENTS AND METHODS

This research followed the tenets of the Declaration of Helsinki, and informed consent was obtained from all patients. Thirty-two eyes of 32 myopic patients were included in this prospective study. In all eyes, best spectacle-corrected visual acuity was better than 20/20. Patients were classified as healthy if they had a normal slit-lamp examination, normal frequency doubling technology by a screening test, and normal corneal topography. The reliable detection of glaucomatous and neurological visual field defects by frequency doubling technology has been well established, and this technique has shown high sensitivity and specificity and can quantify visual field loss accurately.25-27 Corneal topography was assessed using the Tomey TMS-2 (Tomey Corp, Nagoya, Japan). As is customary for refractive surgery candidates, only patients without evidence of corneal abnormalities were selected.

Before and after PRK, the retinal nerve fiber layer thickness was analyzed using the GDx-VCC (software version 5.3.1), a confocal scanning laser polarimeter with a 780-nm polarized light source. The reproducibility and the details of this technique have been described previously.28-31 Briefly, a complete scan consists of 128 × 256 pixels. The angle field used by the system is 40° × 20°. All of the images were acquired through a non-dilated pupil. Only good quality images as determined by the automatic quality assessment software (ie, a score ≥ 8) were selected for analysis. All of the retinal nerve fiber layer images were obtained after a macular scan was performed to evaluate the corneal birefringence.

Immediately after acquiring the data, the algorithm calculated the amount of retardation at each measured retinal position. A retardation map described the changes in the state of polarization (retardation) at each location within the field of view. Each pixel represented the amount of retardation at a particular location. The GDx-VCC compensates for corneal birefringence using an algorithm that allows compensation for each cornea individually.

The following GDx-VCC parameters were considered: temporal-superior-nasal-inferior-temporal average, which is the mean average of the 360° retinal nerve fiber layer thickness; superior and inferior averages; temporal-superior-nasal-inferior-temporal standard deviation, which is the standard deviation of the retinal nerve fiber layer thickness measurements of 360° nerve fiber indicator; symmetry; superior, inferior, and superior/nasal ratios; maximum, inferior, and ellipse modulation; and normalized superior and inferior areas. In addition, to better evaluate the change in the corneal birefringency, the slow polarization axis and the magnitude of the polarization were calculated before and after PRK. The following GDx-VCC analyses were performed in all patients: preoperative macular and retinal nerve fiber layer image, uncorrected postoperative retinal nerve fiber layer image using the same preoperative macular polarization map, and corrected postoperative macular and retinal nerve fiber layer image. In addition, central corneal thickness and intraocular pressure (IOP) were measured before and after PRK in all patients.

All patients underwent PRK using a NIDEK EC-5000 excimer laser (NIDEK Co Ltd, Gamagori, Japan) to correct refractive error. The optical zone was marked at 8 mm, and manual removal of epithelium was performed with a spatula and surgical sponges. Laser application was performed with a minimal optical zone diameter of 6 mm.

Data were analyzed by descriptive analysis. A paired Student t test was used to compare the two sets of data when the distribution of the data was normal. The Wilcoxon matched pair test was used when the distribution of the data was non-normal. Because the number of patients included in this study was relatively small and to avoid labeling differences that occurred by chance as significant, P values <.01 were considered statistically significant.

RESULTS

Patient demographics are shown in Table 1. Thirty-two eyes of 32 patients (14 men and 18 women) were included. Average myopia was −5.14 ± 2.34 diopters (D) (range: −3.00 to −10.50 D), and the average ablation depth was 113 ± 32 μm. Mean time between pre- and postoperative treatment measurements was 107 ± 15 days. After PRK, central corneal thickness (P < .001), polarization axis (P < .001), and magnitude (P = .003) changed significantly (Tables 1 and 2).

Table 3 shows the results of the pre- and postoperative GDx-VCC measurements. In particular, a comparison of the pre- and corrected postoperative measurements found the temporal-superior-nasal-inferior-temporal average and superior maximum increased significantly (P < .001). A comparison of the preoperative and uncorrected postoperative measurements showed changes in the superior, inferior, and superior/nasal ratios; maximum and ellipse modulation; and temporal-superior-nasal-inferior-temporal average and standard deviation were statistically significant (P < .01) (Table 3).
After PRK, some GDx-VCC parameters changed significantly \( (P < .01) \) both when corneal birefringency was corrected and when no correction was applied. Furthermore, when the corrected and uncorrected postoperative data were compared, some parameters changed significantly (Table 3). In particular, superior and superior/nasal ratios, ellipse modulation, and temporal-superior-nasal-inferior-temporal standard deviation changed significantly \( (P < .01) \).

**DISCUSSION**

Using the GDx-FCC, Gurses-Ozden et al\(^{20}\) found total, superior, inferior, nasal, and temporal mean retinal nerve fiber layer thickness was significantly thinner after LASIK. Changes following LASIK could be explained by many different hypotheses such as a change in the corneal birefringent properties or ganglion cell damage due to a damaging increase of IOP during the corneal lamellar cut. Tsai and Lin\(^{13}\) detected a significant effect on retinal nerve fiber layer thickness 1 month after LASIK; they speculated such a finding could be explained either by indirect mechanical damage on ganglion cells or by a change in corneal polarization.

In LASIK candidates, the average refractive error is usually higher than in PRK candidates.\(^{12,20}\) Ozdek et al\(^{12}\) showed retinal nerve fiber layer thinning was proportional to increasing refractive error. These studies showed changes in retinal nerve fiber layer thickness up to 1 month from surgery.\(^{12-15}\)

When GDx-FCC and optical coherence tomography were compared, different results of the retinal nerve fiber layer assessment were obtained. Gurses-Ozden et al\(^{19}\) found significant retinal nerve fiber layer thickness changes after LASIK using scanning laser polarimetry, whereas no change was found when the retinal nerve fiber layer was measured by optical coherence tomography. Carpineto et al\(^{21}\) also found no significant change in retinal nerve fiber layer thickness by optical coherence tomography after PRK, which was a surgical technique without any intraoperative increase of IOP.

In two studies on monkeys, Hayreh et al\(^{32,33}\) showed central retinal artery occlusion for less than 100 minutes produced no apparent morphometric evidence of optic disc damage. In a human study, after increasing IOP by compression for 45 seconds in healthy volunteers, Iester et al\(^{34}\) found no difference in retinal nerve fiber layer thickness 2 minutes or 1 month after the acute increase of IOP. They showed a mild transient increase of IOP is unlikely to create ischemic damage with a consequent loss of fibers. The observed differences in retinal nerve fiber layer thickness before and after compression ranged from 0 µm to 6.3 µm, which correspond to the reproducibility value range of the technique.\(^{28-31}\)

Using the GDx-VCC, Zangwill et al\(^{24}\) obtained similar clinical results. They reported LASIK does not seem to change retinal nerve fiber layer thickness. They suggested that after LASIK, the reduction in retinal nerve fiber layer thickness by GDx-FCC was an artifact measurement most likely caused by erroneous compensation for corneal birefringence. Recently, using GDx-VCC, Choplin et al\(^{16}\) clinically confirmed the hypothesis that acute IOP increase is not involved in retinal ganglion damage.
cell loss. They showed the recorded changes in retinal nerve fiber layer measurements by scanning laser polarimetry after LASIK in patients with high myopia are due to changes in corneal birefringence. These retinal nerve fiber layer changes were not observed when the customized compensation was applied for the cornea. According to these observations, LASIK changes the cornea birefringence but does not affect the retinal nerve fiber layer thickness. In contrast, using the GDx-VCC, Centofanti et al.22 found temporal-superior-nasal-inferior-temporal average and standard deviation, superior thickness, and also nerve fiber indicator were affected by LASIK, although these changes were not clinically significant.

In this study, refractive surgery consisted of PRK. The refractive result was obtained by corneal flattening and thinning (Table 1), which also induced a shift of corneal polarization axis as well as a magnitude change as detected by the GDx-VCC (Table 2).

A significant change in IOP was found following PRK. Intraocular pressure was assessed using a Goldmann applanation tonometer, which essentially quantifies the force needed to flatten a deformable spherical surface to an applanated area of known and fixed diameter.35 After PRK, the corneal changes caused a significant decrease in IOP because a thinner cornea was more easily flattened for applanation.36,37

In this study, when preoperative scans were compared to corrected postoperative scans, only superior maximum and temporal-superior-nasal-inferior-temporal average changed significantly, but when preoperative scans were compared to uncorrected postoperative scans, many of the GDx parameters showed significant differences. Furthermore, when the corrected and uncorrected postoperative scans were compared, some parameters showed significant changes, outlining the role of corneal compensation (Table 3).
There recorded temporal-superior-nasal-inferior-temporal average and the superior maximum changes increased the measured retinal nerve fiber layer thickness after PRK irrespective of the application of the VCC, suggesting individual birefringence compensation may not be capable of fully balancing PRK-induced corneal changes. The nerve fiber indicator slightly improved after PRK, but this change was not clinically significant (Table 3).

The new corneal compensation, applied after PRK, allows minimizing artificial retinal nerve fiber layer thickness changes. However, subtle changes could also be due to the reproducibility, not-fully compensated corneal polarization, or PRK surgery, which could change corneal architecture in yet other unknown ways.

This study showed that after PRK, GDx-VCC parameters changed when the macular image was not re-taken, but when the birefringence correction was recalculated, most of the differences observed were corrected. Even if this finding is likely not to be clinically relevant, mild changes in GDx parameters in some patients could affect the interpretation of the results. Ophthalmologists should be aware of this possibility in patients who undergo PRK and should obtain a repeat macular image after corneal refractive surgery.

REFERENCES


