Richard L. Lindstrom

LINDSTROM'S PERSPECTIVE

One surgeon's impressions after 2 years of cross-linking experience

by Richard L. Lindstrom, MD

In this commentary I would like to discuss my last 2 years' experience working in the CXLUSA investigator-sponsored study of epithelium-on corneal cross-linking, both as a stand-alone treatment and in combination with Intacs, PRK, phototherapeutic keratectomy and conductive keratoplasty.

It must be repeated that no method of CXL has received U.S. Food and Drug Administration approval, and the use of Intacs (Addition Technology), PRK, PTK and CK in combination with CXL is an off-label use.

The combined cases represent an attempt to do refractive CXL, with a goal of reducing residual myopia, astigmatism and higher-order aberrations and enhancing uncorrected and best corrected visual acuity and patient quality of life. These early works are investigational and, to some, controversial, I freely admit. That is the story of my career, and there will be a few arrows to pull out in the field of CXL as well. Still, this is how we learn, and it is important to share openly what we are doing and what we are thinking. I am not going to present data in this commentary, just the personal impressions of a few corneal specialists who have been treating keratoconus patients for up to 4 decades. (But we are collecting data in the CXLUSA study and will report our outcomes as they are analyzed.)

I fully admit that it is likely some of my current thoughts will prove false as more knowledge is gained, and I apologize for the fact that I currently am totally unable to guide you as to which parts will be proven false. It is likely I will be doing at least something different a year from now.

I have been strongly influenced in this field by my good friend Roy Rubinfeld, MD. He is fond of saying, "This is the cool stuff." I agree. The keratoconus cornea is a pretty dysfunctional optical system, usually manifesting in varying degrees of myopia, astigmatism and significant higher-order aberrations, especially coma. Central vertical striae and scarring may also be present. Tear stability is poor, with a rapid tear breakup time.

Most of the patients I see definitely want to avoid a keratoplasty, and like most corneal specialists who see a lot of keratoconus, I have good contact lens fitters available, so stabilizing the cornea with epithelium-off CXL was and is a great advance, as mentioned in last issue's commentary.

Looking for a less invasive approach, I found Rubinfeld and his band of investigators at CXLUSA, including my friends Bill Trattler, MD, Sandy Feldman, MD, Jonathan Talamo, MD, Arthur Cummings, FRCS, and a host of others, working with an epithelium-on treatment regimen that they claimed works.

Now, with nearly 2 years' experience, I find my partners and I agree that epithelium-on collagen CXL can be effective, with an outcome and failure rate using maximum keratometry (Kmax) on the Oculus Pentacam as the marker, with similar outcomes to epithelium-off treatments using the classic Dresden protocol. I understand the controversy, but one surgeon's epithelium-on CXL is often far different from another's. The bottom line for me: You can load the cornea with riboflavin transepithelial, you can treat the cornea with UV light transepithelial, and you can stabilize the cornea with a similar success rate to epithelium-off treatments with a "properly done" epithelium-on CXL. It is much more humane, can be done in a bilateral same-day approach, and is benign enough that even children tolerate the treatment well. For my patients and I, this is a great advance.

What about "the cool stuff" — trying to reduce lower- and higher-order aberrations and enhance uncorrected and best corrected visual acuity? My partners and I did a fairly large series of PRK in mild to moderate keratoconus patients before CXL. Well-informed patients looking for better vision accepted the risk that we might accelerate their disease progression, but in our series, this was rarely — actually, almost never — observed. Many of these patients were ecstatic with their outcomes. So, why not do PRK (wavefront guided, topographic guided, optimized or just standard, based on refraction) or PTK to remove the epithelium and knock down the apex of the cone in combination with epithelium-off CXL? Many prominent surgeons around the world use this approach routinely. In my experience, the haze is worse, epithelial wound healing is delayed, the procedure experience is back to being miserable, and one eye at a time is recommended.

I have some good outcomes, but I am concerned with how to plan around the CXL-induced corneal flattening in combination with the excimer laser plan. I have stopped using this approach, but remain interested in the continuing work of others.

It is best that not everyone studies the same options. Intacs work well with epithelium-on CXL, and two of my partners like this treatment approach, using a femtosecond laser to make the pockets, followed by epithelium-on CXL the same day. I like this option as well, but my long-term visual outcomes with Intacs in keratoconus are not as good as I would like, with many patients experiencing forward light scatter and unwanted night vision symptoms. So, for now, I have abandoned this approach as well.

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I am a long-term user of CK in select cases of presbyopia and astigmatism and have, along with my partner David Hardten, MD, used CK in combination with Intacs with good effect. So, how about CK in combination with epithelium-on CXL for keratoconus? Preliminary results by Rubinfeld, Cummings and I suggest this may be a quite promising way to not only stabilize keratoconus, but also reduce residual astigmatism and improve uncorrected and best corrected visual acuity. As few as three to five CK spots placed under direct observation using a surgical keratoscope such as that manufactured by Mastel or just the ring light on the Visx excimer laser microscope are generating some very gratifying outcomes. It is definitely an art form, but the art of surgery is fun, and placing a few spots, usually at the inferior apex at a 5 mm to 7 mm optical zone or in more oval cones, two spots on the flatter meridian on each side, can greatly improve visual function and quality of life for many patients.

We have much to learn regarding the ideal time interval between CK and CXL. I am doing them same-day sequential, and I am now bold enough to do them bilateral. Rubinfeld waits a day or two in between, and some are looking at a week or more.

Both CK and epithelium-on CXL have a very high level of safety. Recovery is rapid and comfort good with a bandage contact lens for 1 to 3 days and a PRK medical regimen. Patient acceptance has been high. I now offer my patients CK combined with epithelium-on CXL in mild to moderate keratoconus when refractive/topographic astigmatism is 3 D or higher.

I am measuring success not only in Kmax stabilization or reduction, but also in refractive and topographic astigmatism improvement — especially uncorrected and best corrected vision improvement and improved patient-reported outcomes. Sometimes the Pentacam does not look that much better, but the patients' visions are improved, and they are very happy. I am counseling my patients that the earliest we expect improved vision is 6 months. The 1-year outcome is the key time point, and remodeling may occur even longer, but some patients note significant improvement earlier.

I am also offering select patients PRK at 12 to 24 months, once the

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combined CK/CXL has stabilized, and in these late PRKs with 12 seconds of mitomycin C, I am not experiencing significant haze. I always plan to leave at least 350 µm of stromal tissue. Using this approach in select cases, some amazing outcomes can be achieved, even to the level of 20/20 uncorrected vision.

Refractive CXL combined with thermal keratoplasty, Intacs or PRK/PTK to not only stabilize corneas with mild to moderate keratoconus, but also reduce residual refractive error and higher-order aberrations, and improve uncorrected vision, best corrected vision and quality of life is now a very rewarding part of my practice and more fun every day.

There is much to be learned, including the range of keratoconus that will respond to refractive CXL, the stability of the treatments and which treatments work best for which patients. I am willing to be wrong, but I am currently disappointed if 1 to 2 years after CXL in my mild to moderate keratoconus patients, beyond being just stable, they do not have significant improvement in visual function and quality of life.

The next step will be using CXL perhaps in a selective fashion or in combination with thermal keratoplasty as a refractive tool in mildly atypical or normal eyes. Stay tuned: More financial capital and more surgeon and scientist intellectual capital are being focused on CXL, and the innovation cycle in this field is beginning to spin faster. OSN

Disclosure: Lindstrom is a consultant for and/or has equity interest in CXLO, Refractec, Alcon, AMO and Bausch + Lomb.