

Commentary: Bunsen-Roscoe reciprocity – Is it still valid?

In 1997, Wollensak and Spoerl introduced collagen crosslinking with riboflavin with the Standard Corneal Collagen Cross-linkage (S-CXL) for the management of progressive Keratoconus (KC).^[1] The photochemical process induces additional crosslinks between the collagen fibers, which is dependent upon the applied radiant exposure of ultraviolet (UV) light.^[1] The efficacy and long-term safety of S-CXL in adults and children have already been established with many studies in the literature.^[2] The concept of accelerated CXL (A-CXL) was introduced by Schumacher *et al.*^[3] to reduce the treatment duration, improve the patient's comfort, and reduce the risk of microbial keratitis. Later, many settings have been made based on the Bunsen–Roscoe law of reciprocity.^[4] The various settings for A-CXL are at 9 mW/cm² for 10 min, 30 mW/cm² for 3 min, 18 mW/cm² for 5 min, and 45 mW/cm² for 2 min and all deliver a constant energy dose of 5.4 J/cm².^[5] A-CXL also allows thinner corneas to be crosslinked with greater precision.^[6] The A-CXL protocols are slowly replacing the standardized protocols in ophthalmic practice. Previously, many authors have stated that the A-CXL procedure is less efficient in stabilizing KC than S-CXL due to the reduced duration of the procedure and decreased exposure to atmospheric oxygen levels for the photochemical reaction.^[5] So, it is imperative to know the long-term safety and efficacy of A-CXL protocols and understand the predictability of the procedure to stop the progression of the disease. With interest, the authors conducted the present study, which highlights the 5-year results of visual tomographic outcomes and identifies the preoperative risk factors that are predictive of these outcomes with A-CXL (18 mW/cm² for 5 min).^[7] After the publication of the first article by Tomita *et al.*^[8] on comparing S-CXL versus A-CXL, many clinical trials have been conducted to study the results of different types of A-CXL protocols. Shetty *et al.*^[9] made a prospective comparison of different A-CXL protocols and found that A-CXL with 10 min produced significant topographical improvement compared to S-CXL. The authors also highlighted that the procedure's efficiency decreases with increase in the amount of energy delivered. Very few authors have studied A-CXL outcomes with 18 mW/cm² for 5 min. Hashemi *et al.*^[10] conducted a prospective study and compared the long-term (18 months) outcomes of A-CXL (for 5 min) with S-CXL and observed that although visual acuity and safety profile are comparable, corneal flattening is better with S-CXL. The present study has added the following facts to the literature on 5-min A-CXL:

- 1) It has established long-term efficacy in causing significant flattening of mean and maximum K in advanced keratoconus (>58 D) compared to mild to moderate cases, without KC progression throughout the 5-year follow-up. However, Vinciguerra *et al.* reported that S-CXL is ineffective in preventing progression in patients with Kmax value >58 D and reported a 7.4% failure rate at 13 years of follow up.^[11] In addition, Nicula *et al.* recently reported a 3.84% failure rate at 7 years of follow up with A-CXL 10 min, but all patients had allergic conjunctivitis.^[5]
- 2) Long-term stability of Uncorrected distance visual acuity (UDVA), Corrected distance visual acuity (CDVA), manifest cylinder, CCT, steep K, and posterior elevation at the apex, throughout the 5 years

- 3) The stability of endothelial counts was an interesting aspect to note, since 14 patients had advanced disease with K >58 D, which indirectly predicts the safety of high-intensity UV radiation used in A-CXL.
- 4) CCT and Corneal thickness at the thinnest point (TCT) levels were decreased approximately by 12 and 14 μ m, respectively, which is less than S-CXL.
- 5) The complications of microbial keratitis and endothelial decompensation were not observed throughout the 5 years of follow-up.
- 6) Many studies have established that the Kmax is the most commonly used parameter to determine KC progression. This study has found a long term association of high preoperative Kmax values and success of the treatment with A-CXL, similar to the study by Kirgiz *et al.*^[12]

In addition to the limitations mentioned in the present study, the authors felt that evaluation of the demarcation line is of potential interest to the clinicians in the context of the efficacy of 18 mW/cm² A-CXL. The authors are also interested in perceiving the effects of the A-CXL protocol with 5 min in the more beneficial pediatric population. It allows a lesser overall treatment time of 20 min, maintaining high efficacy and patient comfort. The recent literature evidence with various A-CXL protocols is convincing, and the present study provides prospective data with promising outcomes and long-term follow-up results.

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References

1. Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-a-induced collagen crosslinking for the treatment of keratoconus. *Am J Ophthalmol* 2003;135:620-7.
2. Raiskup F, Theuring A, Pillunat LE, Spoerl E. Corneal collagen crosslinking with riboflavin and ultraviolet-A light in progressive keratoconus: Tenyear results. *J Cataract Refract Surg* 2015;41:41-6.
3. Schumacher S, Oeftiger L, Mrochen M. Equivalence of biomechanical changes induced by rapid and standard corneal cross-linking, using riboflavin and ultraviolet radiation. *Invest Ophthalmol Vis Sci* 2011;52:9048-52.
4. Vohra V, Tuteja S, Chawla H. Collagen cross linking for keratoconus. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK562271/>. [Last accessed on 2021 Sep 28].
5. Nicula CA, Nicula D, Rednik AM, Bulboacă AE. Comparative results of "Epi-Off" conventional versus "Epi-Off" accelerated cross-linking procedure at 5-year follow-up. *J Ophthalmol* 2020;2020:4745101.
6. Jacob S, Kumar DA, Agarwal A, Basu S, Sinha P, Agarwal A. Contact lens assisted collagen cross-linking (CACXL): A new technique for cross-linking thin corneas *J Refract Surg* 2014;30:366-72.
7. Chan TC, Tsui RW, Chow VW, Lam JK, Wong VW, Wan KH. Accelerated corneal collagen cross-linking in progressive keratoconus: Five-year results and predictors of visual and topographic outcomes. *Indian J Ophthalmol* 2022;70:2930-5.

8. Tomita M, Mita M, Huseynova T. Accelerated versus conventional corneal collagen crosslinking. *J Cataract Refract Surg* 2014;40:1013-20.
9. Shetty R, Pahuja NK, Nuijts RM, Ajani A, Jayadev C, Sharma C, *et al.* Current protocols of corneal collagen cross-linking: Visual, refractive, and tomographic outcomes. *Am J Ophthalmol* 2015;160:243-9.
10. Hashemi H, Miraftab M, Seyedian MA, Hafezi F, Bahrmandy H, Heidarian S, *et al.* Long-term results of an accelerated corneal cross-linking protocol (18 mW/cm²) for the treatment of progressive keratoconus. *Am J Ophthalmol* 2015;160:1164-70.
11. Vinciguerra P, Albe E, Trazza S, Rosetta P, Vinciguerra R, Seiler T, *et al.* Refractive, topographic, tomographic, and aberrometric analysis of keratoconic eyes undergoing corneal cross-linking. *Ophthalmology* 2009;116:369-78.
12. Kirgiz A, Eliacik M, Yildirim Y. Different accelerated corneal collagen cross-linking treatment modalities in progressive keratoconus. *Eye Vis (Lond)*. 2019;3;6:16.

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