

# Accelerated corneal collagen cross-linking should be modified

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## Dear editor

We have read with interest the recently published comparative study regarding the accelerated versus conventional corneal collagen cross-linking (CXL) in the treatment of mild keratoconus. We would like to underline the importance of the CXL treatment time reduction in this time consuming operation.<sup>1</sup> Accelerated CXL became popular due to patient and doctor comfort in comparison to the previously widespread use of Dresden protocol which is successful in terms of safety and efficacy. Based on the Bunsen-Roscoe law of reciprocity many modifications to the time and irradiation settings have been proposed while the total energy dose delivered to the cornea should be maintained at 5.4 J/cm<sup>2</sup>.<sup>2</sup>

We already proved, by measuring (with the use of anterior segment optical coherence tomography) the demarcation line depth at 1 month postoperatively after CXL, that the treatment depth was significantly different (significantly shallower in accelerated protocol) between the 10 minute accelerated protocol with ultraviolet-A (UV-A) irradiation intensity of 9 mW/cm<sup>2</sup> and the 30 minute standard Dresden protocol with UV-A of 3 mW/cm<sup>2</sup>.<sup>2</sup> Our results suggested that Bunsen-Roscoe law of reciprocity may not directly apply to CXL in living cornea tissue, thus, an increased total energy dose should probably be applied to the keratoconic cornea in order to achieve a treatment effect comparable to the already proven effective standard Dresden CXL protocol.

Consequently, we have proceeded with relevant modifications for the UV-A time settings of the currently proposed accelerated CXL protocol (10 minutes) by increasing the UV-A irradiation time to 14 minutes (40% increase) and we achieved a treatment effect comparable with the Dresden protocol (as indicated by the demarcation line depth).<sup>3</sup>

In the recently published article by Sherif, it is presumed that the accelerated group of patients received CXL treatment according to Bunsen-Roscoe law which should have been 3 minutes of UV-A with irradiation intensity of 30 mW/cm<sup>2</sup> corresponding to 5.4 J/cm<sup>2</sup> total energy dose delivered to the cornea.<sup>1</sup> Interestingly, Sherif mentioned that the accelerated group received UV-A treatment with 30 mW/cm<sup>2</sup> for 4 minutes and 20 seconds; thus the accelerated group received about 40% more UV-A irradiation time, which is comparable to our time setting modifications (from 10 to 14 minutes). Moreover it should be clarified whether the author modified the time settings manually or if these modifications were made according to the UV-A device manufacturer's instructions (Avedro, Inc., Waltham, MA, USA). In addition we would like to enquire whether the author performed measurements (eg, endothelial cell density) concerning the safety of the time and irradiation intensity settings used in this study.<sup>4</sup>

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As we previously published, an indirect and non-contact method to measure the effectiveness of CXL treatment is the demarcation line depth provided with anterior segment optical coherence tomography; our results were the same with the reliable but more invasive (due to contact with the treated cornea) confocal microscopy.<sup>5</sup> Thus, measurement of the demarcation line depth at 1 month postoperatively could provide useful information in suggesting modifications to any of the CXL treatment settings.<sup>6</sup> It should be of great interest whether the author could provide such measurement results concerning the studied groups of this article. Moreover, we should bring to the attention that in cases of mild keratoconus it should probably need a longer follow-up period to establish reliable results concerning the effectiveness of treatment in arresting keratoconus progression.

In conclusion we believe that accelerated CXL treatment settings in agreement to Bunsen-Roscoe law of reciprocity should be revised thoroughly and new modifications have to be carefully made regarding time and irradiation intensity adjustments keeping the safety aspect of CXL treatment as the first priority.

## Disclosure

The authors report no conflicts of interest in this communication.

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## Author's reply

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## Dear editor

I read the valuable comments of Dr Kymionis and Dr Tsoulnaras

Regarding the question relating to the duration of the accelerated cross-linking (CXL), duration was set according to the manufacturer (Avedro, Inc., Waltham, MA, USA) recommendations. The author agrees that Bunsen-Roscoe law of reciprocity may not directly apply for CXL in living cornea tissue as proved by Dr Kymionis et al.<sup>1</sup>

Regarding the question whether the author performed endothelial cell density (ECD): ECD was not performed in the study group but there are several recent publications that evaluated the ECD after accelerated corneal collagen cross-linking.<sup>2-4</sup> The author is currently conducting a study

evaluating different ultra violet-A settings where ECD is among the evaluation criteria. The results will be published in the coming months.

The author agrees with Dr Kymionis and Dr Tsoulnaras that modifications in ultra violet-A settings have to be carefully made regarding time and irradiation intensity keeping the safety aspect of CXL treatment as the first priority.

## Disclosure

The author reports no conflicts of interest in the communication.

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