Advancements

stroma with an intact epithelium by improving the iontophoresis technique. He is also working on a way to add an epithelial map to the excimer laser to have a more precise combined procedure.

"By taking the real epithelial thickness into account, I can use the laser to remove just the right quantity of epithelium that I want on each part of the cornea," he said. "This improves the precision of combining the laser treatment with the cross-linking."

Farhad Hafezi, MD, PhD, one of the original pioneers who brought CXL to the clinical setting since 2003,

continues to improve cross-linking technology through expanding clinical applications and safety measures to ensure high-quality patient care. He said cross-linking procedures were limited because surgeons could not work with corneas thinner than 400 µm. In consequence, many patients with advanced disease who had thinner corneas were left untreated. Having introduced hypo-osmolaric riboflavin to treat thin corneas with Theo Seiler in 2007, his group has now developed what is called the sub400 protocol to address this problem by customizing the UV irradiation duration to each patient's corneal thickness measurement.

"Our research group published an algorithm that could predict the stromal demarcation line depth, and therefore the depth of cross-linking, based on the patient's corneal thickness and the duration and intensity of UV irradiation," he said. "The clinical sub400 protocol modifies the duration of UV irradiation at 3 mW/cm2 to achieve the desired depth needed to cross-link each patient's cornea and leave the 70 µm safety margin."

That intensity of irradiation was selected because it can be achieved by every cross-linking device currently available on the market, ensuring the protocol can be used by anyone.

"However, modern cross-linking devices can perform accelerated procedures at higher intensities, making the procedures faster," Hafezi said. "Thanks to the completion of our clinical validation program, our update to sub400 now includes a distinctly higher fluence and 9 mW/cm2 accelerated cross-linking intensity, opening up shorter customized UV irradiation times for both doctors and patients alike."

His group is also working on techniques to improve epi-off treatments by making them faster and harnessing stronger UV light sources that have been developed since the lower-intensity Dresden protocol was first introduced.

"We now know why accelerating cross-linking reduces the amount of strengthening cross-linking achieves. The UV-riboflavin reaction needs oxygen to diffuse into the stroma from the atmosphere, and higher UV intensities mean that the oxygen is consumed faster than it can diffuse in," he said. "We now know that we can deliver higher UV doses to the stroma without damaging the corneal endothelium than was first thought."

> "We now know why accelerating cross-linking reduces the amount of strengthening cross-linking achieves"
>
> — FARHAD HAFEZI MD, PHD

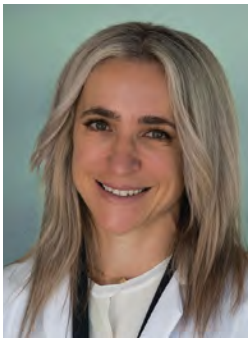
In published preclinical trials, Hafezi and colleagues identified that the accelerated high UV dose epi-off protocol (18 mW/cm2 for 9 minutes 15 seconds) provided a greater stiffening effect than other accelerated protocols, similar to those found in the Dresden protocol.

"We have been using this protocol clinically for over a year now and are preparing the clinical publication," he said.

The final innovation that Hafezi and his team is exploring is whether cross-linking procedures can be done with the patient sitting upright at the slit lamp rather than laying down. To explore the differences, they examined the depth of the demarcation line 1 month after surgery in 23 eyes that underwent cross-linking at the slit lamp.

"The demarcation line is a line visible on corneal OCT imaging after CXL that is thought to represent the interface between cross-linked and non-cross-linked tissue and therefore is a marker of the depth of cross-linking effect," he said. "We then compared those values with those in the literature and, perhaps unsurprisingly, found no difference in the depth of cross-linking effect. This is yet another argument to transfer cross-linking to the slit lamp in an office-based approach."

—by Alex Young



> "I make a smaller epithelial defect compared to the Dresden protocol, and I have found that patients heal much faster, and they are able to get back into their contacts more quickly."
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> — KATHRYN M. HATCH, MD

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Disclosures: Hafezi reports holding patents for cross-linking with EMAGine AG. Hatch reports consulting for CXL Ophthalmics and Glaukos. Rechichi reports no relevant financial disclosures. Rubinfeld reports being a founder, inventor and having a financial interest in CXL Ophthalmics. Trattler reports consulting for Glaukos and having a financial interest in CXL Ophthalmics.