

# Intraocular straylight before and after low myopic photorefractive keratectomy with and without mitomycin C

## *Dispersão de luz intraocular antes e depois da ceratectomia fotorrefrativa para baixa miopia com e sem mitomicina C*

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### ABSTRACT

**Purpose:** To evaluate ocular straylight before and after photorefractive keratectomy (PRK) for low myopia with and without topical mitomycin (MMC) treatment.

**Methods:** Patients who underwent PRK for low myopia were enrolled into the study. PRK without MMC was performed in 21 eyes (12 patients), whereas PRK with topical 0.02% MMC was performed in 25 eyes (14 patients). Both groups were treated using the NIDEK EC5000 excimer laser. Measurements were performed using the C-Quant straylight meter preoperatively and at two and four months postoperatively.

**Results:** The mean patient age was  $30 \pm 4$  years, and the mean spherical equivalent refractive error was  $-2.2 \pm 0.75$  D. The mean preoperative intraocular straylight values were  $1.07 \pm 0.10$  in the PRK without MMC group and  $1.07 \pm 0.11$  log(s) in the PRK with topical MMC group. At two months after surgery, there was a decrease in mean intraocular straylight values in both groups. However, a significant difference was only reached in the PRK with MMC group [ $0.98 \pm 0.09$  log(s),  $p=0.002$ ] compared with preoperative values, which was likely due to a greater scatter of measurements in the PRK without MMC group [ $1.03 \pm 0.13$  log(s),  $p=0.082$ ]. At four months postoperatively, ocular straylight values were not significantly different compared with those at baseline in either the PRK without MMC group [ $1.02 \pm 0.14$  log(s),  $p=0.26$ ] or in the PRK with topical MMC group [ $1.02 \pm 0.11$  log(s),  $p=0.13$ ].

**Conclusion:** PRK for low myopia decreases ocular straylight, and MMC application further reduces straylight in the early postoperative period. However, ocular straylight values do not significantly differ at four months after surgery compared with those at baseline.

**Keywords:** Photorefractive keratectomy; Myopia/surgery; Mitomycin; Wound healing

### RESUMO

**Objetivo:** Avaliar a dispersão de luz intraocular antes e depois da ceratectomia fotorrefrativa (PRK) para baixa miopia com e sem a aplicação tópica de mitomicina C.

**Métodos:** Pacientes submetidos à PRK para baixa miopia foram selecionados para o estudo. PRK sem MMC foi realizado em 21 olhos (12 pacientes) e PRK com MMC tópica a 0,02% foi realizado em 25 olhos (25 pacientes). Ambos os grupos foram tratados com o excimer laser da Nidek EC5000. Avaliações foram realizadas usando o medidor de dispersão de luz C-Quant no pré-operatório e com 2 e 4 meses de pós-operatório.

**Resultados:** A média de idade dos pacientes foi  $30 \pm 4$  anos e a média do equivalente esférico foi  $-2,2 \pm 0,75$  D. As médias da dispersão de luz intraocular no pré-operatório foram  $1,07 \pm 0,10$  no grupo PRK sem MMC e  $1,07 \pm 0,11$  log(s) no grupo PRK com MMC tópica. Após 2 meses da cirurgia houve uma diminuição na média da dispersão de luz intraocular em ambos os grupos. Entretanto uma diferença estatisticamente significativa, comparado com os valores pré-operatórios, foi observada apenas no grupo PRK com MMC ( $0,98 \pm 0,09$  log(s),  $p=0,002$ ), provavelmente devido as medidas com maior espalhamento de luz no grupo sem MMC ( $1,03 \pm 0,13$  log(s),  $p=0,082$ ). Após 4 meses de pós-operatório, os valores de dispersão de luz não apresentavam diferença estatisticamente significantes quando comparados com os valores iniciais, tanto no grupo sem MMC ( $1,02 \pm 0,14$  log(s),  $p=0,26$ ) quanto no grupo com MMC tópica ( $1,02 \pm 0,11$  log(s),  $p=0,13$ ).

**Conclusão:** PRK para baixa miopia diminui a dispersão de luz ocular e a aplicação de MMC contribui para uma ainda menor dispersão de luz no período pós-operatório inicial. Entretanto, quatro meses após a cirurgia a dispersão de luz intraocular não é significativamente diferente das medidas pré-operatórias.

**Descritores:** Ceratectomia fotorrefrativa; Miopia/cirurgia; Mitomicina; Cicatrização

### INTRODUCTION

Cornea laser refractive surgery has become generally accepted as a safe approach for correcting low-to-moderate refractive errors, and satisfactory visual acuity outcomes have been widely reported<sup>(1)</sup>. Nevertheless, the quality of vision may be altered due to changes in contrast sensitivity, glare, and/or higher-order aberrations<sup>(2)</sup>. Many previous studies have shown that corneal laser surgery impacts postoperative corneal aberrations and contrast sensitivity<sup>(3,4)</sup>. Conversely, relatively little work has focused on glare, despite patients frequently reporting

this as a troubling symptom, at least in the early postoperative period, following procedures such as photorefractive keratectomy (PRK).

Disability glare is the veiling of vision due to the forward scattering of light in the eye<sup>(5,6)</sup>. Straylight is a known source of disability glare<sup>(7)</sup>. The cornea can be a major contributor to total intraocular straylight<sup>(8)</sup>. During corneal wound healing, most patients experience transient changes in corneal transparency<sup>(9)</sup>. Injury to the epithelium and removal of the central epithelial basement membrane, which also occur in PRK, initiate a complex sequence of events mediated by

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epithelial-stromal interactions<sup>(10,11)</sup>. Corneal fibroblast and myofibroblast generation, in addition to changes in the quality and quantity of extracellular matrix, are the main alterations contributing to stromal opacity following PRK surgery<sup>(9,12)</sup>. Accordingly, changes in ocular straylight were described in the early postoperative stage after PRK correction in work performed nearly two decades ago<sup>(3)</sup>.

Subsequent to that study<sup>(13)</sup>, the intraoperative use of topical mitomycin C (MMC) has been shown to be an effective adjunct treatment modulating the corneal wound healing response and resulting corneal opacity<sup>(14)</sup>. The effect of MMC on cell replication and the consequent decreased cell density in the anterior stroma, along with changes in the extracellular matrix<sup>(15)</sup>, likely modify ocular straylight after PRK. The current study aimed to evaluate and compare intraocular straylight values in patients who underwent PRK surgery with and without topical MMC application for mild myopia and astigmatism.

## METHODS

### STUDY POPULATION

A total of 46 eyes of 26 patients who underwent PRK treatment were enrolled in the study. Inclusion criteria included patients between 22 and 45 years of age, stable refraction for at least one year, myopia correction of  $\leq 3.00$  diopters (D), astigmatism of  $\leq 1.00$  D, and central corneal thickness of  $>490$   $\mu\text{m}$  measured by ultrasonic pachymetry. Exclusion criteria were as follows: presence of corneal abnormalities suggestive of keratoconus or other corneal ectatic diseases, presence of ocular pathology (dry eye, active infection, clinically significant lens opacification, or clinically significant retina pathology), and pregnancy or lactation.

A complete ophthalmologic examination, including uncorrected visual acuity, best-corrected visual acuity, manifest and cycloplegic refraction, and obtaining clinical history, was performed on all patients. Tonometry, slit lamp examination, and dilated fundus examination were also performed. A Colvard infrared pupillometer (Oasis Medical Inc, Glendora, CA, USA) was used to assess scotopic pupil size. Additional tests performed included ultrasonic pachymetry (Corneo-Gage, Sonogage, Inc., Cleveland, OH), Placido-based corneal topography (EyeSys 2000, EyeSys Co., Houston, TX, USA), corneal tomography (Orbscan IIz, Bausch & Lomb Inc, Rochester, NY, USA), and wavefront analysis (OPD-Scan; NIDEK, Gamagori, Japan).

The institutional review board approved the study, and the tenets of the Declaration of Helsinki were followed. Informed consent was obtained from all patients after detailed discussion, including alternatives and potential complications.

### OCULAR STRAYLIGHT

Undilated straylight measurements were performed preoperatively and at two and four months postoperatively using the C-Quant straylight meter (Oculus Optikgerate GmbH, Wetzlar, Germany), as previously described<sup>(16)</sup>. The C-Quant straylight meter assesses the amount of light scattered toward the retina by a psychophysical approach called the compensation comparison method<sup>(16,17)</sup>. Briefly, the patient was presented with two alternative forced choices and was asked to choose between the stronger of two flickers presented in controlled background lighting<sup>(18)</sup>. The test field was divided into halves: compensation light was presented to one (randomly chosen) half of the test field, while no compensation light was presented to the other half. A bright, ring-shaped, flickering light source corresponding to a  $7^\circ$  scattering angle was used. When light scattering occurs in the eye, part of the flickering light from this ring also reaches the center of the retinal projection of the ring<sup>(19)</sup>. As a result, two flickers are perceived, which differ in modulation depth: one results from straylight only, and the other is a combination of straylight and compensation light flickering in counterphase with the straylight<sup>(16)</sup>. Due to a change in the average luminance of the stimulus and counterphase modulating light, the straylight value of the respective eye is approached when the halves

are balanced. The patients' responses were recorded by a two-alternative, forced-choice procedure. A psychometric curve was fitted to the patients' responses, from which the log (straylight parameter), estimated standard deviation (ESD), and quality factor (Q) were deduced. The measurement was considered reliable when ESD and Q were  $<0.08$  and  $>1.00$ <sup>(20)</sup>, respectively. Straylight values are expressed as log(s). Higher values indicate more straylight.

Measurements were taken under low-mesopic conditions by the same technician. Three straylight measurements were taken per eye at each time point, and mean values were calculated and recorded for data analysis.

### REFRACTIVE SURGERY PROCEDURE

Stromal tissue ablations were performed with the NIDEK EC 5000 CXIII excimer laser system (NIDEK, Gamagori, Japan). The epithelium was mechanically removed using a blunt blade, and an optical zone of 6.0 mm with a 7.5-mm transition zone was used in all cases. When used, 0.02% MMC was applied for 30 s after tissue ablation, and the cornea was subsequently irrigated with balanced salt solution.

All eyes were treated with 0.5% moxifloxacin hydrochloride ophthalmic solution four times daily for one week after PRK. Further, 1% prednisolone acetate ophthalmic suspension was administered as one drop four times daily for the first week, three times daily for the second week, twice daily for the third week, and once daily for the last week. In addition, artificial tears were used four to eight times a day as needed after surgery. Bandage contact lenses were worn for five to seven days after surgery.

### STATISTICAL ANALYSIS

Statistical analysis was performed with SPSS version 20.0 software (SPSS, Inc, Chicago, IL). All datasets were tested for normality using the Kolmogorov-Smirnov test. Data are expressed as the mean  $\pm$  standard deviation. All data were normally distributed. The comparison of pre- and postoperative straylight values was performed using the paired *t*-test, and differences between the groups were determined by the independent *t*-test. Correlations between ocular straylight, wavefront error, and spherical equivalent values were investigated using Pearson's correlation analysis. A *p*-value of  $<0.05$  was considered to be statistically significant.

### RESULTS

A total of 46 eyes of 26 patients (21 women and 5 men) were enrolled into the study. The mean age was  $30 \pm 4$  years (range, 25-45 years); the mean myopic error was  $1.96 \pm 0.69$  diopters (D) (range,  $-0.75$  –  $-3.00$ ); the mean astigmatism was  $0.43 \pm 0.42$  D (range, 0-1.00 D); the mean spherical equivalent was  $-2.2 \pm 0.75$  D (range, 1.00-3.50 D). PRK surgery without MMC was performed in 21 eyes of 12 patients and PRK surgery with topical 0.02% MMC was performed in 25 eyes of 14 patients. The demographic and baseline clinical characteristics of the patients stratified by the application of MMC are provided in table 1.

The mean preoperative intraocular straylight values were  $1.07 \pm 0.10$  log(s) and  $1.07 \pm 0.11$  log(s) in the PRK without MMC and PRK with topical MMC groups, respectively. During postoperative follow-up, all patients had complete epithelial healing within 5 to 7 days after surgery, and no late haze was noted after the first month. Values on pre- and postoperative ocular straylight, wavefront error, and spherical equivalent in both PRK groups are summarized in table 2. At two months after surgery, there was a decrease in the mean intraocular straylight values in both groups compared with those at baseline; however, a significant difference was observed only in the PRK with MMC group ( $p=0.002$ ) and not in the PRK without topical MMC group ( $p=0.082$ ). At four months after surgery, there was an increase in straylight in the PRK with topical MMC group when compared with the

two-month value; however, it failed to reach a significant difference (p=0.107). In the PRK without topical MMC group, the intraocular straylight value remained unchanged at four months when compared with the two-month value after surgery (p=0.74). In addition, at four months postoperatively, ocular straylight values were not significantly different compared with those at baseline in the PRK without MMC group (p=0.26) or the PRK with topical MMC group (p=0.13).

Regarding wavefront analyses, there was a trend toward increasing higher-order aberration (HOA) in both groups after surgery (Table 2) (p=0.074, PRK without MMC group at four months after surgery compared with baseline; p=0.037, PRK with MMC group at four months after surgery compared with baseline). However, between the groups, HOA values were not statistically significant different at any time point. Finally, no correlation was found between ocular straylight and wavefront error values and between ocular straylight values and spherical equivalent correction.

**DISCUSSION**

The current study revealed that low myopic PRK correction tends to decrease ocular straylight values either with or without topical MMC application. In addition, straylight reduction was more pronounced in the early postoperative period at 2 months after PRK with MMC treatment. At four months after refractive surgery, however, such reduction was not significantly different in any of the two groups

compared with baseline values. To the best of our knowledge, no prior study has evaluated the impact of topical MMC on ocular straylight after PRK surgery.

Many structures are involved in the generation and modulation of ocular straylight, including the cornea, lens, iris, and intraocular media<sup>(21)</sup>. Light scattered by lenses tends to increase with age and increases with cataract<sup>(19)</sup>. Corneal scattered light is relatively constant<sup>(22)</sup>, although it may change after corneal refractive procedures<sup>(21)</sup>. Considering other corneal factors that might also affect ocular straylight, Li and Wang<sup>(21)</sup> reported that central corneal thickness and anterior chamber depth have no significant association with ocular straylight.

Our findings are in agreement with previous studies that have also shown a decrease in postoperative ocular straylight values after refractive surgery<sup>(23,24)</sup>. Lapid-Gortzak et al.<sup>(24)</sup> found a decrease in ocular straylight values at three months after laser *in situ* keratomileusis (LASIK) and laser-assisted subepithelial keratectomy for myopic correction. In that study, the authors referred to ocular straylight as a parameter of corneal clarity and suggested that it is correlated to the stromal cellular response to surgery. It has been recognized that the anterior stromal cell density decreases after PRK correction<sup>(15,25)</sup>, and the depletion of keratocytes in the anterior stroma has been shown to be higher after MMC application<sup>(14)</sup>. It is also known that stromal corneal fibroblasts and keratocytes contribute to the total amount of ocular light scattered<sup>(26)</sup>. Thus, we believe that the observed changes in ocular straylight values in the early two-month period after PRK occurred due to a reduction of the anterior stromal cell density. In the PRK with MMC group, the effect was likely greater due to the inhibition of keratocyte replication by the drug<sup>(15)</sup>. In that group, it is likely that at least partial recovery of stromal cell density at four months after surgery led to an increase in the intraocular straylight value compared with the two-month value. It could also be speculated that the higher reduction in straylight in the PRK with MMC group compared with that in the PRK without MMC group is related to a higher ablation depth (higher spherical equivalent correction)<sup>(18)</sup>. However, a previous study failed to show any relationship between ocular straylight and ablation depth<sup>(21)</sup>. In concordance with our findings, other studies have shown that after an initial decrease, ocular straylight values slowly return to the preoperative state<sup>(23,24)</sup>.

It is important to note that many previous studies found an increase in ocular straylight values after laser correction surgery. However, most of these investigations were based on LASIK surgery where corneal flap creation appeared to be a critical factor in increases in ocular straylight<sup>(20,21)</sup>. Flap generation may lead to microfolds and particles at the interface<sup>(27)</sup>, which may contribute to increased ocular straylight. According to Wallau and Campos<sup>(28)</sup>, eyes undergoing PRK with MMC have less higher-order aberrations and better contrast sensitivity than LASIK eyes when the level of correction is similar in both groups, emphasizing the role of the corneal LASIK flap in the quality of vision. Moreover, the level of myopic correction in previous studies was also higher<sup>(21,29)</sup>, which is likely to trigger a more exuberant wound healing response, possibly associated with generation of

**Table 1. Demographic and baseline clinical data of patients in the photorefractive keratectomy (PRK) without topical mitomycin (MMC) group and the PRK with topical MMC group**

	Treatment group		p-value
	PRK without MMC	PRK with MMC	
Patients (n)	12	14	
Sex	11F/1M	10F/4M	
Eyes (n)	21	25	
Age (years)	30 ± 4 (25-34)	30 ± 5 (25-56)	0.067
Preop myopia (D)			
Mean ± SD	-1.47 ± 0.47	-2.37 ± 0.56	0.001
Range	-0.75 to -2.0	-1.25 to -3.0	
Preop astigmatism (D)			
Mean ± SD	-0.26 ± 0.36	-0.59 ± 0.42	0.002
Range	0 to -1.00	0 to -1.00	
Preop mean keratometry (D)	42.78 ± 1.98	43.74 ± 1.24	0.072
Low-mesopic pupil size (mm)	6.02 ± 0.5	6.02 ± 0.7	0.085
Total of HOA	0.33 ± 0.10	0.32 ± 0.07	0.079

F= female; M= male; D= diopter; HOA= higher-order aberration.

**Table 2. Mean values ± standard deviations of pre-and postoperative intraocular straylight [log(s)] values, wavefront error (µm), and spherical equivalent (D) after photorefractive keratectomy (PRK) without topical mitomycin C (MMC) and PRK with topical MMC**

	Intraocular straylight			Wavefront error			Spherical equivalent		
	Preop	Postop 2 months	Postop 4 months	Preop	Postop 2 months	Postop 4 months	Preop	Postop 2 months	Postop 4 months
	PRK without MMC	1.07 ± 0.10	1.03 ± 0.13	1.02 ± 0.14	0.33 ± 0.10	0.417 ± 0.127	0.388 ± 0.106	-1.63 ± 0.57	-0.37 ± 0.41
PRK with MMC	1.07 ± 0.11	0.98 ± 0.09	1.02 ± 0.11	0.32 ± 0.07	0.387 ± 0.064	0.412 ± 0.083	-2.66 ± 0.54	-0.30 ± 0.83	-0.05 ± 0.34

myofibroblasts and greater production of disorganized extracellular matrix as well as activated keratocytes (corneal fibroblasts), thus increasing ocular straylight. There are several reports<sup>(13,30)</sup> of haze as a cause of increased straylight, and we agree that the development of moderate-to-severe haze is an important factor<sup>(24)</sup>. In the present study, the overall low myopic correction, with and without MMC application, likely led to the faster recovery of corneal transparency.

Study limitations include the relatively small number of eyes included in each group and the lack of ultrastructural assessment.

At four months postoperatively, which is a relatively short follow-up period, the straylight values in both the PRK with MMC group and the PRK without MMC group were similar; hence, the use of topical MMC is not likely to influence the quality of vision with regard to straylight.

Further long-term follow-up studies with confocal microscopy could advance our understanding of factors contributing to ocular straylight after laser corneal surgery<sup>(21)</sup>. The present study shows that low myopic PRK correction, decreased ocular straylight at two months after surgery, and topical MMC application likely contribute to ocular straylight reduction. However, at four months after PRK surgery, this reduction appears to not be substantial. The role of ocular straylight in overall patient satisfaction following corneal laser surgical procedures remains to be elucidated.

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