Improvement of Spatial Contrast Sensitivity Threshold after Surgical Reduction of Intraocular Pressure in Unilateral High-Tension Glaucoma

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Purpose. To measure the effect of a surgical reduction of IOP on the spatial contrast sensitivity threshold in eyes showing a considerably increased IOP but no glaucomatous visual field defect, on white-on-white computer-assisted static perimetry.

Methods. Prospective clinical trial, lasting 36 months; 10 consecutive subjects with untreated IOP $\geq$ 30 mm Hg in one eye and $\leq$18 mm Hg in the fellow eye, no evidence of field damage in both eyes, best corrected visual acuity $\geq$ 20/20 in both eyes, and scheduled for a primary trabeculectomy in the eye showing a high IOP. The spatial contrast sensitivity threshold was measured before surgery and at each follow-up visit.

Results. Preoperative spatial contrast sensitivity was worse in those eyes bearing a high IOP relative to the normal fellow eyes (paired samples *t*-test, $P < 0.0005$). An improvement of contrast sensitivity threshold, exceeding the 95% confidence limits of the preoperative test–retest variability, was observed at 3, 6, and 12 cyc/deg in each surgical eye at the end of follow-up. No change was observed in the fellow untreated normal eyes. The improvement correlated directly with the amount of decrease in pressure obtained by surgery.

Conclusions. Eyes with no field defects on white-on-white computer-assisted static perimetry, but bearing a IOP $\geq$ 30 mm Hg, show a decreased spatial contrast sensitivity. A surgically obtained reduction of IOP is paralleled by an improvement of spatial contrast sensitivity. (*Invest Ophthalmol Vis Sci.* 2005; 46:197–201) DOI:10.1167/iovs.04-0199

Glaucomatous damage to visual function is considered to be irreversible. Actually, recovery of visual field damage was reported in some patients on reduction of intraocular pressure (IOP). This improvement, when present, was related to the amount of pressure reduction achieved in each eye.[1–5] However, the existence of this phenomenon is still a matter for discussion.[6,7] Different stages of the disease in the tested eyes, different levels of IOP at baseline, differences in the treatment modalities (i.e., medical, surgical, laser), and spontaneous fluctuations of the visual field have been hypothesized as a possible explanation for the observed discrepancies among the individual surveys.[8]

During the natural history of a glaucomatous optic neuropathy, certain type of functional visual loss may occur substantially sooner than shown by standard visual fields.[9] In particular, defects in contrast sensitivity have been reported in some subjects before observable nerve fiber damage or visual field loss on standard achromatic computer-assisted perimetry.[10–13] While testing the reproducibility of a novel chart, developed for measuring spatial contrast sensitivity, Pomerance and Evans[14] showed, in a limited series of glaucomatous eyes, an improvement of foveal spatial contrast sensitivity threshold after a short-term course of topical β-blockers.

In this prospective, investigator-masked clinical trial, we tested foveal spatial contrast sensitivity before and after glaucoma surgery. The enrolled eyes had to show (1) an untreated IOP between 30 and 36 mm Hg at baseline and (2) a very early stage of the disease (i.e., pathologic cupping and normal results in white-on-white automatic perimetry).

Patients and Methods

Subjects already scheduled for a primary trabeculectomy in one eye at the glaucoma service of our institute and meeting the eligibility criteria listed in Table 1, agreed to be enrolled in the study. They signed a routine informed consent for surgery and a proper consent for having contrast sensitivity tested and the collected clinical data used for scientific purposes. The protocol adhered to the tenets of the Declaration of Helsinki and was approved by the local ethics committee. The fellow untreated eye of each subject was arbitrarily considered as the internal control.

Foveal spatial contrast sensitivity was tested by using a translucent chart (CSV-1000 system; Vector Vision, Arcanum, OH). The system provides a fluorescent luminance source that retroilluminates the chart. The instrument houses a series of photocells that automatically monitor and calibrate the instrument light level to 85 cd/m^2$\pm$ 0.1 log unit. At the testing distance of 8 feet, the translucent chart presents four spatial frequencies on a separate row of the test: 3, 6, 12, and 18 cyc/deg. Sensitivity levels at each frequency range from 0.7 to 2.08 (3 cyc/deg), 0.91 to 2.29 (6 cyc/deg), 0.61 to 1.99 (12 cyc/deg), and 0.17 to 1.55 (18 cyc/deg) log units.

Contrast sensitivity was measured three times (allowing a 2-minute interval between each test) in both eyes the day before surgery, according to the procedure described by Pomerance and Evans.[14] The third determination was considered the baseline. In this way, we offset the subjects for any short-term "learning effect." In fact, a slight improvement between the first and the second determination was observed in six subjects. No significant difference was detected between the second and the third measurements (data not shown).

A conventional limbus-based trabeculectomy at the 11 o'clock position was performed in all patients by the same surgeon (SAG). Six eyes needed postoperative argon laser suture lysis. Postoperative subconjunctival administration of up to 25 mg of 5-fluorouracil (5 mg/injection, at a weekly interval) was administered in nine eyes.

Spatial contrast sensitivity was measured 2, 6, 9, 12, 18, 24, 30, and 36 months after surgery in both eyes of each subject. Diurnal IOP curves were scheduled and performed concurrently (six readings, 8 AM to 6 PM) and the average of the two highest values was used for comparison with preoperative values.

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Table 1. Eligibility Criteria

- Normal visual field (G1 program; *Octopus,* Koeniz-Berne, Switzerland) in both eyes, as detailed by Caprioli.[15]
- IOP ≥ 30 mmHg in one eye and IOP ≤ 18 mmHg in the fellow eye (average of the two highest readings of the diurnal curve from 8 AM to 6 PM, six readings).
- A >0.2 difference in cup-to-disk ratio between the study eye and the contralateral normal eye, evaluated by indirect opthalmoscopy performed at the slit lamp.
- Visual acuity (best corrected) ≥ 20/20 in both eyes.
- Lens Opacities Classification Study II score = C_0, N_0, P_0.
- Refractive error between −5 and +3 diopters
- No previous treatment with any antiglaucoma medication.
- No concurrent treatment with systemic β-blockers.
- No history of diabetes

Central corneal thickness was measured by means of an ultrasound pachymeter (model AP2000; Nidek, Gamagori, Japan), 10 to 15 minutes before the first IOP reading of the phasing, at baseline, and at months 2 and 36 after surgery. Three readings in the central corneal region were performed every time, and the values were averaged for analysis.

Best corrected visual acuity (BCVA) was tested in both eyes of each subjects on admission in the study and at every follow up visit. The Early Treatment Diabetic Retinopathy Study (ETDRS) far-distance chart was adopted. LogMAR was calculated as reported elsewhere.[16]

The study was investigator masked. Therefore, each study variable was collected by personnel who were masked to treatment. The sample size provided a power of 90% for a minimal expected difference of 0.35 log with an estimated variance of 0.15 log. The paired and unpaired samples Student's *t*-test was adopted when analyzing the spatial contrast sensitivity changes.

Results

Ten patients (all were white; seven were male; age range, 36–62 years; median age, 48 years) were enrolled. The diagnosis on presentation were post-traumatic angle recession (n = 4), pigmentary dispersion (n = 3), pseudoexfoliative glaucoma (n = 2), and secondary glaucoma (n = 1). Each patient completed the follow-up. A transient <2-mm hyphema was observed in two eyes the day after surgery. Hyphema cleared uneventfully 48 hours later.

Figure 1 shows the mean IOP in the treated and untreated fellow eyes through follow-up. IOP was stable in the untreated eyes. A relevant IOP decrease was observed after surgery. This was followed by a progressive increase with time (mean preoperative IOP at 2 and at 36 months after surgery was 38.4 ± 4.5, 14.4 ± 1.7, and 17.8 ± 2.0 mm Hg ± SD). In no case was adjunctive medical treatment considered.

The mean changes of spatial contrast sensitivity observed at the end of follow-up are displayed in Figure 2. The preoperative spatial contrast sensitivities of the study eyes were lower than those measured in the fellow eyes at every spatial frequency ($P < 0.001$). At the end of the follow-up, the contrast sensitivity showed a significant improvement in the surgical eyes: in fact, the 3, 6, and 12 cyc/deg spatial contrast sensitivity threshold of the study eyes approached the values concurrently recorded in the fellow untreated eyes ($P > 0.2$).

Figure 3 displays the spatial contrast sensitivity threshold measured at the 36-month follow-up visit in both study and

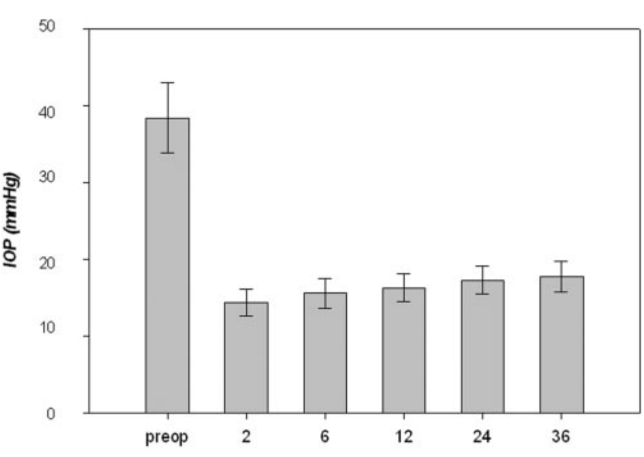

Figure 1. Mean IOP in the study eyes through follow-up. The IOP difference between before surgery and month 36 was statistically significant ($P < 0.001$).

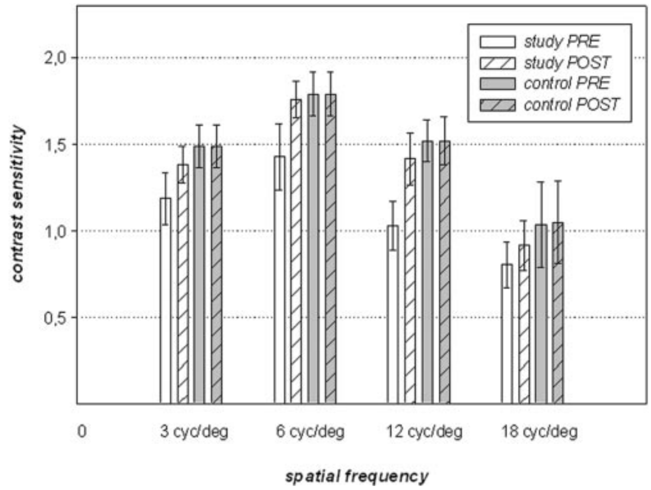

Figure 2. Changes in spatial contrast sensitivity between the pre- and the postoperative phase (36-month follow-up) in the study and control eyes. Bars, 95% confidence limits. Study PRE, study eyes at the preoperative evaluation; study POST, study eyes at the final (36 months) follow-up visit; control PRE, control eyes at the preoperative evaluation; and control POST, control eyes at the final (36-month) follow-up visit.

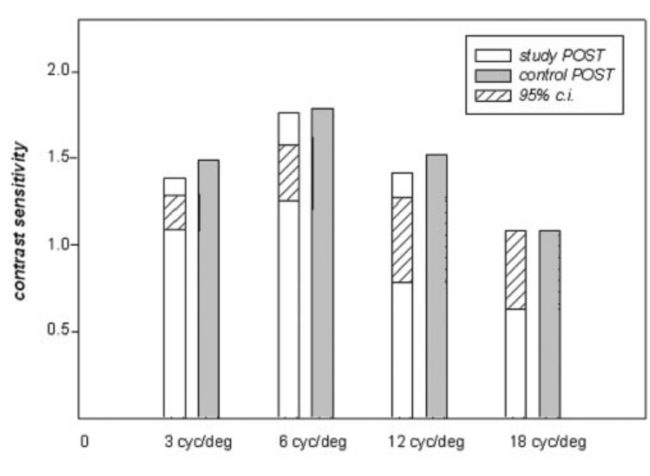

Figure 3. The columns show the SCS threshold at the end of the follow-up (36 months) in the study eyes (□) and in the control eyes (▩). *Hashed areas*: 95% confidence interval for the test variability in study eyes before surgery (coefficient of repeatability). study POST, study eyes at the final (36-month) follow-up visit: control POST, control eyes at the final (36-month) follow-up visit.

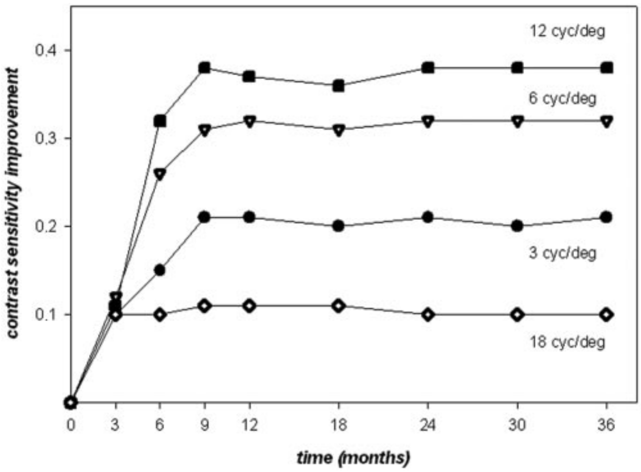

FIGURE 4. Spacial contrast sensitivity threshold changes in study eyes for each spatial frequency during the entire follow-up.

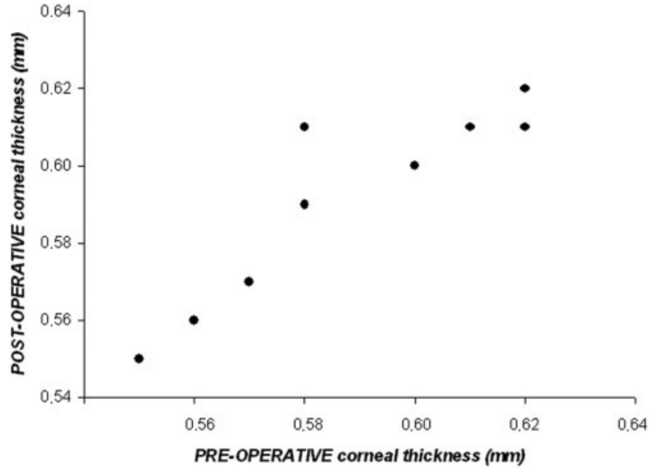

FIGURE 6. Pre- and postoperative (36-month follow-up) corneal thickness in the study eyes.

fellow eyes. The coefficient of repeatability (COR, i.e., 1.96 times the SD of the test–retest difference proposed by Bland and Altman for normally distributed data[17]) describes the 95% confidence interval for the variability in a test. The dashed areas show the 95% confidence interval of the contrast sensitivity measured in the study eyes before surgery. The postoperative values of contrast sensitivity in the surgical eyes exceeded the upper limit of the preoperative 95% confidence interval for test–retest variance at 3, 6, and 12 cyc/deg. Conversely, the improvement of contrast sensitivity was barely detectable at 18 cyc/deg (Figs. 2, 3).

Figure 4 shows the time course of the changes in contrast sensitivity observed in the surgical eyes. An improvement in spatial contrast sensitivity was evident at the first follow-up visit (2 months after surgery) at each frequency tested. Whereas at the 18-cyc/deg frequency no further improvement was observed, at the 3-, 6-, and 12-cyc/deg frequencies, tested continued to improve up to the 9-month visit.

Figures 5 and 6 show pre- and postoperative values of visual acuity and corneal thickness respectively, in the study eyes. No significant change was observed in both groups (statistics not shown).

Figure 7 shows the correlation between the amounts of contrast sensitivity threshold improvement (ΔSCS) measured at the end of follow-up and the amount of IOP reduction (ΔIOP) obtained after surgery in the study eyes. The highest level of correlation (detailed for each spatial frequency in Fig. 5) was found at 3 cyc/deg ($R^2 = 0.67$) and the lowest at 18 cyc/deg ($R^2 = 0.13$).

DISCUSSION

Spatial contrast sensitivity decreased in a cohort of human eyes showing no glaucomatous visual field defects on achromatic computer-assisted static perimetry but showing an increased IOP and an increased cupping of the optic disc. An improvement was observed on reducing the pressure by means of an uncomplicated surgical procedure.

Changes in brain function may induce significant modifications of spatial contrast sensitivity threshold.[18] When this oc-

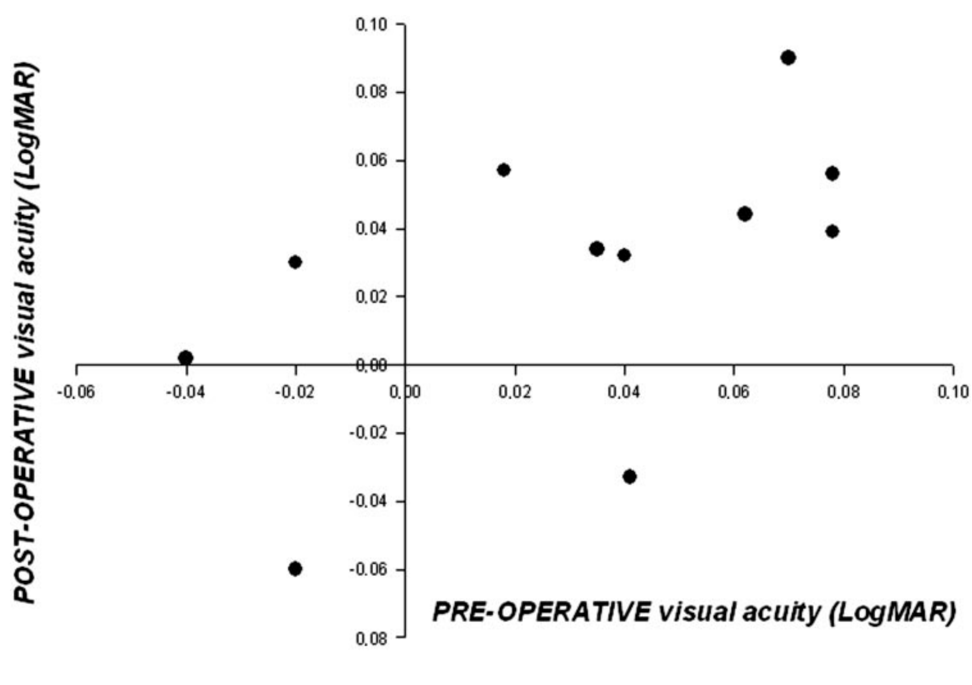

FIGURE 5. Pre- and postoperative (36-month follow-up) visual acuity in the study eyes.

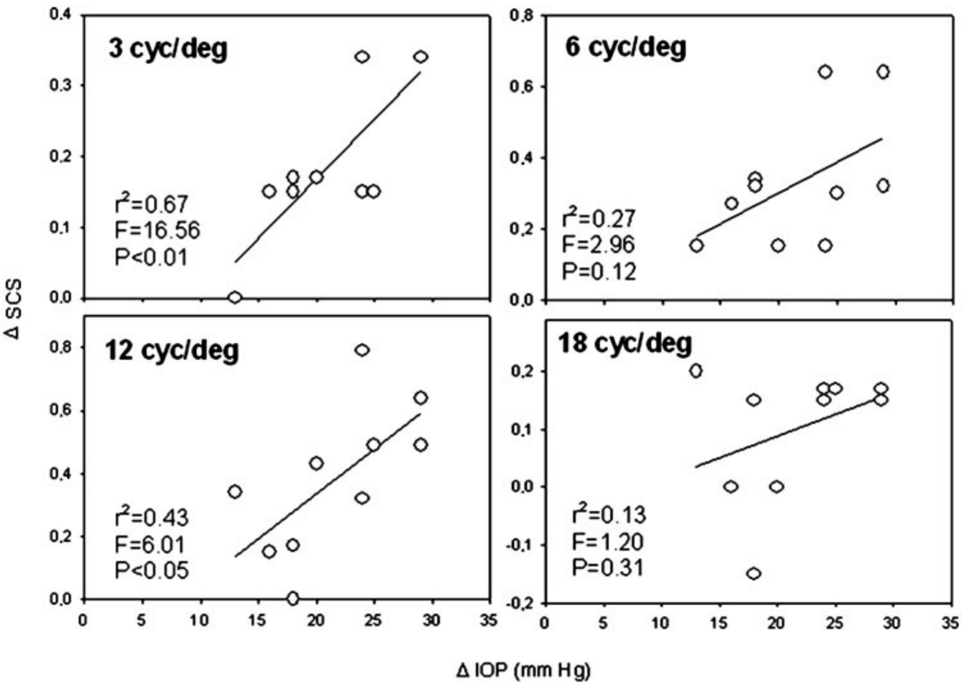

FIGURE 7. Correlation between contrast sensitivity threshold improvement (ΔSCS) and IOP reduction (ΔIOP) for each spatial frequency in the study eyes.

curs, both eyes of an individual patient are simultaneously affected. In our study, we observed no change of contrast sensitivity threshold in the fellow normal untreated eye during follow-up. Therefore, we can assume that the improvement of contrast sensitivity, observed in the surgical eye, was not related to changes in brain activity.

The improvement of spatial contrast sensitivity was not paralleled by changes in both BCVA and corneal thickness. In fact, the corneal thicknesses were within normal limits in both the treated and the untreated normal fellow eyes. Epithelial edema, with a consequent decrease in vision, ". . . does not occur until the cornea has swollen to 0.65 to 0.75 mm."[19] However, if the IOP is high, as it was in the eyes enrolled in our study, epithelial edema may occur at lesser thicknesses.[19] Should the postsurgical improvement of contrast be linked to a better transmission of light through the optical media (i.e., to a decreased blurring of the image), it would become more and more significant with increasing the spatial frequency of the stimuli. Actually, the improvement was observed at 3, 6, and 12 cyc/deg. The shift of threshold observed at 18 cyc/deg, albeit reaching a moderate statistical significance according to Student's *t*-test, was within the 95% confidence interval of the test–retest repeatability. The improvement of contrast sensitivity, when present, was a progressive phenomenon, the best threshold being reached 9 months after surgery (Fig. 4). Talks et al.,[20] while observing the recovery of the visual evoked potential (VEP) in 34 patients after an acute episode of accelerated hypertension, observed a progressive improvement of the P_{100} latency, which leveled out not earlier than 6 months after the pathologic event.[20]

The mechanism for the improvement in vision, as measured by contrast sensitivity, remains unknown. Ganglion cells die by apoptosis in glaucoma. A pressure-related decrease in the retrograde axonal transport has been suggested to trigger apoptotic phenomena in the nuclei.[21,22] Should the observed improvement of visual function match an improvement in the "living conditions" of the single cells, one might speculate that the surgery-induced decrease in IOP led to a better axonal flow across the optic nerve (i.e., the greater the drop, the greater the improvement). Of note, the amount of improvement of contrast sensitivity was related to the extent of IOP reduction obtained in each eye on surgery. When spatial contrast sensitivity is tested, ganglion cells represent the dominant component of the response to low-frequency stimuli.[23] Again, the best correlation between the amount of decrease in IOP and the amount of improvement was observed at 3 cyc/deg (i.e., the lowest spatial frequency tested by the CSV1000 chart; Vector Vision) in our cohort of patients.

An improvement of visual field has been described on pressure reduction in human glaucomatous eyes.[3,4,5,24,25] These data have not been confirmed by other reports.[6,7] When discussing this issue, Shields and Cooke[8] concluded that ". . . these conflicting findings may indicate that a critical level of pressure reduction and/or intervention at a critical time in the disease process is needed to achieve reversal of field loss." Spaeth[26] suggested that "glaucoma cannot with certainty be considered controlled unless the IOP has been lowered to a level associated with improvement in the disc or field."

Our data can be interpreted according to Spaeth's hypothesis. Therefore, the possibility that an improvement of contrast sensitivity could be adopted to identify the target IOP in glaucomatous eyes deserves further investigation.

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