Corneal Collagen Cross Linking

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Conductive Keratoplasty and Corneal Cross Linking (CK-CXL)

One of the applications for CXL currently being investigated is using it to stabilize the refractive changes produced by CK. CK or CXL alone is not sufficient to markedly improve vision for most patients with KC or corneal ectasia. According to Raiskup-Wolf 1-year study [123], the CDVA improved at least 1 line in 53 % of 142 eyes and remained stable in 20 % of eyes. Kato et al [248] reported a case series of CK alone (without CXL) for 21 eyes with advanced KC in which UDVA, CDVA, corneal topography, and MRSE all improved but had regressed by the 3-month postoperative visit. Kymionis et al [249] reported on 2 patients that underwent same day CK plus CXL for KC. All parameters here improved too but had regressed by 3 months postoperatively. In traditional CK, the surgeon uses a radiofrequency probe inserted into the cornea to a depth of about 500 μm to increase the temperature in a circumferential series of eight or more spots placed 6, 7, or 8 mm from the corneal center. The heat causes controlled shrinkage of the tissue, resulting in a tightening effect on the mid-peripheral cornea, increasing refractive power. CK has been used to treat astigmatism, decentered ablations, KC and trauma, as well as to produce a moderate refractive correction. In general, the procedure has lost some of its appeal due to the tendency for the refractive changes to regress over time. Researchers realized, however, that CXL might minimize or eliminate that drawback. Surgeons and patients alike are frustrated with the visual outcomes of CXL alone and frustrated with the stability of CK procedures. Over the past several years, researchers have been doing CK to regularize the corneal shape, followed by CXL, both to lock in the beneficial effects of the CK and to stabilize the cornea. This is referred to as CK-Plus or refractive CXL by the CXLUSA investigator group (Richard Lindstrom, MD, Personal communication, 2013). CK is a noninvasive, very well-tested and safe procedure that has been around for a long time, but one of its limitations has always been the tendency for the improved visual results to regress. When it is combined with CXL, visual improvement has been demonstrated to become more permanent. One- and two-year data demonstrate substantial, statistically significant clinical improvement in both UDVA and CDVA. Patients and surgeons have found the combination treatment very gratifying. Standalone CXL is very effective at stopping vision loss from progressive ectasia, but for most patients it is generally not very effective at significantly improving the patient's vision. CK combined with CXL: On the one hand the corneal shape and vision are improved without removing any corneal tissue, and on the other hand the cornea is made stronger by the CXL. It took investigators some time to figure out the sequence in which the procedures should be done (Richard Lindstrom, MD, Personal communication, 2015). The literature shows that when you do CK at the same time as CXL, the results are likely to regress. Work done by Arthur Cummings [250] in Dublin, Ireland found that leaving an interval between the CK and CXL helped to prevent the effect from regressing. The typical interval therefore between the CK procedure and the CXL procedure is 1 day. Final data are still outstanding but those who had the procedures a day apart have had notably better long-term data that those who were done on the same day. The CK is performed with real-time keratometric monitoring (and, in some cases,

serial scans) enabling the surgeon to watch and monitor the corneal shape intraoperatively while doing the CK.

An unpublished study by Roy Rubinfeld, Arthur Cummings and Olivia Dryjski looking at 244 eyes demonstrated that CK plus the proprietary, patent pending Epi-On CXL treatment on the next day was safe and effective. As shown in Fig. 4.30, this noninvasive treatment improved vision up to 15 months postoperatively with statistically significant improvements in UDVA and CDVA noted at all time points except CDVA at postoperative month one. Benefits definitely appeared to last for much longer than with CK alone. A greater benefit was observed in eyes with worse preoperative vision (88 eyes with CDVA 20/40 or less).

As of August 2015, our nomogram shows that apical spots improved clinical data even more (as shown in Figs. 4.30, 4.31, and 4.32). The optical zones have been reduced by incremental amounts starting at an optical zone of 10 mm and eventually getting down to 2–3 mm recently. There has not been a good option to improve vision in central cones for many years now and CK may be filling that gap.

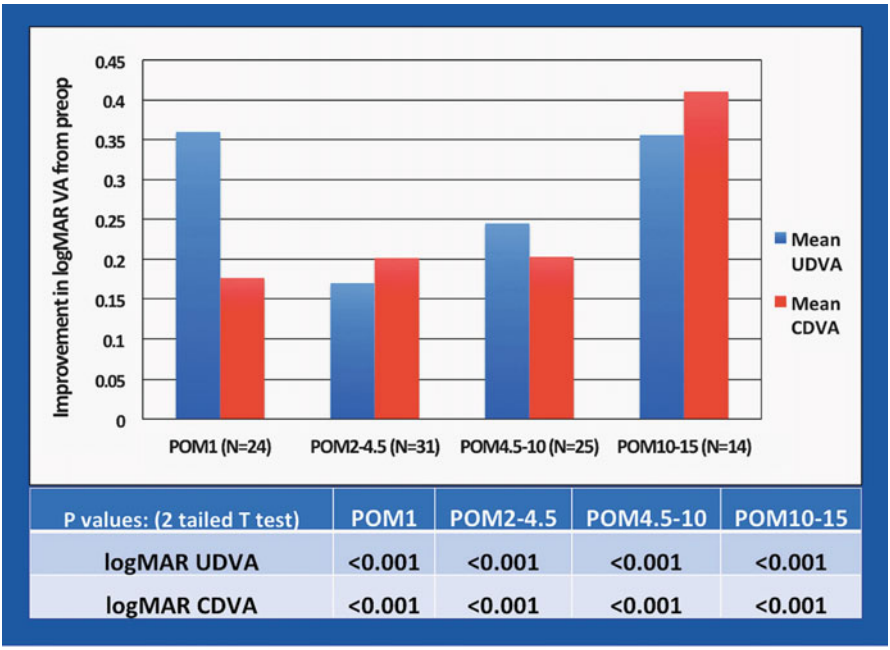
Take-Home Message

- CXL is effective at stopping progressive vision loss in keratoconus and ectasia but usually does not markedly improve vision.
- CK is a safe, well tested, nonsubtractive procedure that can be used to safely and effectively flatten the apex of the cone and subsequent CXL the next day appears to lock in the significantly improved vision in these patients in long term follow-up.
- Corneal flattening with CK combined with proprietary, effective Epi-On CXL yield improved vision and high safety for the treatment of ectasia.
- Keraflex is a novel thermal procedure that provides very significant corneal flattening in keratoconus cases directly after application.
- In some cases, this corneal flattening is maintained and even flattens further after the subsequent CXL.
- The best time for the CXL application is deemed to be 24 h or more after the Keraflex procedure.
- More studies are required to determine if Keraflex will become an accepted treatment for keratoconus. At this point it does not look promising as a long-term solution for the treatment of keratoconus.

Refractive Lens Exchange and Phakic Intraocular Lenses

Refractive Lens Exchange

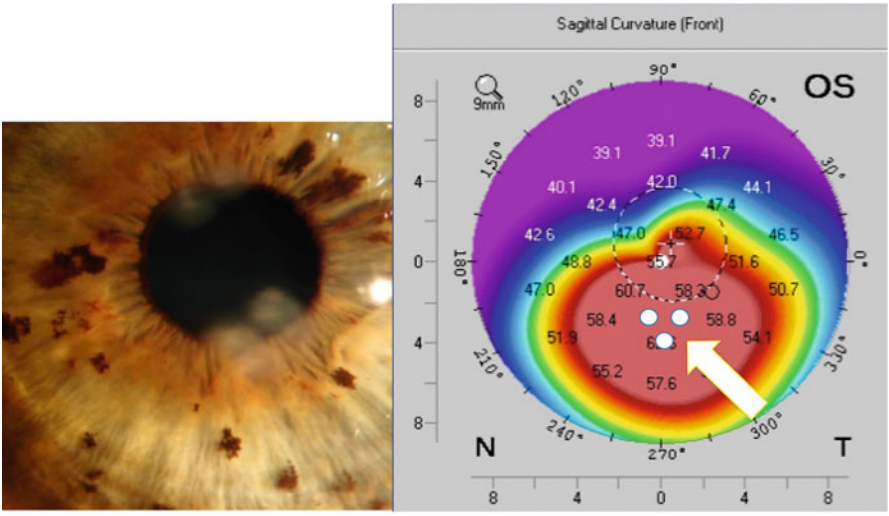
Surgical correction of the spherical and cylindrical errors associated with KC remains a challenge. Laser in situ keratomilleusis in KC may cause corneal ectasia. Photorefractive keratectomy has been used by some researchers to treat myopia



P values: (2 tailed T test)	POM1	POM2-4.5	POM4.5-10	POM10-15
logMAR UDVA	<0.001	<0.001	<0.001	<0.001
logMAR CDVA	<0.001	<0.001	<0.001	<0.001

Eyes with CK: 1 day before CXL and preop CDVA of 20/40 or worse

Fig. 4.30 Improvement in logMAR UDVA and CDVA in eyes with CK performed 1 day before CXL and with a preoperative CDVA of 20/40 or worse. All time points are statically significant ($p<0.001$)



Typical Placement of Initial Apical CK Spots @ 3-6 mm OZ

Fig. 4.31 Typical placement of the initial apical CK spots is at the 3-6mm optical zone

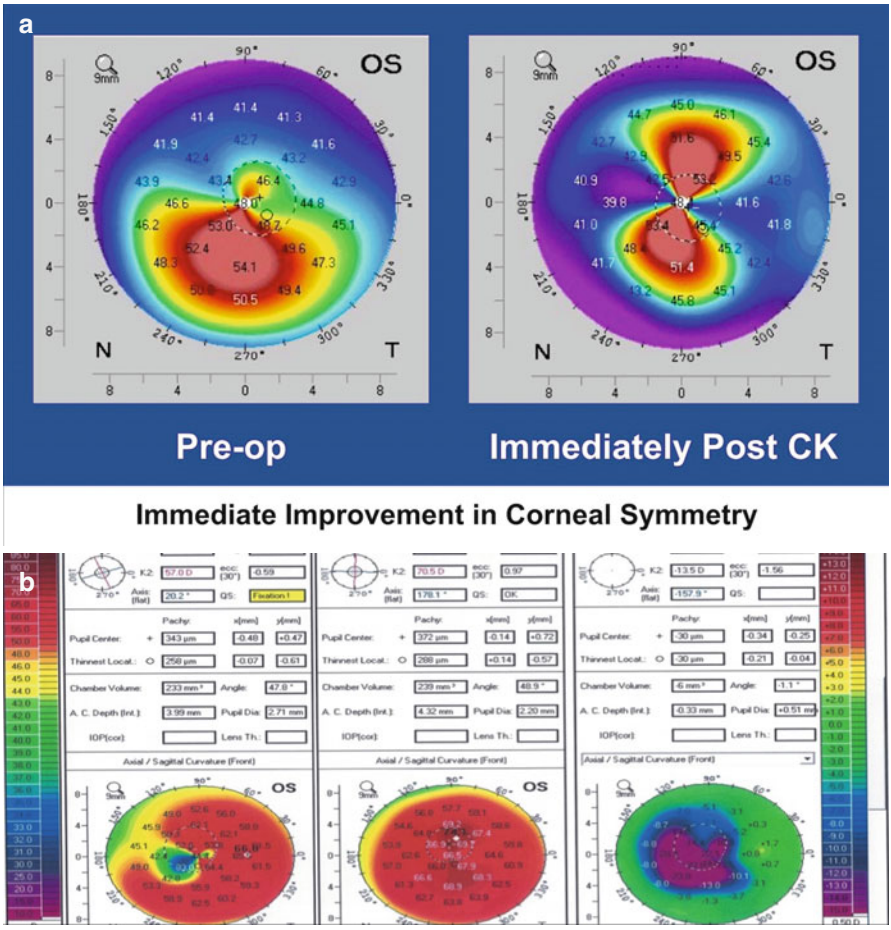


Fig. 4.32 Immediate improvement in corneal symmetry is noted after CK

associated with KC, but thinning of keratoconic corneas raises long-term safety concerns. PIOLs are generally not implanted in patients older than 45 years of age. Other techniques, such as ISCR, can improve visual acuity and reduce corneal curvature in KC, but correction of the spherical error is limited. Refractive lens exchange (RLE), also called "clear lens extraction," consists of phacoemulsification of the clear crystalline lens and in-the-bag implantation of an appropriately powered intraocular lens (IOL). It is generally used to correct large spherical errors in patients in the presbyopic age range because it causes loss of accommodation. Myopia associated with KC is not routinely considered an indication for RLE because of difficult IOL power calculation. Despite the difficulties in obtaining accurate preoperative refraction, and keratometric readings, RLE may be indicated for presbyopic patients with higher spherical errors. In such cases, astigmatism can be addressed by a toric IOL [251].