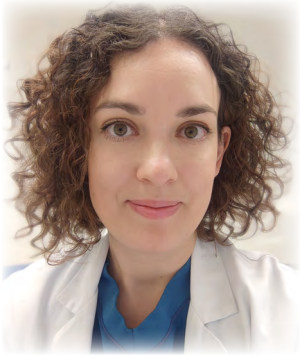
Can Porcine Collagen Replace Human Donor Corneas?

On December 9, 2022, Maria Xeroudaki defended her thesis "Advanced Surgeries, Medicines and Materials for Corneal Regeneration" at the Faculty of Medicine and Health Sciences, Linköping University, Sweden. Her main supervisor was Neil Lagali, Professor of Experimental Ophthalmology, Department of Biomedical and Clinical Sciences, Linköping University. Her two co-supervisors were Beatrice Bourghardt Peebo, Adjunct Assistant Professor, and Per Fagerholm, Professor Emeritus.



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Introduction

Corneal blindness is a leading cause of visual impairment, and corneal transplantation with human donor tissue is the only treatment for advanced corneal diseases. Two main challenges must be addressed in corneal transplantation surgery: limited access to suitable corneal donors, especially in low-income countries where the need is highest, and challenging corneal surgeries with many postoperative complications. Stimulating the body's repair mechanism is now considered the gold standard for the functional healing of damaged tissues. Novel drugs and biomaterials that could promote the regenerative properties of the cornea would be the ideal treatment for corneal diseases.

In my thesis, we developed cell-free substitutes for human corneal stroma made of porcine collagen, a purified byproduct from the food industry that is already FDA-approved. Abundance, cost-effectiveness, low rejection risk due to acellularity, high purity, and worldwide availability are among the main advantages of porcine collagen compared to human donors and other corneal stromal substitutes. The biomaterials were transparent and could be manufactured in different sizes and in core-and-skirt forms with different degradation rates. They could be successfully loaded with nerve growth factor and dexamethasone without sacrificing transparency, and both drugs could be released in vitro. The biological activity of dexamethasone released by the implants could also be confirmed in vivo in a high-risk keratoplasty model. The biomaterials could be safely implanted in rabbit (**Figure 1**), minipig, and human corneas with advanced keratoconus using minimally invasive femtosecond-laser-assisted intrastromal keratoplasty procedures. No graft rejection occurred, the anatomy of the surrounding tissue was maintained, and the biomaterials remained intact with only a few host cells found in the implant–host interface or in the periphery of the implanted biomaterials. The inflammatory response following the operation depended on the individual response to injury and was not stimulated by biomaterial implantation. In the human studies, transparency was maintained at the highest level in all subjects after two years, with no signs of inflammation. The topographic indices and best corrected visual acuity were improved, all patients could tolerate contact lenses, and no patients were considered legally blind. A compatible packaging and sterilization process was developed that could enable worldwide distribution of the implants and storage at room temperature or in a refrigerator for up two years.

We performed a randomized, blinded, placebo-controlled preclinical study to evaluate the role of regenerating agent (RGTA) eye drops in corneal wound healing following therapeutic laser ablation of the cornea. RGTA eye drops following excimer laser ablation of the anterior healthy rabbit cornea did not affect the epithelial closure. Sub-basal nerves were found to repopulate both groups, and all corneas were clinically transparent following laser.

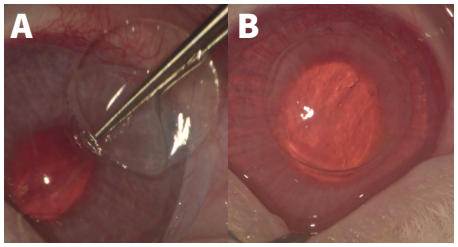

Figure 1. (A) Manual insertion of the biomaterial into the stromal pocket created by femtosecond laser in a rabbit cornea. (B) Biomaterial in the intrastromal pocket.

Key points:

- Biomaterials based on porcine collagen can be simpler, cheaper, more broadly available, and as effective and safe as human donor tissue for lamellar keratoplasty.
- They can be customized and loaded with therapeutic substances.
- Laser-assisted procedures ensure safe intrastromal implantation.
- RGTA administration following laser ablation of the cornea has no advantage regarding epithelial healing or transparency.

Conclusion

Our results show that biomaterials made of bioengineered porcine collagen are a safe alternative to human donor tissue for lamellar corneal transplantation and that femtosecond laser enables safe intrastromal implantation with fewer postoperative complications. Regenerating agent eye drops do not affect the already rapid wound healing following laser ablation of the healthy cornea.

Future directions:

- Refinement and standardization of the implant and surgical technique that allow custom-made biomaterial implantation to optimize visual gain.
- Approved clinical trials for presbyopia correction with bioengineered porcine collagen constructs implanted in a stromal pocket created with femtosecond laser.
- Treatment of neurotrophic keratopathy with drug-loaded biomaterials.

References

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