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CORRESPONDENCE

Sir,

**Femtosecond-assisted intrastromal corneal cross-linking for early and moderate keratoconus**

Collagen cross-linking by UVA light augmented by riboflavin was proposed to improve the biomechanical properties of keratoconic corneas.[1] As an alternative to the standard technique (riboflavin saturation of stroma through denuded corneal surface, followed by UVA irradiation[2–4]) we developed a femtosecond-assisted intrastromal pocket for riboflavin induction.

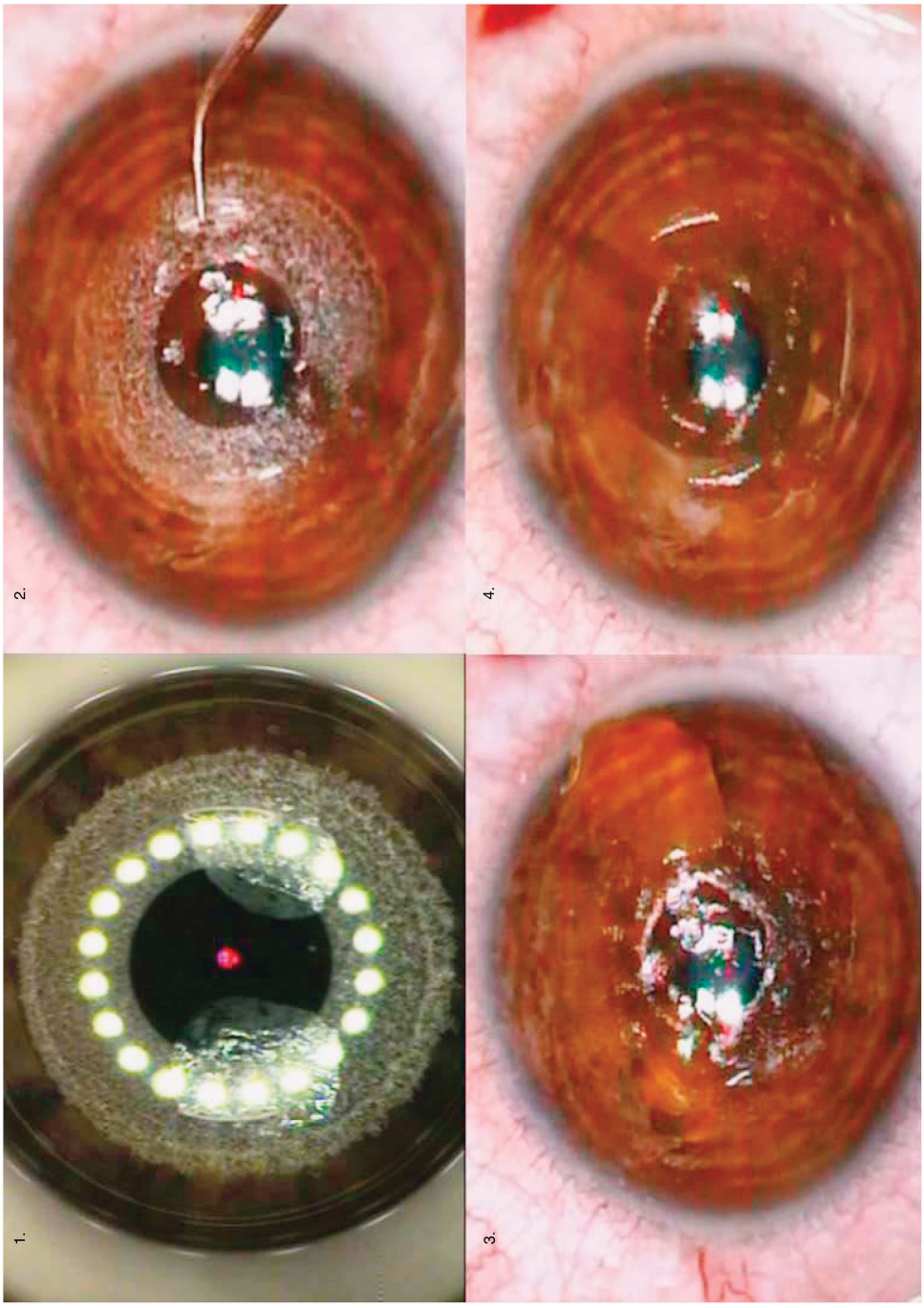


**Figure 1** (1) Creation of a 6-mm-diameter circular intrastromal pocket, by means of the femtosecond laser, leaving a clear optical zone of 3 mm. (2) Creation of two 0.5-mm-width entry channels 180° apart. Following the pocket creation, a tapered Intacs spatula mall Jameson muscle hook was used to enter and bluntly dissect the pocket. (3) Infusion of 0.3 ml of 0.1% riboflavin solution into the pocket using an Intacs stromal channel irrigation cannula. Infusion continued until the entire pocket was colored bright yellow due to the presence of the riboflavin solution. (4) A UVA irradiation source of ~370 nm wavelength (365–375 nm) was used for corneal surface irradiation.

*Case report*

Twelve eyes of 9 patients (mean age 29.75 ± 9.3 years) with early progressive keratoconus (K-readings > 48D, skewed steepest radial axis > 22°, superior–inferior difference on the 5 mm circle > 2.5D, inferior–superior difference > 1.5 D, minimum corneal thickness > 380 μm) were included. Progression was confirmed by K-reading increase of ≥ 1 D, or thickness decrease ≥ 5 μm in two consecutive Orbscan corneal tomographies.

A 6-mm-diameter doughnut-shaped intrastromal pocket was created at 200 μm depth by the Technolas Femtec 520 (Technolas Perfect Vision GmbH, Munich, Germany), leaving a 3 mm clear central optical zone (Figure 1, 1). Two 0.5 × 0.5 mm entry channels 180° apart were created, for riboflavin infusion and depressurization; a tapered Intacs spatula hook was used to bluntly dissect the pocket (Figure 1, 2). In all, 0.3 ml of 0.1% riboflavin in 20% dextran solution was introduced into the pocket using Intacs stromal channel irrigation cannula, until the entire pocket was coloured bright yellow (Figure 1, 3). Cornea was irradiated with UVA 365–375 nm light (3 mW/cm$^2$ irradiance) for 30 min. Total fluency at the corneal plane was 5.4 J/cm$^2$.

CDVA initially decreased at the first month ($P = 0.157$), followed by marked improvement at the 3rd and 12th months postoperatively ($P = 0.042$) (Figure 2). Significant reduction was observed in astigmatic power ($P = 0.016$), eccentricity ($P = 0.044$), and thinnest point corneal thickness 1 year postoperatively ($P = 0.043$). Keratoconus remained stable 12 months postoperatively, Kmax remaining unchanged and Kmin increasing after the first postoperative month ($P = 0.034$) (Table 1).

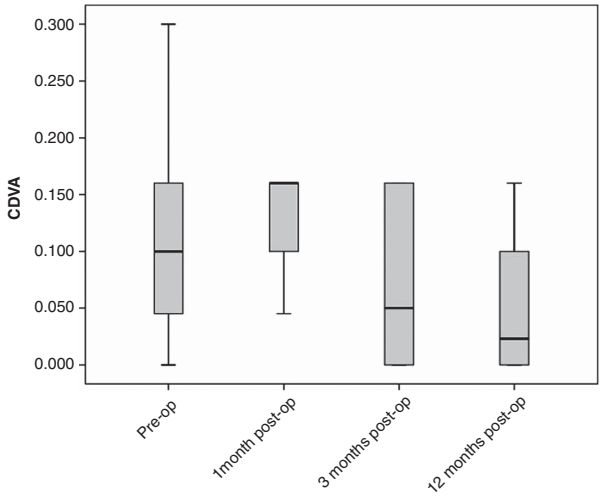


**Figure 2** Change in corrected distance visual acuity.

**Comment**

Riboflavin injected intrastromally into a precisely designed pocket is a painless procedure, with fast rehabilitation, reinforcing collagen at a selected location. The greatest effect of UVA light occurs at the area of maximal absorbance and its close vicinity.[5] Riboflavin introduced at the mid-stromal ring 200 μm deep will maximize the cross-linking effect around the protrusion.

This procedure's safety was proven by the unchanged endothelial cell density and morphology. As long as the cornea treated has a minimum thickness of 380 μm, the corneal endothelium (and deeper structures) will not experience damage.[6]

There was a significant improvement in CDVA, with concomitant stabilization for 12 months. Concerns about biomechanical instability from the femto ring have been countered.[7]

This surgical approach merits additional exploration in a larger cohort to further confirm the safety of the technique.

**Table 1** Preoperative, 1st, 3rd and 12nd postoperative month follow-up mean and standard deviation for corrected distant visual acuity (CDVA) (log MAR), Kmax, Kmin, and eccentricity (Ecc) (Topolyser, Oculus Instruments), thinnest point (μm) (thin), and irregularity in 3 mm (Irr) (Corneal Topography System—Bausch & Lomb—ORBSCAN II)

| | *Pre-op* | *1st* | *3rd* | *12nd* |
|---|---|---|---|---|
| CDVA | 0.1 ± 0.09[a] | 0.13 ± 0.05 | 0.07 ± 0.08 | 0.05 ± 0.06 |
| Kmax | 49.7 ± 2.86 | 48.6 ± 2.24 | 49 ± 3.11 | 50 ± 2.57 |
| Kmin | 45.6 ± 2.36[a] | 45.7 ± 2.46 | 46.2 ± 2.59 | 46.4 ± 2.28 |
| Ecc | 0.9 ± 0.3[a] | [b]0.8 ± 0.2 | [c]0.9 ± 0.3 | [d]1 ± 0.2 |
| Thin point | 417 ± 31.4[a] | 317 ± 23.3 | 357 ± 18.7 | 357 ± 30.8 |
| Irr | 4.7 ± 2.2 | 5.6 ± 0.2 | 4.6 ± 3.2 | 4.4 ± 2.7 |

Statistically important differences are marked as:
[a] Preoperative *vs* 1 year ($P < 0.05$).
[b] 1 month *vs* 1 year ($P < 0.05$).
[c] 3 months *vs* 1 month ($P < 0.05$).
[d] 3 months *vs* 1 year ($P < 0.05$).

## Conflict of interest

The authors declare no conflict of interest.

## References

1 Kohlhaas M, Spoerl E, Schilde T, Unger G, Wittig C, Pillunat LE. Biomechanical evidence of the distribution of cross-links in corneas treated with riboflavin and ultraviolet a light. *J Cataract Refract Surg* 2006; **32**: 279–283.
2 Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-a-induced collagen crosslinking for the treatment of keratoconus. *Am J Ophthalmol* 2003; **135**: 620–627.
3 Wollensak G. Crosslinking treatment of progressive keratoconus: new hope. *Curr Opin Ophthalmol* 2006; **17**: 356–360.
4 Tu KL, Aslanides IM. Orbscan II anterior elevation changes following corneal collagen cross-linking treatment for keratoconus. *J Refract Surg* 2009; **25**: 715–722.
5 Malhotra C, Shetty R, Kumar RS, Veluri H, Nagaraj H, Shetty KB. In vivo imaging of riboflavin penetration during collagen cross-linking with hand-held spectral domain optical coherence tomography. *J Refract Surg* **28**: 776–780.
6 Spoerl E, Mrochen M, Sliney D, Trokel S, Seiler T. Safety of UVA-riboflavin cross-linking of the cornea. *Cornea* 2007; **26**: 385–389.
7 Kanellopoulos AJ. Collagen cross-linking in early keratoconus with riboflavin in a Femtosecond laser-created pocket: initial clinical results. *J Refract Surg* 2009; **25**: 1034–1037; 86.

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**Sir,**

## Perfluropropane ($C_3F_8$) gas injection followed by deep anterior lamellar keratoplasty (DALK) in severe keratoconus

Acute corneal hydrops is the rapid development of corneal edema due to tears in the Descemet's membrane. Perfluropropane gas ($C_3F_8$) injection has been found useful in early resolution of hydrops.[1] Although gas injection has been found to accelerate the recovery of corneal hydrops, hydrops resolves spontaneously in most cases and reports of accelerated recovery do not refer to any control group. We present a case of hydrops in severe keratoconus managed by $C_3F_8$ injection and visually rehabilitated by deep anterior lamellar keratoplasty (DALK).

### *Case report*

A 19-year-old male presented in December 2012 with corneal hydrops of 3 weeks duration in his left eye. The Descemet's tear was central and localized. Non-expansile 14% $C_3F_8$ gas was injected in the operating room. Three weeks following injection, edema totally resolved (Figure 1). OCT showed extensive thinning of the entire cornea (Figure 2).

On 31 March 2013, DALK was performed. Partial thickness trephination was done with 9 mm trephine, which was decentered inferiorly to include the cone. Lamellar dissection was done manually without injection of air into the corneal stroma. Donor graft (9.5 mm) was sutured to the bed after removing the DM.

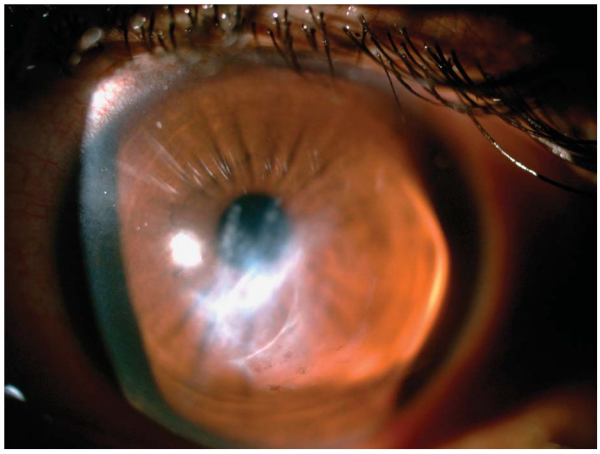

**Figure 1** Diffuse slit-lamp view showing resolved hydrops following $C_3F_8$ injection.

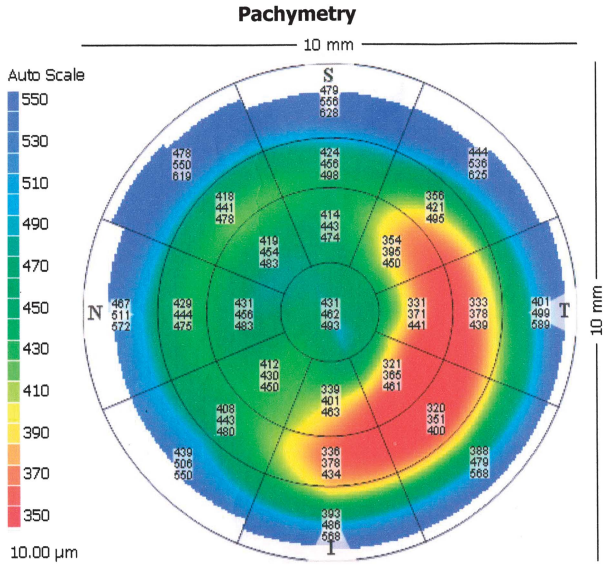


**Figure 2** OCT image after resolution of hydrops.