Advances in Treatment of Corneal Disease:

Gamma-Irradiated Sterile Cornea (VisionGraft®) Provides Safe, Effective Alternative for Non-Endothelial Cornea Surgery

CorneaGen™

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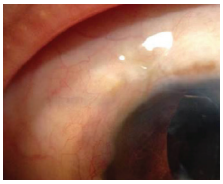
INTRODUCTION

Worldwide, corneal disease is responsible for almost one-fifth of all blindness.[1,2] Among the approximately eight million people who suffer from corneal disease annually, an estimated 100,000 receive corneal transplants.[1,2] Corneal transplantation is one of the most common and most successful solid tissue transplantation surgeries performed today.[3] In the U.S., more than 49,000 cornea transplantations were completed in 2019 alone.

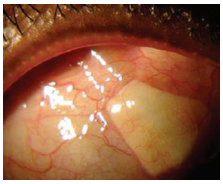
Despite the general success of corneal surgical procedures, conventional corneal transplantation still faces a number of challenges. One of the greatest challenges is a supply issue due to donor shortages. In the U.S., less than 60 percent of donated corneas are deemed suitable for transplant.[1] Additionally, donated corneas can be of low quality or have short distribution periods.[2] This further complicates transplantations in remote areas. In high-risk populations, corneal transplants often have a high failure rate subsequent to immune rejection of donor tissue.[2] Recent studies have indicated that gamma-irradiated corneal tissue could address several of these issues by increasing the supply of donor cornea tissue, making it stable over longer periods of time, and reducing donor immunogenicity.[1,2]

Traditionally, treatment of corneal defects has been managed through utilization of tissue adhesives,[4] conjunctival flaps,[5] amniotic membrane grafting,[6] patching with scleral tissue,[7] or patching with fresh corneal tissue,[8] or patching with glycerin or cryopreserved corneal tissue.[9] Although commonly used, glycerin-cryopreserved corneal tissue, poses several challenges for surgeons. Glycerin-cryopreserved corneas must be rehydrated and repeatedly rinsed of residual glycerin prior to use in any procedure. Additionally, manipulation and handling by surgeons can change the cornea's thickness and clarity. Once implanted, the glycerin-treated corneas may take several weeks before complete stromal clearing, potentially leading to more complications and medical management.[10]

A CLEAR ALTERNATIVE



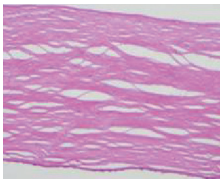
VisionGraft® Patch



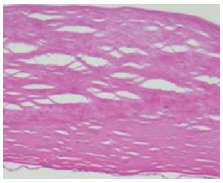
Sclera Patch

Several studies show that using VisionGraft®, a sterile, gamma-irradiated cornea allograft made available by CorneaGen, may provide a safe and effective alternative for non-endothelial corneal procedures. A recent study documenting clinical outcomes for lamellar keratoplasty found that gamma-irradiated corneal tissue not only was clear out of the package, but remained clear through epithelialization and a follow-up period of 7 to 36 months.[11] A similar study of sterile, gamma-irradiated cornea in penetrating keratoplasty reported that VisionGraft® remained clearer and thinner than fresh corneal grafts without endothelium up to one week postoperatively.[12]

Figure 1.



Irradiated Cornea



Fresh Cornea

In a study that tested the optical properties of 20 donor corneas, researchers found that tissue sterilized with irradiation had pachymetry, deeper stromal histology (see Figure 1.), and ultrastructural characteristics comparable with non-irradiated tissues and should be suitable for such clinical applications as tectonic keratoplasty and keratoprosthesis implementation.

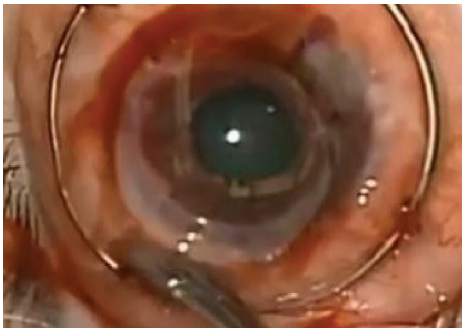
Gamma-irradiated corneal allografts also convey other benefits that can alleviate the shortage of donor corneal tissue. The process of gamma-irradiation virtually eliminates the risk of infection while also enhancing the allograft's stability and shelf-life.[1] Within 24 hours of initial recovery, grafts are sterilized by a validated gamma-irradiation procedure (AAMI American National Standard: Sterilization of health care products-radiation, ANSI/AAMI/ISO 11137, Parts 1-3:2009).[13] Sterility is verified via two-week microbiological testing, and lots are released subsequent to receipt of testing results.[14]

Another benefit of gamma-irradiation is its ability to destroy antigen-presenting cells, thereby reducing the likelihood of allograft rejection. Researchers found that, in gamma-irradiated corneas, viable corneal cells were universally absent; all were positive for ethidium homodimer-1, indicating cell membrane disruption and widespread cell death.[14] The use of VisionGraft® tissue could be especially advantageous in cases with underlying inflammation or where the graft needs to be placed close to the limbus.[11] In one case, in which a fungal infection resulted in corneal perforation, the use of VisionGraft® improved the patient's chances for a successful second graft by using a sterile corneal graft with reduced immunogenicity (see Figure 2.).[15]

In addition, gamma-irradiated corneas convey storage advantages over the standard glycerin and optisol methods. Gamma-irradiated allografts offer sterility as well as a long shelf life – at least one year of surgical quality when conveniently stored in albumin at room temperature.[1,11]

This makes VisionGraft® ideal for both emergencies and scheduled surgeries, as well as for use in remote areas.[11,12]

Figure 2.



Moreover, sterile gamma-irradiated corneal tissue is ready to use and easy to handle. According to a study of gamma-irradiated corneal grafts in lamellar keratoplasty, VisionGraft® tissue appeared clear in the storage bottle and did not require rinsing in saline prior to surgical use.[11] VisionGraft® corneas were reported to handle identically to fresh corneas, due to similar thickness and tensile strength.[11] One study reporting 150 patient outcomes using irradiated corneas in non-endothelial surgical applications found that VisionGraft® was "suitable for any use where a clear human tissue is needed."[1] The 19 surgeons surveyed in the study used 198 irradiated donor corneas and reported positive impressions of VisionGraft® regarding its ease of use, clarity, thickness, tensile strength, and suturing, as well as epithelialization and biological incorporation.[1]

COMPARABLE TO FRESH CORNEAS

VisionGraft® sterile corneas are comparable to, and offer a number of advantages over, fresh corneas:

- Sterile gamma-irradiated corneas have the same thickness as fresh corneas and handling is identical.[11]
- The tissue does not require rehydration prior to surgery and is clear when implanted.
- Gamma-irradiation offers additional patient safety, compared to fresh corneas, and virtually eliminates the risk of bacterial or fungal disease.[1]
- A key benefit of VisionGraft® is its demonstrated ability to deplete antigen-presenting cells transferred within the donor tissue; due to gamma-irradiation processing, this reduces the likelihood of graft rejection by "preventing…direct sensitization".[11]
- VisionGraft® offers a shelf life of two years at room temperature, a low 2.5% erosion rate, and demonstrated positive clinical outcomes for up to 24 months.

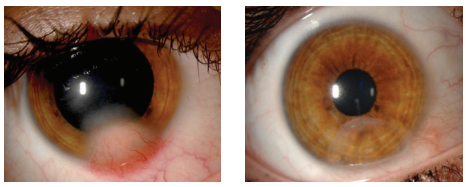
Studies have also demonstrated that VisionGraft® is easier to work with than other patch graft materials, provides better durability and tensile strength, and reduces or eliminates erosions.[1,11] Moreover, there was no incidence of immune rejection, infection, significant opacification, or neovascularization of donor tissues during the follow-up period.[14]

Lab testing on the VisionGraft® tissue included suture pull-through testing, which demonstrated comparable strength with that of fresh corneal tissue, histopathology studies that demonstrated normal collagen structure, and electron microscopy testing, which demonstrated similar mean interfibrillar distance and fibril diameter to that of non-irradiated fresh corneas.[16]

A SOLUTION FOR NON-ENDOTHELIAL SURGICAL APPLICATIONS

Despite the success of corneal transplants, a shortage of donor tissue remains one of the most serious hurdles. Gamma-irradiation provides a sterile graft for non-endothelial surgical procedures. Recent studies have demonstrated that sterile, gamma-irradiated corneal tissue is suitable for use in patch grafts – both corneal and glaucoma – as well as in keratoprothesis and lamellar corneal procedures.[1,11,17] Using VisionGraft® corneal tissue for non-endothelial applications can increase the supply of corneal tissue suitable for transplantation in situations that require viable endothelium.

Figure 3.



Before After

VisionGraft® tissue also maintains its shape, strength, and optical clarity.[1] Thus, sterile gamma-irradiated tissue can serve as an effective alternative in non-endothelial surgical applications, can be immediately accessed in remote areas or emergency situations (see Figure 3.).

Comparison: Gamma-irradiation vs. Other Current Storage Methods for Cornea Tissue

Properties	Irradiated Cornea	Glycerin Cornea	Cryopreservation
Steile (yes or no)	Yes	No	No
Surgeon preparation	None required	Yes	Yes
Tissue quality	Very Good	Thicker, rubbery	Thinner
Storage - Duration Condition	2 years	5 years	2 weeks
Clarity	Clear	Inconsistent	Clear

Synopsis

Indications for Surgical Procedures Similar to Fresh Corneas

- Histopathology demonstrates normal collagen structure
- Similar mean interfibrillar distance and fibril diameter
- Thickness and handling (whole corneas)
- Comparable suture pull-through strength

VisionGraft® Characteristics

- Gamma-irradiated corneal tissue, sterile
- Stable shelf-life at room temperature for two years
- No rehydration required / ready to use
- Clear when transplanted
- Durable, maintains shape with manipulation

Benefits of Irradiation

- Reduces the likelihood of graft rejection
- No antigen-presenting cells transferred with donor tissue
- Eliminates risk of bacterial or fungal disease
- Does not change the tensile strength of corneal tissue

Similar to Fresh Corneas

- Histopathology demonstrates normal collagen structure
- Similar mean interfibrillar distance and fibril diameter
- Thickness and handling (whole corneas)
- Comparable suture pull-through strength

Surgeon Perspective of VisionGraft®

- Good re-epithelialization
- Reduces or eliminates erosion
- Reduces re-operations
- Provides a diagnostic window to the valve

Patient Perspective of VisionGraft®

- Provides translucent outcome
- Reduces or eliminates the need for repeated surgeries to replace eroded tissue

Alternative Solutions

- Sclera
- Glycerine-preserved cornea
- Pericardium
- Amnion

CONCLUSION

In summary, the findings of the studies mentioned in this paper indicate that VisionGraft® sterile, gamma-irradiated corneal allografts provide a safe and effective alternative to conventionally prepared corneal tissue in non-endothelial surgical applications.

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