Corneal Collagen Cross-Linking for the Treatment of *Acanthamoeba* Keratitis

To the Editor:

Berra et al recently published an in vivo experimental study of corneal collagen cross-linking (CXL) on *Acanthamoeba* keratitis.[1] The authors analyzed the effects of CXL in rabbit corneas infected by stromal injection of 0.05 mL *Acanthamoeba*-containing suspension (40% trophozoites/60% cysts). On the basis of the analysis of corneal parasite concentration after CXL, the authors concluded, "Treatment of *Acanthamoeba* keratitis by corneal CXL with riboflavin and UV-A did not prove effective in decreasing the intensity and severity of *Acanthamoeba* keratitis." Considering the importance of this conclusion, we would like to highlight a number of aspects that merit further attention.

First, the infective form of *Acanthamoeba* is the trophozoites and not the cysts. The latter represent the resistive form of the parasite. The occurrence and relative amount of these 2 forms mainly depend on the phase of the disease. Therefore, correct interpretation of the CXL effect on *Acanthamoeba* keratitis requires an accurate verification of the disease phase, differentiating between the active infectious components and the chronic resistive elements.[2]

Second, the authors injected 8500 parasites (5100 trophozoites/3400 cysts). This number is extremely high and can be found only in chronic *Acanthamoeba* keratitis.[3]

Third, the authors do not report the depth of injection, which is an important parameter because the absorption rate of riboflavin 0.1% shows a logarithmic decay (Fig. 1), with most of the CXL energy absorbed in the first 100 μm. Hence, CXL effectiveness is highest in the first 100 μm of the corneal stroma, and its efficacy decreases with increasing depth.[4]

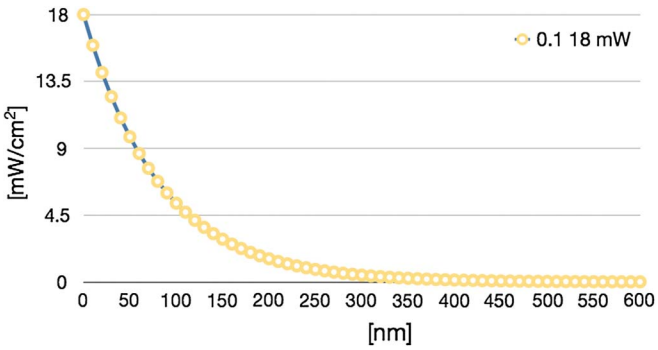

FIGURE 1. The figure shows the energy in the cornea depending on the corneal depth during a cross-linking with 18 mW/cm².

We believe that this study demonstrates the limitations of CXL treatment for chronic *Acanthamoeba* keratitis, but our data (unpublished) indicate that CXL may be a valuable tool for the treatment of acute *Acanthamoeba* infections localized mostly in the superficial corneal stroma with a low number of parasites and high proportion of trophozoites, which are more sensitive than cysts.

Financial disclosures/conflicts of interest: None reported.

Olivier Richoz*
Zisis Gatzioufas*
Farhad Hafezi*†

*Department of Ophthalmology, Geneva University Hospitals, Geneva, Switzerland
†Department of Ophthalmology, Doheny Eye Institute, Keck School of Medicine, University of Southern California, Los Angeles, CA

REFERENCES

1. Berra M, Galperín G, Boscaro G, et al. Treatment of Acanthamoeba keratitis by corneal cross-linking. *Cornea*. 2013;32:174–178.
2. Siddiqui R, Khan NA. Biology and pathogenesis of Acanthamoeba. *Parasit Vectors*. 2012; 5:6.
3. Thomas V, McDonnell G, Denyer SP, et al. Free-living amoebae and their intracellular pathogenic microorganisms: risks for water quality. *FEMS Microbiol Rev*. 2010;34:231–259.
4. Spoerl E, Mrochen M, Sliney D, et al. Safety of UVA-riboflavin cross-linking of the cornea. *Cornea*. 2007;26:385–389.