High Fluence Iontophoretic Corneal Collagen Cross-linking: In Vivo OCT Imaging of Riboflavin Penetration

To the Editor:

We read with interest the excellent article by Malhotra et al.[1] regarding in vivo estimation of riboflavin penetration using anterior segment optical coherence tomography (OCT). The article evaluates the effect of complete versus grid-like epithelial removal on riboflavin penetration during collagen cross-linking (CXL) in vivo using hand-held OCT. Twenty eyes of 20 patients were imaged intraoperatively at 30 and 60 minutes after starting the procedure. Results showed a homogeneous hyperreflective band extending to a mean depth of 54.2 µm after 30 minutes. In the grid-like removal group, the band was reported uneven in the epi-on areas.

We agree with the authors on the use of OCT for in vivo evaluation of riboflavin's penetration inside the stroma. Moreover, we agree that grid removal of the epithelium is not able to soak the corneal stroma evenly like the epi-off procedure.[2] In our study, we report the in vivo riboflavin penetration during CXL performed with iontophoresis versus conventional epithelium-off protocol using high-resolution OCT.

Six eyes (6 patients) undergoing CXL were measured preoperatively, intraoperatively, and postoperatively using high-resolution OCT. The epithelium was removed completely in the central 9-mm zone in 3 eyes (epi-off group), whereas riboflavin penetration through intact epithelium was promoted by an iontophoresis device in the remaining 3 eyes (iontophoresis group). The iontophoresis device for corneal application (8 mm in diameter) is placed on the cornea using an annular suction ring (low suction created by a syringe connected on the suction annulus). The device is filled with approximately 0.5 mL solution from the open proximal side, until the electrode (stainless steel mesh) is covered (**Figure 1A**). The device is connected to a constant current generator (I-ON XL, Sooft, Italy) set at 1 mA (the total dose of 5 mA × min is monitored by the generator).

The depth of the hyperreflective band (representing penetration of riboflavin) in the anterior corneal stroma was measured. In the conventional epi-off group, after 30 minutes of passive impregnation, a homogeneous hyperreflective band without fading effect was measured at mean depth of 80 µm (**Figure 1C**). In the iontophoresis group, we observed a less homogeneous hyperreflective band with a fading effect extending through the anterior 200 µm of the cornea (**Figure 1D**). This band was not visible until the end of irradiation time.

Intraoperative OCT imaging could be a useful technique to evaluate in vivo penetration of riboflavin inside the cornea. Although we still cannot demon-

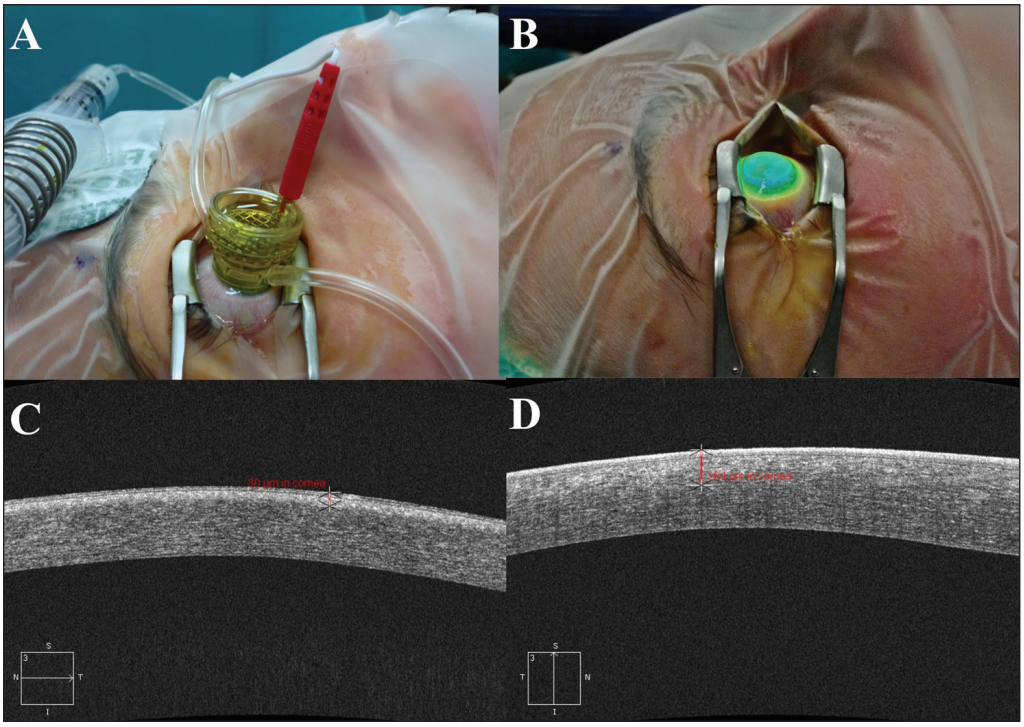

Figure 1. Iontophoresis impregnation phase (A) throughout an intact epithelium and (B) the irradiation phase in which it is possible to see a intense fluorescence. Intraoperative high-resolution optical coherence tomography images show (C) a homogeneous hyperreflective band at a mean depth of 80 μm in the epi-off group and (D) a less uniform band with a fading effect extending through the anterior 200 μm of the cornea.

strate the correlation between the band's intensity and riboflavin stromal concentration, we speculate that a higher OCT reflectivity should be positively correlated with it.

These results confirm early pre-clinical evidence that iontophoresis allows penetration of riboflavin through an intact epithelium. According to our hypothesis, the in vivo OCT results of the iontophoresis group showed a lower concentration of riboflavin in the stroma compared to the epi-off technique. More studies are needed to evaluate whether this difference could correlate with clinical CXL results.

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The authors have no financial or proprietary interest in the materials presented herein.

AUTHOR QUERIES

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