OCT) study was performed using the radial lines protocol, in which 512 pixels per line were obtained. In addition to these 6 radial lines, a fast macular thickness protocol was performed, resulting in a map with the values of the retinal thickness in the central 1-, 3-, and 6-mm area. Because of the nature of the irradiating 6 radial lines, the further from the foveal center, the higher the chance of missing small retinal cysts. In spectral-domain OCT machines, scanning protocols of vertical and horizontal lines can be chosen, but in clinical practice, there is always a compromise in choosing the scan width and a chance of missing abnormalities. It is possible theoretically that some of our discrepancies were caused by missing small isolated retinal cysts in between the scanning lines in a retina of normal thickness. However, it is more probable that the FA-positive/OCT-negative discrepancies were caused by true differences in combination with the limited resolution of the TD OCT scan, although the highest resolution (512 pixels/line) was used.

In their comment, Khanduja and associates suggest that atrophic retinas with macular edema (ME) could be discovered on OCT by the presence of cysts. However, diffuse macular edema manifests without cysts.[2,3] Purely relying on the presence of retinal cysts can be misleading. Retinal thickening in an already atrophic retina resulting from long-standing edema or inflammation then may remain unnoticed. Longitudinal measurements of the changes in the retinal thickness are needed to note an excess of fluid present in an atrophic retina and to make the diagnosis of ME.

The suggestion to compare the patients with a first attack, a recurrent attack, and inactive uveitis is valuable. Our study was based mainly on patients with chronic macular edema and including the patients with macular edema in its very early phase may reveal different percentages of discrepancies compared with our results. However, we assessed our population for the duration of the uveitis and ME, and we did make the difference between active versus inactive uveitis and found that the duration of the ME and the activity of uveitis did not differ between the FA-positive/OCT-negative group and the FA-positive/OCT-positive group.

We agree that, in addition to the higher-resolution OCT, the differences in the composition of the study group of Khanduja and associates and our study groups might have contributed to the differences in the prevalence of the discrepancies between FA and OCT imaging.

In conclusion, we point out that discrepancies between the FA and OCT findings occur because these 2 investigations reveal different ME characteristics, specifically morphologic and functional features. The ophthalmologists caring for the patients with ME should be aware of possible pitfalls using only 1 of these imaging methods.

JEANNETTE OSSEWAARDE-VAN NOREL
Utrecht, The Netherlands
ANIKI ROTHOVA
Utrecht and Rotterdam, The Netherlands

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Persistent Corneal Edema After Collagen Cross-Linking for Keratoconus

EDITOR:

SHARMA AND ASSOCIATES RECENTLY PUBLISHED AN INTEResting retrospective case series of patients who manifested persistent corneal edema after collagen cross-linking (CXL) for keratoconus.[1] The authors analyzed the clinical data of 350 patients with keratoconus who underwent CXL and identified 10 patients with postoperative corneal edema (2.9%). Corneal edema improved in 4 and resolved in 1 patient, whereas 5 patients underwent penetrating keratoplasty for visual restoration. Based on these findings, the authors underscore the potential risk for endothelial damage and consequent corneal edema after CXL, although they recognize that CXL is a procedure demonstrating a strong overall safety profile.

Considering the importance of the reported clinical data, we would like to highlight a number of aspects, which merit further attention. First, the authors applied the Dresden protocol for CXL procedure using isotonic riboflavin 0.1% drops (20% Dextrane; IROC Innocross AG, Zug, Switzerland). CLX was performed after removal of corneal epithelium and subsequent measurement of central corneal thickness to ensure that central corneal thickness remained at more than 400 μm in all cases. However, corneal thickness (CT) was measured neither at the end of riboflavin solution instillation nor during ultraviolet A irradiation,

although it is well established that CT may decrease significantly during CXL in which corneal epithelium is removed because of corneal dehydration from epithelial debridement.[2,3] Intra-CXL corneal thinning is transient and reversible,[3] but it may expose the corneal endothelium to severe danger if a minimal preoperative stromal thickness of 330 μm is not respected.[4] Therefore, careful evaluation of CT after riboflavin solution instillation, as well as repeated intratreatment CT measurements with administration of hypotonic riboflavin solution for CT values of less than 330 μm, should be part of the routine CXL protocol. This was not the case in this study.

Second, only 1 case report on endothelial damage after CXL has been published so far, whereas dozens of studies have reported the absence of irradiation damage to the endothelium in the past years.[5] This case report also did not measure corneal thickness during surgery, similar to the cases reported here.

Third, another potential source of endothelial damage that often is underestimated is associated with the imprecise estimation of preoperative and intraoperative corneal pachymetry. The measured CT, as evaluated by portable ultrasound devices, does not always correspond to the thinnest corneal point, which is the crucial pachymetric reading determining the decision tree in a CXL procedure. In our opinion, it is of paramount importance that physicians perform preoperative and intraoperative corneal pachymetry with simultaneous evaluation of the corresponding corneal topographic data to measure the thinnest point corneal pachymetry in the area of the cone.

Finally, frequent equipment calibration also is essential for avoidance of ultraviolet light toxicity resulting from inadvertent delivery of excessive energy. In conclusion, we believe that meticulous adherence to the procedural precautions mentioned above would have prevented the endothelial damage reported here.

ZISIS GATZIOUFAS
OLIVIER RICHOZ
Geneva, Switzerland
EBERHARD SPOERL
Dresden, Germany
FARHAD HAFEZI
Geneva, Switzerland, and Los Angeles, California

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REPLY

WE THANK GATZIOUFAS AND ASSOCIATES FOR THEIR interested in our case series of persistent corneal edema after collagen cross-linking for keratoconus and for initiating a discussion of the various methods to prevent this condition in the future.[1] Gatzioufas et al proposed various causes for the persistent corneal edema after CXL treatment with epithelium off, including corneal dehydration during the ultraviolet A exposure, imprecise estimation of preoperative and intraoperative corneal pachymetry, and poor calibration of equipment.

We agree that this potential complication has been documented only as a single case report.[2] Because endothelial damage and corneal edema can affect vision significantly, we believed it was important to report the additional 10 cases of the same condition. As stated in the study, we could only speculate on the exact cause of the findings. We do concur with Gatzioufas and associates regarding the variables that may prevent endothelial cell toxicity.

We agree that accurate measurements of preoperative and intraoperative corneal thickness are vital to avoid endothelial damage. It is possible that the ultrasonic devices may miss the thinnest corneal point, so we obtained our preoperative pachymetry readings from a Pentacam (Pentacam Oculyzer; Oculus Optikgerate GmbH, Heidelberg, Germany).

Calibration of the equipment is of paramount importance to prevent inadvertent delivery of excessive energy and resultant ultraviolet light toxicity. We are very conscientious of this fact and checked the irradiance using a calibrated ultraviolet meter to confirm 3.0-mW/cm^2 emissions before each treatment session.

With respect to the issue of possible corneal dehydration during the ultraviolet A emission, we agree that the corneal thickness measurement should have been rechecked during ultraviolet A exposure to confirm hydration and stability of the corneal thickness. In a recent study, an intraoperative corneal thickness decrease from more than 400 to 350 μm in 80% of eyes during a 60-minute epithelium-off CXL treatment has been reported.[3] However, despite the decreased thickness, corneal edema or endothelial cell damage did not occur. In another study by Kymionis and associates, they did not find a statistically significant change

in the corneal thickness during ultraviolet A irradiation or any endothelial cell loss.[4] The mean preoperative pachymetry reading in our study was 472.6 ± 17.5 μm. Considering the preoperative pachymetry readings and the results of these studies, even with some corneal dehydration, the intraoperative CCT may not have decreased to less than 350 μm. This hypothesis cannot be confirmed secondary to the retrospective nature of the study. Because studies have shown some corneal dehydration with ultraviolet A exposure, we do agree that CXL protocols should include checking pachymetry during the ultraviolet exposure stage of the procedure and corneal rehydration or cessation of the procedure if the corneal thickness drops substantially. We thank Gatzioufas and associates once again for their interest and good insight.

ASHOK SHARMA
KANISH MIRCHIA
KANWAR MOHAN
Chandigarh, India
RAJAN SHARMA
Ambala, India
JENNIFER M. NOTTAGE
Owings Mills, Maryland
VERINDER S. NIRANKARI
Owings Mills and Baltimore, Maryland

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Two-Year Corneal Cross-Linking Results in Patients Younger Than 18 Years With Documented Progressive Keratoconus

EDITOR:

I READ WITH INTEREST THE PAPER BY VINCIGUERRA AND associates and congratulate the authors on their work.[1] The area of collagen cross-linking (CXL) applications for younger patients is surely going to be the topic of much conversation and publication of data in the near future.[2–6]

My concern regarding this paper has nothing to do with the science, but rather the title. After finding it initially by seeing it in the *Journal*, I tried to find it again in PubMed and found it extremely challenging to do so. I believe the use of accurate but nonstandard nomenclature is the source of the issue and would like to propose a solution for authors moving forward.

In PubMed (www.pubmed.org; accessed October 4, 2012) the search term *cross-linking* yielded more than 42 000 results, an enormous number that is not feasible to search. Using additive or refined search terms, *corneal cross-linking* yielded 500 references; in that subset, this article was number 39 on the list. Using *pediatric cross-linking* yielded 428 results, most of which were not relevant to this topic, and this article was not listed in the first 60 references. *Pediatric corneal cross-linking* yielded only 2 results, neither of which were this article. Further, when related citations from one of these articles were searched, this paper was not among the first 80 references listed.[2]

Thus, this study, of excellent quality with important results, risks not being found readily in literature searches unless an individual either knows specifically what they are looking for or is extremely diligent in their search. Because this is an area where publications are just beginning to surface in the literature and where numerous other publications are likely to make it to print soon, standardized nomenclature will improve the results for authors, researchers, and readers alike by facilitating a more complete and accurate search.

Most sources, including the United Nations Children's Fund and the World Health Organization (http://www.who.int) define children as those 2 to 11 years of age and adolescents as those between 12 and 18 years of age, although the range occasionally differs by 1 to 2 years on either end based on the source. Therefore, neither term individually technically would be correct for this study or many others, where the individuals treated are usually between 8 and 18 years of age in mixed populations. However, *pediatric* is a more general term referring to both children and adolescents. In recent submissions to the *Journal of Refractive Surgery*,[3–6] original titles included the terms *children*, *adolescents*, and *juveniles*; these were all edited to include the term *pediatric* so that all of these articles, discussing a similar topic, will be available readily through a simple literature search.

I, therefore, propose that all papers relevant to this particular topic use *pediatric corneal cross-linking* in their titles in some form. If the scientific community uses this terminology, it will facilitate greatly a more complete understanding of the literature by