



# Late-onset corneal haze after intrastromal corneal ring implantation in an eye with previous topography-guided PRK

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## ABSTRACT

**Purpose:** To report a case of late-onset corneal haze 3 months after intrastromal corneal ring segment (ICRS) implantation in an eye with previous transepithelial topography-guided photorefractive keratectomy (TG-PRK). **Observations:** A 40-year-old woman with stable keratoconus for 10 years underwent limited TG-PRK with mitomycin C in both eyes for mixed astigmatism. After four years, with atopic symptoms worsening and eye rubbing, the patient presented keratoconus progression in the left eye with increased irregular astigmatism. An ICRS was implanted with initial improvement in vision. Three months later severe subepithelial haze was observed along the ring groove.

**Conclusion and importance:** This is the first report of subepithelial haze after ICRS implantation. This report increases the evidence that permanent corneal wound healing changes occur after PRK and that late-onset haze may be triggered by corneal remodeling, as little inflammation or epithelial defect occurs after ICRS implantation. We do believe the detection of triggers, identification of risk factors of late-onset haze and appropriate preoperative counselling have an increasing importance due to the rising number of patients that have undergone PRK.

## 1. Introduction

Photorefractive keratectomy (PRK) is a technique used to correct myopia, hyperopia and astigmatism for over 30 years.<sup>1</sup> Corneal wound healing process following PRK is a complex inflammatory cascade eventually leading to some degree of anterior subepithelial haze.<sup>2</sup> Mild haze usually appears between one and three months after surgery and does not cause clinical symptoms.<sup>3</sup> Some of the clinical factors that have been correlated with haze formation are the length of time required for epithelial defect healing, depth of ablation, removal of the epithelial basement membrane, ablation of Bowman's layer and the smoothness of stromal surface after the ablation.<sup>3,4</sup>

Late-onset corneal haze is described as when the onset starts 6 months or more after surgery.<sup>3</sup> Fortunately, this type of haze is not common after isolated PRK but may occur after different stimuli in eyes previously submitted to PRK. It also has less tendency to spontaneously resolve over time.<sup>3</sup> Persistent defects in the regenerated corneal epithelial basement membrane seems to play a critical role in late haze formation.<sup>4</sup>

Age-related changes of corneal collagen fibers observed in

biomechanical studies have shown a tendency toward progressive corneal stiffness.<sup>5</sup> Continuous corneal crosslinking (CXL) takes place with aging and halts the progression of keratoconus.<sup>5,6</sup> Many controversy resides when a surface ablation treatment could be suitable for a keratoconic patient, however different studies have shown good refractive and visual results and lack of keratoconus progression in older patients with stable keratoconus.<sup>5,7,8</sup>

In this paper we describe a case of late onset haze which was triggered by the implantation of an intracorneal ring segment (ICRS) in a keratoconic patient who had been previously submitted to topography-guided PRK (TG-PRK) for corneal regularization and mixed astigmatism treatment.

## 2. Case report

A 40-year-old woman with stable keratoconus for 10 years presenting a pre-operative refraction of +1.00–1.75 × 70 in the right eye (OD) and +1.00–4.25 × 115 in the left eye (OS), underwent transepithelial TG-PRK in both eyes. Corrected distance visual acuity was 20/25 in OD and 20/30 in OS. Central corneal thickness was 469 μm in OD and 453 in

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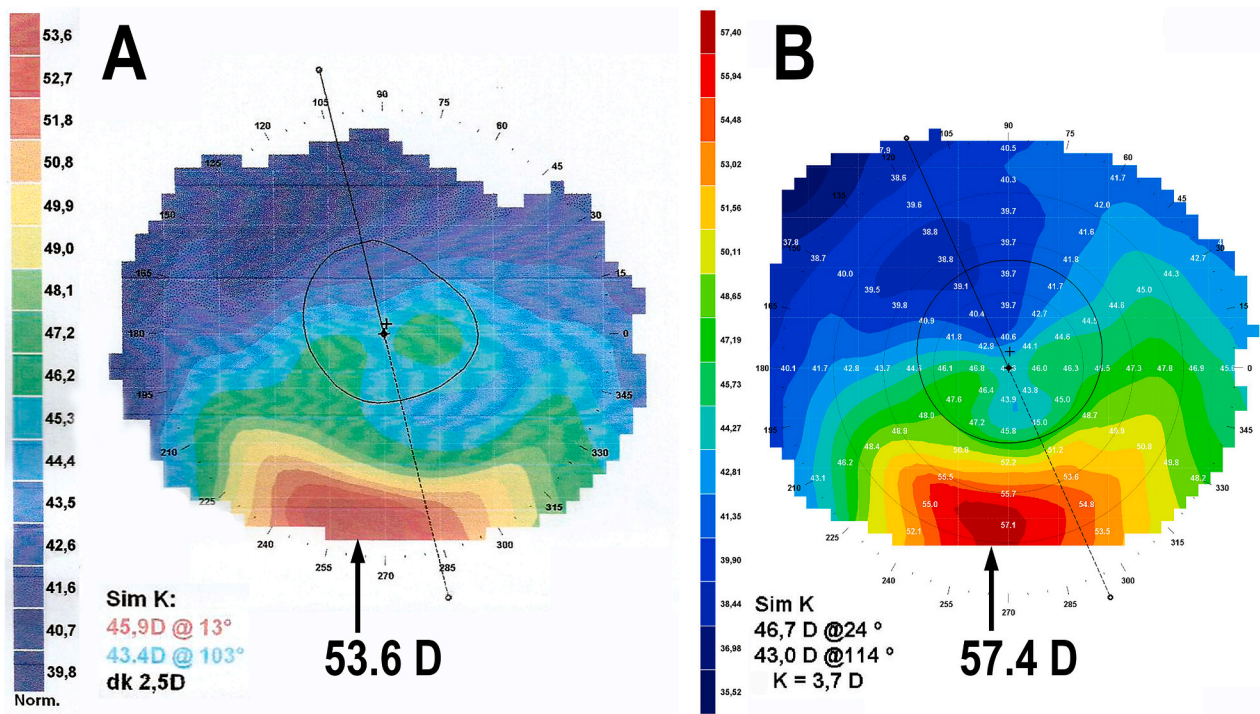


Fig. 1. A. Topography three months after TG-PRK. B. Four years later keratoconus progression was observed, with increased apical keratometry and irregular astigmatism.

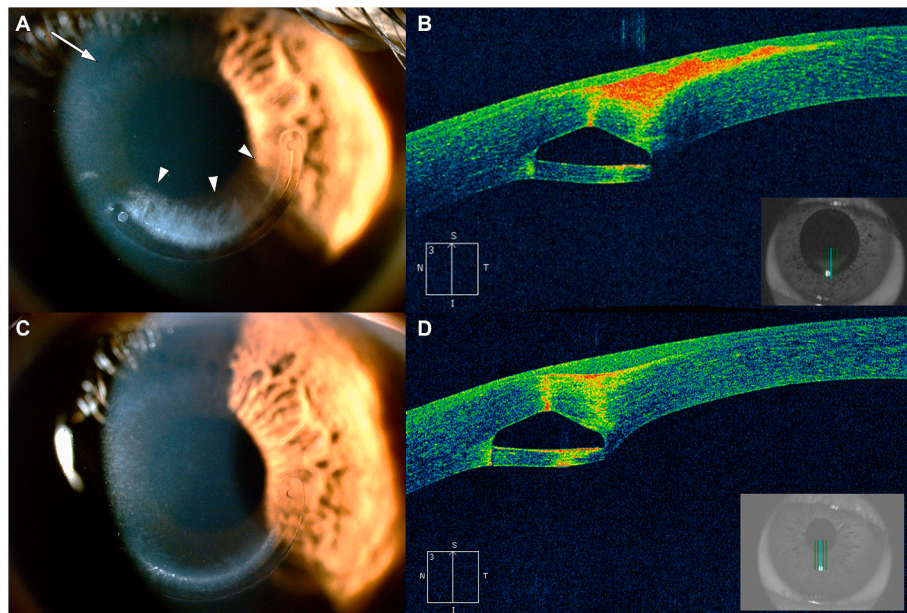


Fig. 2. A. Grade 3+ subepithelial haze formation along the ring groove 3 months after ICRS implantation. B. Hyperreflectivity in the subepithelial layer and anterior stroma in anterior segment OCT 3 months after ICRS implantation, comparable to PRK haze. C and D. One year after haze treatment important improvement was observed.

OS. A Schwind Amaris 500 Hz excimer laser (Kleinostheim, Germany) was used with an optical zone of 6.5mm in OD (calculated central and maximum stromal ablations of 19.64µm and 39.96µm, respectively) and 6.0mm in OS (calculated central and maximum stromal ablations of 42.12µm and 65.93µm, respectively). Mitomycin C (MMC) 0.02% was applied in both eyes for 1 min after ablation. Postoperative was uneventful and after 3 months uncorrected distance visual acuity (UDVA) was 20/30 OD and 20/40 OS, with trace subepithelial peripheral haze in both eyes. Four years later, the patient returned complaining of

decreased vision in OS over the last year with worsening ocular atopic symptoms and eye rubbing. UDVA was 20/100 and topography showed keratoconus progression, with an increase in apical keratometry from 53.6 D to 57.4 D (Fig. 1 A and B). There were no signs of haze at this time. Dynamic refraction in OS was +2.75–4.00 × 75 (20/30). It was decided to intensely treat the ocular allergy and to implant one 160° arc/200µm-thickness Ferrara ring segment at axis 22°. Surgery was uneventful, performed with manual technique. After one week the patient improved to 20/40 UDVA. Three months later, she returned

complaining of progressive blurred vision. Biomicroscopy showed grade 3+ subepithelial haze formation along the ring groove (Fig. 2A). Anterior segment OCT showed hyperreflectivity in the subepithelial layer and anterior stroma, equivalent to PRK haze (Fig. 2B). After six months, there was no improvement on haze or vision despite adequate topical corticosteroid therapy. Refraction was  $+2.00-4.00 \times 105$  (20/30). With the purpose of reducing the haze, after manual epithelial scraping, a small optical zone (4mm) aspheric PRK was performed for  $+1.50-4.00 \times 105$  using the Schwind Amaris 1050 Hz laser (Kleinostheim, Germany), followed by application of MMC 0.02% for 2 minutes. Maximum ablation depth was  $26\mu\text{m}$  and occurred in the area of haze. One year later UDVA was 20/25 and dynamic refraction was  $+0.25-1.25 \times 115$  (20/20). Important haze regression was observed (Fig. 2C and D). After three years UDVA was 20/20; dynamic refraction was  $0.00-0.50 \times 110$  (20/20) and topography was stable.

### 3. Discussion

Late onset corneal haze in eyes with previous PRK has been reported with intervals varying from two to 20 years, following different stimuli, from cataract surgery, LASIK and vitreoretinal surgery to blunt trauma, corneal infections and UV-light exposure.<sup>1,9</sup> Despite the widespread use of ICRS in different scenarios, corneal haze has not been previously reported after its use in virgin eyes except from the mild subepithelial haze that occurs around the ring and tends to disappear in the following months.<sup>10</sup> The occurrence of haze after ICRS in an eye with a long-time history of PRK supports the evidence that permanent corneal wound healing changes occur after PRK. It also supports a different trigger for late-onset haze after PRK, namely corneal remodeling, as little inflammation or epithelial defect occurs after ICRS implantation.

The organization of the extracellular matrix is altered in the anterior stroma after PRK, with changes in cellular density and phenotype.<sup>2,4</sup> Stromal cells are activated under the influence of cytokines such as transforming growth factor beta (TGF $\beta$ ) and platelet-derived growth factor (PDGF) released from the epithelium.<sup>4</sup> Alteration in corneal permeability likely due to defective basement membrane regeneration and increased epithelium-derived TGF $\beta$  signaling to the stroma have been described as possible mechanisms.<sup>4</sup> Thus, a minimal corneal injury may initiate an inflammatory cascade leading to the contact of cytokines, growth factors and components from the lacrimal glands and conjunctiva with the corneal stroma, ultimately leading to haze formation.<sup>4</sup>

A smooth corneal surface after refractive surgery has been reported to decrease the possibility of defective basement membrane regeneration.<sup>4</sup> In our case, transepithelial TG-PRK was applied for corneal regularization and mixed-astigmatism treatment in a keratoconus patient. Topography-guided ablations tend to be deeper and more irregular than aspheric ablations, with a greater potential for irregular epithelial basement membrane regeneration, increasing the risk of this complication in our case. It is also important to emphasize that surface ablations are not usually recommended for keratoconic patients due to the increased risk of biomechanical instability. Particularly in this case, a 40-year-old patient presented topographically stable keratoconus for over ten years, and mixed astigmatism which allow a lower amount of tissue removal. Although we do recognize that a combined treatment of CXL and TG-PRK could potentially decrease the odds of biomechanical decompensation of the cornea, there is an increased risk of other complications, such as stromal haze and scar and late corneal remodeling.

### 4. Conclusion

This report increases the evidence that permanent corneal wound healing changes occur after PRK and that late-onset haze may be triggered by corneal remodeling, as little inflammation or epithelial defect occurs after ICRS implantation. Detection of triggers, identification of risk factors of late-onset haze and appropriate preoperative counselling have an increasing importance due to the rising number of patients that have undergone PRK.

### Patient consent

Written consent to publish this case has not been obtained. This report does not contain any personal identifying information.

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None.

### Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

### Declaration of competing interest

The authors do not have a commercial or proprietary interest in this work.

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### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ajoc.2020.100820>.

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