AMD. *Br J Ophthalmol* 2014; e-pub ahead of print 7 July 2014; doi:10.1136/bjophthalmol-2014-305252.
3 Xu L, Lu T, Tuomi L *et al*. Pharmacokinetics of ranibizumab in patients with neovascular age-related macular degeneration: a population approach. *Invest Ophthalmol Vis Sci* 2013; **54**: 1616–1624.
4 Hanhart J, Tiosano L, Averbuckh E, Banin E, Hemo I, Chowers I. Fellow eye effect of unilateral intravitreal bevacizumab injection in eyes with diabetic macular edema. *Eye* 2014; **28**: 646–653.
5 IVAN Study Investigators, Chakravarthy U, Harding SP, Rogers CA, Downes SM, Lotery AJ *et al*. Ranibizumab versus bevacizumab to treat neovascular age-related macular degeneration: one-year findings from the IVAN randomized trial. *Ophthalmology* 2012; **119**(7): 1399–1411.

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Sir,
Is accelerated corneal cross-linking for keratoconus the way forward? Yes or No

While I congratulate the Journal for encouraging such interesting debates and the authors for their hard work in presenting their points of view, I feel it is necessary to point out two inaccuracies presented and repeated in both articles.[1,2]

The first is equating the degree, depth, and safety of cross-linking to the depth of the demarcation line. There is currently no evidence to support this direct correlation. The so-called stromal demarcation line, first described by Seiler and Hafezi,[3] can be easily delineated by anterior segment optical coherence tomography, has been shown to possibly be shallower in older patients and those with more severe ectatic disease.[4] It has been found to be thicker centrally and thinner peripherally[5] and possibly related to an increased density of the extracellular matrix.[6] Although a deeper demarcation line has been associated with a larger decrease in corneal thickness,[7] its depth has not been shown to be correlated to either visual or keratometric changes at 6 months post-operatively.[4] It may simply represent natural wound healing responses rather than delineate the true area between cross-linked and uncross-linked tissue. Clearly a lot more research is required to ascertain the true nature of this demarcation line and its relationship with the actual cross-linking process.

Finally, in both articles it is stated that keratoconus in its early stages is a posterior corneal disease. Although posterior corneal curvature changes can indeed be detected before anterior alterations in sub-clinical disease, this is almost certainly due to the epithelium masking early anterior changes. This has been elegantly demonstrated by Reinstein *et al*[8] using high-resolution ultrasound.

Conflict of interest

The author declares no conflict of interest.

References

1 Tsatsos M, MacGregor C, Kopsachilis N, Anderson D. Is accelerated corneal collagen cross-linking for keratoconus the way forward? Yes. *Eye (Lond)* 2014; **28**(7): 784–785.
2 MacGregor C, Tsatsos M, Hossain P. Is accelerated corneal collagen cross-linking for keratoconus the way forward? No. *Eye (Lond)* 2014; **28**(7): 786–787.
3 Seiler T, Hafezi F. Corneal cross-linking induced stromal demarcation line. *Cornea* 2006; **25**(9): 1057–1059.
4 Yam JC, Chan CW, Cheng AC. Corneal collagen cross-linking demarcation line depth assessed by Visante OCT After CXL for keratoconus and corneal ectasia. *J Refract Surg* 2012; **28**(7): 475–481.
5 Kymionis GD, Grentzelos MA, Plaka AD, Stojanovic N, Tsoulnaras KI, Mikropoulos DG *et al*. Evaluation of the corneal collagen cross-linking demarcation line profile using anterior segment optical coherence tomography. *Cornea* 2013; **32**(7): 907–910.
6 Mazzotta C, Balestrazzi A, Traversi C, Baiocchi S, Caporossi T, Tommasi C *et al*. Treatment of progressive keratoconus by riboflavin UVA induced cross linking of corneal collagen: ultrastructural analysis by Heidelberg retinal tomography II in vivo confocal microscopy in humans. *Cornea* 2007; **26**(4): 390–397.
7 Doors M, Tahzib NG, Eggink FA, Berendschot TT, Webers CA, Nuijts RM. Use of anterior segment optical coherence tomography to study corneal changes after collagen cross-linking. *Am J Ophthalmol* 2009; **148**(6): 844–851.
8 Reinstein DZ, Archer TJ, Gobbe M. Corneal epithelial thickness profile in the diagnosis of keratoconus. *J Refract Surg* 2009; **25**(7): 604–610.

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