



INNOVATION IN TISSUE STORAGE

XTRA4™: Next-Generation
Solution for Hypothermic
Corneal Storage

WHITE PAPER

Commissioned
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REDEFINING CORNEAL STORAGE MEDIA PERFORMANCE

1. EXECUTIVE SUMMARY

As global demand for high-quality corneal grafts continues to rise, the need for advanced corneal preservation technologies has become increasingly important. Developed through Moria's dedicated research and development team, XTRA4™, an optimized corneal storage medium, represents a significant advancement over conventional hypothermic storage solutions.

This white paper presents key findings from preclinical evaluations conducted independently by three eye banks. The results consistently demonstrate that XTRA4 allows excellent corneal preservation.

Notably, corneal thickness remains stable with minimal swelling and reduced stromal folds, even in the absence of an intact epithelium. The absence of corneal swelling helps preserve the architecture of the stroma and Descemet's membrane, thereby minimizing mechanical stress on the endothelial cells. This, in turn, supports the maintenance of endothelial cell viability throughout the entire hypothermic storage period.

These findings suggest that XTRA4 provides practical benefits for both eye banks and surgeons. By improving workflow efficiency, XTRA4 has the potential to significantly increase global access to sight-restoring corneal procedures.

2. INTRODUCTION

The Unmet Need for Corneal Storage Innovation

Hypothermic storage remains the most widely used method of corneal preservation in North America. Over the last 30 years, Optisol-GS® has been the most widely used corneal storage medium in U.S. eye banks, maintaining endothelial cell viability for up to 14 days at 4°C.¹

In recent years, several alternative hypothermic storage media have been introduced, including Life4°C (NuMedis, Inc., Isanti, MN) and Eusol-C™ (Moria, France and Italy).² These alternatives gained prominence during the COVID-19 pandemic, when global supply chain disruptions led to widespread shortages of Optisol-GS. The situation was further complicated by the discontinuation of Life4°C production in April 2022.² However, with the supply chain issues, a significant drop in transplant volume has been observed with both domestic and international transplant numbers in 2024 which is still lagging slightly behind pre-COVID levels.³

This highlights the **need for sustainable, scalable, and reliable corneal storage solutions.**⁴

3. XTRA4: A SCIENCE-DRIVEN, OPTIMIZED FORMULATION

In response to the unmet need for improved cold storage solutions, and thanks to the expertise of the Moria R&D team in corneal storage media formulation and optimization, Moria has developed **XTRA4 – an optimized hypothermic corneal storage medium.**

Distinct from previous formulations, XTRA4 is dextran-free, addressing concerns over potential uptake of this component by the preserved corneal tissue.⁵ As described by Dr. Jana D. Tóthová, Moria innovation is R&D-driven where we developed hundreds of prototypes and tested several alternatives for essential components. XTRA4 is a rich, carefully optimized formulation that was only finalized after extensive experimentation to identify the most safe and effective ingredients.”

Specifically, XTRA4 is a sterile, iso-osmolar culture medium including vitamins, amino acids, sodium pyruvate as an ATP precursor, and a deswelling agent to help maintain the cornea’s proper hydration and prevent excessive stromal swelling. The formulation is buffered with sodium bicarbonate and minimum essential medium (MEM) to maintain a physiological pH range. For broad-spectrum antimicrobial protection, it is supplemented with gentamicin sulfate and streptomycin sulfate.⁶

Meeting the Benchmarks: Safety Backed by Iterative Validation

Accelerated aging studies have confirmed that all parameters remain within specification limits throughout the 2-year product shelf-life.⁷ In terms of biocompatibility, XTRA4 has demonstrated excellent safety according to cytotoxicity, skin sensitization and ocular irritation testing.⁸⁻¹⁰

More importantly, preliminary scientific investigations from three independent eye banks including VisionGift (Portland, Oregon),¹¹ Eversight (Cleveland, Ohio),¹² and Fondazione Banca degli Occhi del Veneto (Venice, Italy),¹³ suggest that XTRA4 outperforms Optisol-GS in preserving corneal tissue quality and may extend preservation time in the future. These early findings suggest that **XTRA4 has the potential to establish a new benchmark in corneal preservation.**

4. WHY CHOOSE XTRA4?

I. Stable Corneal Thickness Profile

A primary objective in the development of corneal storage media is to **preserve the physiological features of the donor cornea including both its structure and function.**

Moreover, it is well established that prolonged hypothermic corneal storage time can negatively impact corneal physiology. Post-storage corneal thickness is expected to increase as preservation time is extended.¹⁴

Comparative studies show that:

- Corneas stored in Optisol-GS exhibit a progressive thickening by day 14, with significant corneal thickness throughout storage.¹¹⁻¹³
- Corneas preserved in XTRA4 maintain a stable thickness profile that remains close to baseline values up to and beyond 14 days.¹¹⁻¹³
- Average central corneal thickness (CCT) increased by 2.4% in the XTRA4 group, and 10% in the Optisol-GS group between Day 1 and Day 14.

XTRA4 maintains physiological corneal thickness, which is directly associated with the absence of stromal and Descemet’s membrane folds, thereby minimizing mechanical stress and endothelial cell loss during storage. This stable corneal thickness profile under hypothermic conditions enables optimal preservation of endothelial viability.

Both XTRA4 and Optisol-GS have demonstrated excellent endothelial survival in vitro for up to 14 days, with preservation of normal endothelial cell morphology. Across multiple validation studies, XTRA4 has shown comparable outcomes to Optisol-GS in terms of endothelial cell density (ECD) and cell morphology.¹¹⁻¹³ However, extended preliminary observation shows minimal changes in endothelial cell viability after even longer periods of storage in XTRA4.¹¹⁻¹³

II. Stromal Preservation Independent of the Intact Epithelium

To further evaluate the performance of XTRA4, donor corneas were stored in XTRA4 at 4°C for six days following epithelial removal (Figure 1). In contrast to corneas stored in Optisol-GS, those preserved in XTRA4 did not develop stromal swelling or edema despite the absence of epithelium.

Stromal preservation independent of the epithelium

Epithelium was removed and corneas were stored for 6 days at 4°C

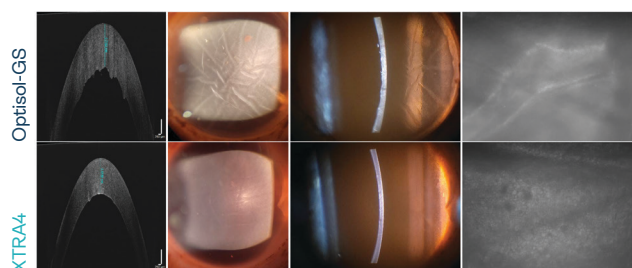


Figure 1. Comparative imaging of corneas stored in Optisol-GS and XTRA4 using anterior segment OCT (A), slit-lamp photography (B, C), specular microscopy (D). The images illustrate differences in corneal morphology and thickness following storage in each medium. (Images courtesy of VisionGift, Portland, Oregon).

While thinner corneas are not inherently a marker of better preservation, maintenance of stromal clarity and thickness even in the presence of epithelial defects, **offers practical advantages for eye banks:**

- Consistent corneal thickness and stromal clarity during storage has the potential to improve eye bank workflows by facilitating tissue assessment and allowing for greater flexibility in tissue selection and surgical scheduling.
- Reduced corneal swelling can allow accurate preoperative assessment with specular microscopy, which can facilitate better intraoperative planning and even potentially improve visual outcomes in the early postoperative period.

No epithelial defect-related folds and edema

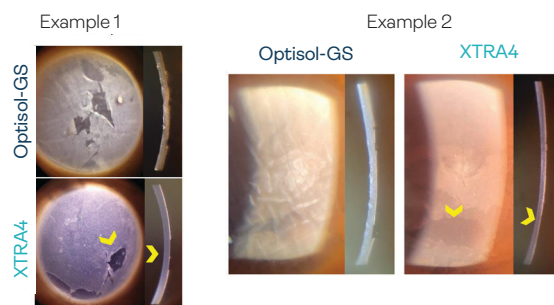


Figure 2. Slit-lamp photographs demonstrating that, unlike corneas stored in Optisol-GS, those stored in XTRA4 show no epithelial defect-related stromal folds or edema.¹¹ (Image obtained from VisionGift, Portland, Oregon).

III. Optimized for DSAEK: Predictable Thickness, Improved Workflow

Two independent studies evaluated the performance of XTRA4 against other commonly used hypothermic media for Descemet stripping automated endothelial keratoplasty (DSAEK) graft preparation. The Fondazione Banca degli Occhi del Veneto in Venice, Italy compared XTRA4 to Eusol-C, while Eversight in Cleveland, Ohio, conducted a parallel evaluation against Optisol-GS.¹³

In both evaluations, XTRA4-stored DSAEK tissues demonstrated comparable outcomes in terms of endothelial cell morphology, density, and viability within the first 7 to 10 days of storage at 4°C.

- DSAEK grafts stored in XTRA4 showed only a 7% increase in thickness after 72-96 hours.¹³ These findings were also independently replicated in another study by VisionGift comparing XTRA4 and Optisol-GS.¹¹

This consistent tissue profile offers tangible benefits for both eye banks and surgeons. In the United States, the increasing preference for endothelial keratoplasty has placed greater emphasis on tissue quality.³ By preserving corneal thickness more effectively, XTRA4 helps reduce variability during DSAEK graft preparation.

Dr. Khoa Tran, PhD of VisionGift highlighted this advantage, stating, "Whatever you see in the cornea stored in XTRA4 on day one is what you get when you go back to prepare it for surgery."

Dr. Onkar Sawant, PhD of Eversight added, "It provides confidence to eye bankers to tell their surgeons that the thickness of the tissue we cut is likely to remain very close to that during surgery."

Predictability in graft thickness is particularly important when preloading ultrathin DSAEK tissue, as even modest swelling can exceed injector lumen capacities and contribute to endothelial cell loss.¹⁵ A cornea preserved in XTRA4 remains near its original thickness, reducing variability during graft preparation. This stability is especially valuable for DSAEK graft preparation and viability where excessive swelling can complicate microkeratome dissection, while reducing EC viability during preloading and tissue delivery. (Figure 3).

Reduction of swelling associated cell loss in XTRA4 stored grafts

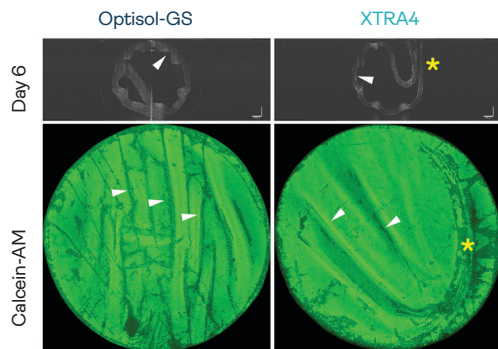


Figure 3. Comparative imaging of preloaded DSAEK grafts stored in Optisol-GS versus XTRA4. The graft stored in Optisol-GS swells to a greater extent during storage, unlike the graft stored in XTRA4 which maintains thickness once preloaded. Excessive swelling can cause cell death along extreme folds (indicated by white arrowhead).

IV. Compatibility with Standard Eye Bank Protocols

Representing a promising advancement in hypothermic corneal storage, XTRA4 offers seamless integration into existing eye bank workflows. “XTRA4 fits easily into current protocols without the need for specialized storage techniques,” noted Dr. Tóthová from Moria. Dr. Tran of VisionGift added, “It is compatible with what eye banks are already doing, which makes it very practical, not just for domestic use, but also for international tissue distribution.” This ease of adoption positions XTRA4 as a scalable and forward-looking solution for the evolving needs of corneal transplantation.

V. Potential for Greater Flexibility in Graft Allocation and Surgical Planning

XTRA4 potentially helps maintain tissue eligibility for endothelial keratoplasty and could significantly reduce the likelihood of having to downgrade grafts to penetrating keratoplasty, thereby effectively expanding the usable donor pool.

Dr. Sawant explained, “We do rule out some corneal tissue that is too thick and therefore can’t meet criteria for DSAEK.” He added “The data suggest that XTRA4 could increase tissue suitability for endothelial keratoplasty processing. Additionally, the potential for a longer storage window in the future would also give surgeons greater flexibility to reschedule procedures or reassign tissue to other patients, as needed.”

Dr. Matthew Feng, MD (Indianapolis, Indiana) pointed to the practical advantages in the operating room, particularly when preparing delicate DMEK grafts. “When we prepare a DMEK graft, we often encounter stress lines related to stromal folds,” he said. “It’s believed those stress lines represent localized endothelial loss, so these donor corneas are probably weaker. Generally, it’s preferred to have a donor cornea that is more compact. Descemet membrane then peels in a more consistent, more uniform way. Thus, if donors have compact stroma with fewer stress lines, we expect our outcomes will be better.”

These advantages could also translate to clinical benefits in the postoperative phase. “Improved endothelial preservation, as evidenced by more compact stroma in the preoperative, untouched donor state, is going to result in a healthier graft in vivo across all types of keratoplasty, whether DMEK, DSAEK, or PK,” Dr. Feng added.

The consistent tissue profile observed with XTRA4 may also deliver tangible benefits for both surgeons and patients. As Dr. Feng emphasized, having a storage medium that helps preserve endothelial function, particularly over a longer duration, can be a real asset. “Preserving stromal thickness may support better epithelial healing following PK and deep anterior lamellar keratoplasty (DALK) procedures. Also, having a donor storage media that is going to preserve endothelium more consistently, not to mention prolong preservation, is going to be a real asset to reduce the risk of graft detachment following DMEK,” he explained. “Every possible advantage to maintain endothelial function, at every step along the donor cornea’s journey, is going to benefit the patient.”

Eversight conducted independent research on XTRA4 supported by funding from Moria to offset costs related to tissue procurement, processing and data analysis. Eversight also utilizes Moria instrumentation and supplies in the course of its operations. The findings and conclusions presented reflect Eversight’s objective scientific evaluation.

VisionGift conducted independent research on XTRA4, supported by a High Impact Grant from the Eye Bank Association of America (EBAA) awarded to Dr. Khoa Tran and Dr. Mark Greiner, with matching funds provided by Moria to help offset research-related costs. The investigators retained full control over data interpretation and the dissemination of results. Findings from this study have been presented at the Cornea and Eye Banking Forum (2024), the European Eye Bank Association Annual Meeting (2025), the World Cornea Congress (2025), and ARVO (2025). A manuscript detailing the results is currently under review.

XTRA4 has received FDA clearance and is now available for sale in the United States.
This paper was commissioned by MORIA and developed by Medevise Consulting based on literature review, scientific data and expert interviews.

CONCLUSIONS

The development of XTRA4, an advanced hypothermic corneal storage medium, represents a major leap forward in donor tissue preservation. Validated through independent studies by leading eye banks, XTRA4 demonstrates superior performance over conventional media.

XTRA4 delivers four key advantages in corneal preservation:

1. **Stable corneal thickness** is maintained throughout storage, with minimal stromal swelling and fold formation.
2. **Preserved stromal architecture**, even in the absence of an intact epithelium, significantly enhancing tissue evaluation.
3. **Sustained endothelial cell viability** proven for 14 days with the potential for extended storage.
4. **Seamless integration into existing workflows** supports efficient tissue evaluation, logistics, and distribution without requiring procedural changes.

These features enable safe and effective storage of donor corneas for extended storage, offering both clinical and logistical benefits.

Benefits for Eye Bank Technicians

XTRA4 is developed with the goal to support the operational needs of eye bank professionals by providing:

- **Consistent tissue profiles** that simplify processing and enhance evaluation.
- **Enhanced imaging clarity** for accurate endothelial cell assessment.
- **Workflow compatibility**, allowing adoption without disrupting established protocols.
- **Extended preservation time**, improving inventory management.

Prospective Benefits for Surgeons

When approved, XTRA4 will be evaluated in practice. Studies will examine prospective benefits in clinical use, operational workflow and patient outcomes – including:

- **Predictable graft thickness**, essential for procedures like DSAEK where surgeons are seeking smoother and more predictable injection characteristics.
- **Minimized stromal distortion**, potentially aiding in smoother DMEK graft preparation and insertion.
- **Excellent endothelial preservation**, potentially reducing the risk of postoperative complications.
- **Superior graft success rates**, potentially reducing the incidence of patients requiring rebubbling.
- **Greater scheduling flexibility**, without compromising graft viability or quality.

In summary, XTRA4 is a next-generation hypothermic corneal storage solution that meets the distinct operational and clinical needs of both eye bank technicians and corneal surgeons. By setting a new benchmark in tissue preservation for both domestic and international tissue use, XTRA4 is poised to reshape global standards in corneal storage, expand access to high-quality donor tissue, and ultimately enhance patient care across both developed and underserved healthcare systems.

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