New advances in corneal crosslinking:

Making vision treatment gentler and more precise

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On December 6, 2024, Sofie Elving defended her thesis "Advanced crosslinking for keratoconus and low-grade myopia" at the Dept. of Clinical Sciences/Ophthalmology, Umeå University. The PhD project was conducted at the Umeå University Hospital. Her main supervisor was Prof. Anders Behndig, and her co-supervisor was Gauti Jóhannesson, MD, PhD, both at the Dept. of Clinical Science/ Ophthalmology, Umeå University.

In people with keratoconus, the cornea becomes thinner and gradually bulges outward, creating blurred and distorted sight. If untreated, this condition can make glasses or contact lenses insufficient and may lead to significant visual impairment. Over the past two decades, a treatment called corneal crosslinking (CXL) has revolutionized care for keratoconus. The procedure uses ultraviolet (UV) light together with vitamin B2 (riboflavin) to strengthen the corneal tissue. This process creates new "crosslinks" in the corneal stroma, making the cornea more stable and preventing further bulging.

Given the established use of CXL in the current treatment arsenal for keratoconus, advancing the treatment to achieve better visual outcomes, less ocular discomfort, and faster post-treatment recovery has great potential value, particularly because the disease often affects young patients and is chronic in nature. In this thesis, a next-generation version of the treatment—called Advanced CXL—was developed and evaluated. Our goal was not only to stop disease progression in keratoconus but also to explore whether the same technology could be used to improve vision in mild myopia.

One key development was the use of the transepithelial (epi-on) technique, where the epithelium is left intact. In traditional CXL, this layer is removed (epi-off), which can cause discomfort and prolong healing time. By keeping the epithelium in place and adding high oxygen levels, Advanced CXL aims to make the treatment safer, gentler, and faster to recover from.

The thesis includes three clinical studies that tested different aspects of Advanced CXL. In Studies I and II, we treated healthy volunteers with mild myopia with a form of Advanced CXL, called photorefractive intrastromal crosslinking (PiXL). This technique reshapes the cornea, reducing myopia without surgery or laser correction. The studies compared different light patterns to find the most effective and comfortable design. All treatments improved uncorrected vision and reduced myopia, with results remaining stable for two years. Treatments using ring-shaped light patterns caused less early discomfort, while smaller rings gave slightly better vision but a temporary reduction in low-contrast vision. Importantly, all protocols were safe and no loss of visual quality or damage to the cornea was seen. In Study III, we treated patients with progressive keratoconus. Here, customized, topography-guided epi-on CXL in high oxygen was compared with the conventional epi-off method over 2 years. Both treatments successfully stopped the disease and improved visual acuity. However, patients treated with the epi-on technique experienced less pain and faster recovery, while achieving comparable results in vision and corneal stability.

Key points:

- Advanced epi-on CXL in high oxygen effectively halts keratoconus progression, improves high- and low-contrast vision, and reduces post-treatment discomfort, allowing faster recovery and potential same-day bilateral treatment.
- PiXL for low-grade myopia safely improves uncorrected vision.

Together, this thesis showed that Advanced CXL can be tailored both for disease treatment and vision correction. For patients with keratoconus, it offers a gentler, equally effective alternative to traditional methods. For people with mild myopia, it opens a new, non-invasive way to improve eyesight without laser surgery. In conclusion, by optimizing factors like light patterns, oxygen levels, and individualized treatment planning, these developments in this thesis suggest a future where CXL protocols are increasingly oriented toward refractive improvement, in addition to halting disease, making treatment more comfortable, precise, and patient-friendly.

Future directions:

- Refinement of customized epi-on CXL: Improve targeting of the cornea's weakest areas to reduce total illumination, minimize post-treatment discomfort, and enhance visual outcomes.
- Evaluate the potential of PiXL: Optimization of PiXL protocols for myopia to maximize refractive effect while balancing patient comfort.

References

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