

Letter to the editor

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It is with great interest that we read the publication by Kanellopoulos.¹ In this the author shows in a group of 21 patients with 46 months of mean follow-up that the new CXL protocol described, where higher fluence UV light is used with shorter exposure, appears to be a safe, comfortable and effective treatment for stabilizing a progressive keratoconus. This is a very valuable observation. The author also concludes, that collagen cross linking may be a promising adjunct treatment in cases, where a risk of post-LASIK-keratectasia is suspected. LASIK for correction of keratectasia is still controversially discussed. If used as a prophylactic treatment to prevent post-LASIK keratectasia, we would like to point out that the cross linking should be performed preferably after the LASIK procedure because the first will impact various steps of the refractive laser treatment.

In 2010 we showed in porcine eyes that CXL reduces the amount of refractive change after a myopic LASIK and results in an increased flap thickness although the laser ablation rate is unaltered. Our study suggests the need for adjustment of microkeratome and laser parameters for LASIK after CXL and indirectly endorses the theory of a immediate stiffening effect of CXL.²

Meanwhile Kanellopoulos et al also published their results of simultaneous same-day PRK and CXL in which they follow this suggestion. They found that stabilizing the cornea (with CXL) and rehabilitating the vision (with topography-guided PRK) seems to be a promising concept to delay or even avoid corneal transplantation in young adults with progressive keratoconus.^{1,3-7}

Since the indications for refractive laser surgery seem to be progressively expanding, the ophthalmic community needs to reconsider carefully the list of contraindications for ablative surgery weakening the corneal strength and also to be aware that a previous CXL treatment impacts the biomechanical properties of the cornea and microkeratome-assisted refractive surgery. It will remain in the individual surgeon's responsibility to reassure that a patient seeking LASIK surgery has not been treated with CXL for early keratoconus or other indications previously.

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References

1. Kanellopoulos AJ. Long term results of a prospective randomized bilateral eye comparison trial of higher fluence, shorter duration ultraviolet A radiation, and riboflavin collagen cross linking for progressive keratoconus. *Clin Ophthalmol*. 2012;6:97–101.
2. Kampik D, Ralla B, et al. Influence of corneal collagen crosslinking with riboflavin and ultraviolet-a irradiation on excimer laser surgery. *Invest Ophthalmol Vis Sci*. 2010;51(8):3929–3934.

3. Kanellopoulos AJ. Comparison of sequential vs same-day simultaneous collagen cross-linking and topography-guided PRK for treatment of keratoconus. *J Refract Surg*. 2009;25(9):S812–S818.
4. Krueger RR, Kanellopoulos AJ. Stability of simultaneous topography-guided photorefractive keratectomy and riboflavin/UVA cross-linking for progressive keratoconus: case reports. *J Refract Surg*. 2010;26(10):S827–S832.
5. Kanellopoulos AJ, Binder PS. Management of corneal ectasia after LASIK with combined, same-day, topography-guided partial transepithelial PRK and collagen cross-linking: the athens protocol. *J Refract Surg*. 2011;27(5):323–331.
6. Kanellopoulos AJ. The management of cornea blindness from severe corneal scarring, with the Athens Protocol (transepithelial topography-guided PRK therapeutic remodeling, combined with same-day, collagen cross-linking). *Clin Ophthalmol*. 2012;6:87–90.
7. Kanellopoulos AJ. Long-term safety and efficacy follow-up of prophylactic higher fluence collagen cross-linking in high myopic laser-assisted in situ keratomileusis. *Clin Ophthalmol*. 2012;6:1125–1130.

Author's response

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We would like to thank the esteemed group from the University Hospital of Dusseldorf for their very useful comments on our publication on high-fluence short duration collagen crosslinking for progressing keratoconus. I am in total agreement with the authors on the fact that collagen crosslinking definitely changes the refractive index of the cornea. This is evident in the bias that it adds to Scheimpflug imaging in underestimating the actual cornea thickness for years to come after collagen crosslinking of corneas. It is also evident, as we have published, in the fact that it is difficult to design a normogram in using topography-guided Excimer normalization of the corneas that have been previously crosslinked.

The additional point that I wanted to make is that in our paper of high-fluence collagen crosslinking and also in our paper with long-term follow-up of prophylactic crosslinking in routine LASIK cases, we do not advocate that the latter technique is used to correct keratoectasia with LASIK. The intention of using prophylactic collagen crosslinking in LASIK cases is to identify cases that could potentially have the risk for ectasia and, at the end of the LASIK procedure, add a collagen crosslinking reinforcement of the cornea, in order to prevent such an occurrence. In this technique, more commonly called LASIK Xtra in our days, the actual collagen crosslinking is performed after the laser ablation, so it should not interfere with normograms. We have shown that in this short duration a higher fluence collagen crosslinking, because we actually use 30 mW for a minute, (the total energy equivalent of the standard Dresden protocol at 30 mW would have been delivered in three minutes), does not affect the normogram.

It is interesting that one would question the biomechanical effect of this treatment to the outcome of LASIK procedures. I think the answer to that came to us indirectly in a study published this year in the Journal of Refractive Surgery supplement in November, where we studied using LASIK Xtra in hyperopic LASIK. To our amazement, we found a dramatic difference in a contralateral eye study, making the crosslinked LASIK hyperopic cases far more stable long term (2–3 years) than routine cases, and the difference started at six months. We have since used this technique as our routine in hyperopic LASIK. We theorize that it reinforces the fact that it although employs

a fragment of the original total energy and crosslinking effect intended with a Dresden Protocol, LASIK Xtra seems to add biomechanical stability in the cornea and of course, it remains to be seen in larger studies by multiple centers whether this will benefit long-term fluctuations and regressions of hyperopic, and more importantly the more common myopic LASIK, and reduction of the incidence of ectasia following laser in situ keratomileusis.

We practice in southern Europe, and the intricacy of our patient population is very high incidence of keratoconus. We have performed many LASIK procedures in young adults (20 to 30) who often looked perfectly “normal” for LASIK, without any existing topographic and Scheimpflug criteria for potential ectasia, such as the Randleman criteria, the Pentacam Ambrosio/Belin indices, the Klyce and Raboniwicz criteria. These patients often show up for routine follow-up with a sibling interested in LASIK that has overt keratoconus. We estimate (personal assessment) that 1 out of 80 young adults in Greece has topography and/or topometry signs of keratoconic changes. This was our main drive to design, introduce and preemptively employ a potentially useful tool such as LASIK Xtra in preventing the potential of ectasia.

It has been estimated by Marshal (personal communication), that even thin flap (100–120 µm flap) LASIK reduces cornea biomechanical stability by about 20%. We propose that if we continue to do LASIK, which we find an excellent technique as far as the rapidity and relative stability of visual rehabilitation, we will need to employ some kind of a “return” of this reduction in biomechanical instability. In our clinical experience LASIK Xtra offers that. Many clinicians may argue that they have for decades performed thousands of successful and stable procedures. There are few studies that document long and very long term stability of refraction, acuity and more importantly in our opinion stable keratometry measurements.

Of course, we have introduced this concept and although it remains a clinical concept that has proven effective in our practice, we are yet to see a significant number of long-term studies, especially from other centers, to reproduce and validate our theories and data.

References

1. Kanellopoulos AJ, Binder PS. Collagen cross-linking (CCL) with sequential topography-guided PRK: a temporizing alternative for keratoconus to penetrating keratoplasty. *Cornea*. 2007 Aug;26(7):891–895.
2. Kanellopoulos AJ. Post-LASIK ectasia. *Ophthalmology*. 2007 Jun;114(6):1230.
3. Kampik D, Ralla B, et al. Influence of corneal collagen crosslinking with riboflavin and ultraviolet-a irradiation on excimer laser surgery. *Invest Ophthalmol Vis Sci*. 2010;51(8):3929–3934.

4. Kanellopoulos AJ. Comparison of sequential vs same-day simultaneous collagen cross-linking and topography-guided PRK for treatment of keratoconus. *J Refract Surg*. 2009;25(9):S812–S818.
5. Krueger RR, Kanellopoulos AJ. Stability of simultaneous topography-guided photorefractive keratectomy and riboflavin/UVA cross-linking for progressive keratoconus: case reports. *J Refract Surg*. 2010;26(10):S827–S832.
6. Kanellopoulos AJ, Binder PS. Management of corneal ectasia after LASIK with combined, same-day, topography-guided partial transepithelial PRK and collagen cross-linking: the athens protocol. *J Refract Surg*. 2011;27(5):323–331.
7. Kanellopoulos AJ. The management of cornea blindness from severe corneal scarring, with the Athens Protocol (transepithelial topography-guided PRK therapeutic remodeling, combined with same-day, collagen cross-linking). *Clin Ophthalmol*. 2012;6:87–90.
8. Kanellopoulos AJ. Comparison of sequential vs same-day simultaneous collagen cross-linking and topography-guided PRK for treatment of keratoconus. *J Refract Surg*. 2009 Sep;25(9):S812–S818.
9. Kanellopoulos AJ. Long-term safety and efficacy follow-up of prophylactic higher fluence collagen cross-linking in high myopic laser-assisted in situ keratomileusis. *Clin Ophthalmol*. 2012;6:1125–1130.
10. Kanellopoulos AJ. Long term results of a prospective randomized bilateral eye comparison trial of higher fluence, shorter duration ultraviolet A radiation, and riboflavin collagen cross linking for progressive keratoconus. *Clin Ophthalmol*. 2012;6:97–101.

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