Will CXL Get Approval in 2014?
A leading researcher weighs in on crosslinking trials

There are currently three corneal crosslinking (CXL) clinical trials in the FDA pipeline, and researchers hope the “original” US CXL trial, which began in 2008, will be approved in the United States in 2014. CXL uses ultraviolet light and riboflavin drops to form links between collagen molecules that strengthen the cornea and impede the progression of keratoconus (KC).

The first CXL trial, which was conducted in 10 sites with nearly 500 eyes treated, is in final stages of the FDA approval process. That trial began enrolling participants in 2008, and treatments were completed about two years later. Follow-ups were done with all patients for a year, before data was analyzed, reviewed and prepared for FDA review.

“All treatments have been done, the follow-up has been completed, the data analysis has been done, and it is currently in the approval process,” says Dr. Peter Hersh, medical monitor of the crosslinking clinical trials, director and founder of the Cornea and Laser Eye Institute – Hersh Vision Group in New Jersey, and director of the Cornea and Refractive Surgery Division at Rutgers New Jersey Medical School. “From my point of view, it meets all the expectations we want: It shows crosslinking is effective and a safe procedure for patients with keratoconus and, indeed, it is effective in diminishing the progression of keratoconus compared with patients who received placebo drops, so we know it is really working.”

“From a medical viewpoint, there is no reason not to expect FDA approval,” Hersh says. “The FDA has been actively involved and is aware... (continued inside)
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of the need for the procedure. If all goes well, in terms of the approval process, I would hope it would be approved in the new year.”

A second clinical trial using a new ultraviolet device for accelerated crosslinking was completed earlier this year. It uses higher power, so treatment can be completed in a shorter amount of time. This trial, which treated 220 eyes in a randomized trial comparing it with a placebo, is currently in the patient follow-up phase.

Hersh and his colleagues are starting a third randomized crosslinking trial using pulsed CXL, which employs a noncontinuous beam of light. The reason for this study is CXL scientists have demonstrated that additional oxygen within the cornea during the procedure may lead to a greater crosslinking effect. “It’s a whole new approach and a new modality,” Hersh says. This trial will take place in 10 study sites and follow all guidelines for FDA approval.

There are also physician-sponsored CXL trials being conducted throughout the country; these trials aren’t necessarily being done specifically for FDA approval, though they usually are done under strict regulatory oversight. One such trial is being conducted by the American-European Congress of Ophthalmic Surgery (ACOS) to look at using different UV powers during CXL. The ACOS trial is quite large — up to 4,000 subjects at 100 sites — and is looking at the efficacy of different UV powers on crosslinking results, Hersh says.

All CXL trials currently looking toward FDA approval use the “epi-off” technique of CXL, in which the epithelium is removed.

“Is the amount of corneal crosslinking and the longevity of the crosslinking equivalent with epi-on? And if it’s less, is it worth the advantage of a shorter healing time? That’s the ultimate question,” Hersh says.

If you’d like to help researchers find out the answer, look into physician-sponsored clinical trials currently underway studying just that.

For information about CXL clinical trials, visit www.nkcf.org/clinical-trials.
In the late 1980s, Richard Solomon’s father told him about his deteriorating eyesight. “I suspect he’d been dealing with it for a while, but at around age 70, he began to talk about it,” Solomon says. “In retrospect, I think that’s when his AMD went from dry to wet.”

“My dad had several laser surgeries to seal some of the blood vessels in his eye to keep them from leaking,” he says. “The surgeries left scar tissue in his macula, and he said looking out through his eyes was like looking through a piece of Swiss cheese — there were these holes in his vision where the scar tissue was. I remember that very well.

“At one level, my dad was pretty resilient: He listened to books on tape; he played tennis until he couldn’t see the ball at all; he used a talking watch that he liked to show off; he drove until he took himself off the road following a minor accident. On the other hand, he struggled to maintain his independence and occasionally grew frustrated and discouraged. It was poignant, as a son, watching a parent go through this.”

Watching his father cope with vision loss spurred Solomon to find out all he could about age-related macular degeneration (AMD); he learned the disease was probably in his future, as well. Solomon subscribed to the Macular Degeneration Partnership (MDP) Update and the DEF newsletter. He got his first Amsler grid from MDP, checked it regularly and even developed his own: “As a psychologist, I did in-depth interviews with patients every day. I took notes on lined paper, so I had my own version of an Amsler grid, where I could track my vision.”

It wasn’t until 2010, just before Solomon and his wife moved from Santa Barbara to Oakland, Calif., to be closer to their granddaughter, that he started noticing real distortion on the grid, with an increase in the waviness of the lines. “Instead of the one or two areas of minor distortion I saw 10 years ago, now it’s five or six,” he reports. Luckily, Solomon has seen no real effect on his ability to read or drive — or golf, which has been his passion since age 12.

“I don’t let myself sit and ruminate about what is going to happen to my sight,” Solomon says. “I learned from my mom that worrying doesn’t help you. Do what you can at the moment and go on, then face it when it happens. That’s how she lived her life.

“When I do start to worry about the future in regard to having AMD, I recall that research and medicines to treat wet AMD have progressed a great deal in the 17 years since I was diagnosed, and that there are research projects going on for treating dry AMD, too. These are things I have learned in reading AMD.org updates, and they give me hope.”
Amy Yahoo's son, Mark, was 20 years old when he told her he couldn't see the television. And, by the way, he'd made the font on his computer screen as big as it could get and still couldn't really see it.

"Are you kidding?" she asked. "How long has this been going on?"

"A while," Mark answered.

"So typical," Yahoo says four years later. "They don't tell you anything right away. They wait. This is the same kid who walked around on a broken foot for a day before he bothered to tell us."

Yahoo took her son to an eye doctor, who took one look at Mark's eyes and said, "Keratoconus." Having never heard the word, she immediately started Googling. She found the National Keratoconus Foundation website (www.nkcf.org), which helped her begin to understand the disease and Mark's treatment options. It's also where she first learned about corneal crosslinking (CXL), as well as the fact that a CXL clinical trial was underway less than an hour from their central New Jersey home.

When another eye doctor confirmed Mark's diagnosis, Yahoo asked him about corneal crosslinking and whether the procedure and the trial might be a good fit for Mark. "He told me if it were his child, that's what he would do," Yahoo says.

Mark has keratoconus (KC) in both eyes. Within two months of his first visit to the doctor conducting the clinical trial, there was progression in one eye — a criterion to enter the trial — and he underwent CXL four years ago. The other eye started progressing last year, so he underwent CXL in that eye, too. There has been no progression since the procedures, and Yahoo believes Mark even has experienced some correction.

When he was first diagnosed, Mark was in school studying computers. "He had his screen at the largest font, and he still couldn't see, plus he had a hard time even watching TV. That's pretty extreme," Yahoo says. "He could never get enough correction from glasses, he couldn't tolerate contact lenses, and we ruled out Intacs, because the thought of something implanted in his eye freaked him out. I did a lot of research. The key was the degree of impact KC was already having on Mark's life. For him, the loss of vision was scarier than the prospect of surgery. We didn't see any other options. He was 20 years old, and he couldn't see. We didn't know how fast the KC would progress, and why take that chance?"

Yahoo's advice to parents in a similar situation? "Be proactive. You only get one set of eyes."

It was the right move for the Yahoo family. "So far, so good," Yahoo says. "Knock on wood."
Pediatric Eye Disease: Research on Cystinosis

A child’s visual system is fundamentally different from an adult’s in that it undergoes rapid and important maturational changes during the first few years of life," says Dr. Jennifer Simpson, a pediatric ophthalmologist and professor of ophthalmology at the Gavin Herbert Eye Institute at UC Irvine. "Any disease process that interferes with the normal visual development during this critical early period can have a profound, lifelong impact on a child’s global development and ability to learn."

As a clinician and researcher, Simpson focuses her research on the vision needs that exist in her young patient population. "My primary goal is to identify unmet needs in pediatric eye disease and take those needs back to the lab, where I can focus my research efforts on pursuing novel therapies that can be translated back to my patients," she says.

Simpson investigates novel drug and stem cell therapies for cystinosis, which is a rare hereditary disease that results in the abnormal accumulation of an amino acid called cystine in nearly all cells, tissues and organs of those affected by the disease. This amino acid accumulates so much that it forms crystals in the cells. These crystals damage critical organs such as the kidneys, brain and cornea.

"From an early age, children with cystinosis are forced to deal with the effects of corneal crystals, including light sensitivity, eye pain, irritation and blurred vision," Simpson says. "Currently, hourly drops are the only treatment for this painful condition, but the frequency of this regimen is very burdensome for both patients and their families."

Simpson’s research uses a two-pronged approach. With researchers at Baylor College of Medicine, she is testing the effectiveness of a nano-based drug-delivery system that has the potential to reduce corneal crystals in a sustained-release manner over a day rather than drops every hour.

“Our goal is to reduce the burden of both the disease and the therapy for these patients,” she says.

In a parallel project, Simpson is pursuing the use of stem cell therapy as a potential cure for corneal cystinosis. She believes a multi-faceted approach to translational research has the potential to speed up progress in both understanding a disease state and investigating potential cures.

“I have firsthand knowledge of the devastating effects vision loss can have on children and their families,” she says. “I’m very mindful that the clock is ticking.”
Hey call this the season of giving, so won’t you consider a year-end gift to The Discovery Eye Foundation?

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We are excited to report DEF has been given a prestigious 2013 Top-Rated Award by GreatNonprofits. The rating is based on the large number of positive reviews received from volunteers, donors and clients, which makes it even more gratifying. GreatNonprofits provides reviews and ratings of nonprofits, and this award recognizes the ongoing credibility of DEF.

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To learn more about our Legacy Society or to sign up for our estate-planning e-newsletter, visit www.discoveryeye.org.

Try Some Tart-Healthy Foods

What would holidays be without dessert? While adding some decadence to your meals and celebrations, why not make sure your sweets include some eye-healthy ingredients, such as those in a cranberry pear tart?

Cranberries provide antioxidant and anti-inflammatory benefits and are also an excellent source of vitamin C, which protects against ultraviolet light damage. Pears have nutrients that protect against type 2 diabetes, heart disease, cancer, osteoporosis and eye diseases, such as AMD and, possibly, cataracts. Pears are also considered hypoallergenic, which means if you have food allergies, you should be fine with pears.

The recipe for the simple, delicious and healthy (well, sort of) tart pictured above is in the “Eye Cook” section of our website at www.discoveryeye.org (under “Events & News”). Now if only someone would bake it for us …

Give Until it Feels Good

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