# Sterile Irradiated Tissue: A Practical Solution for Glaucoma Treatment


## ABSTRACT

Glaucoma is a leading cause of blindness worldwide, and serious cases are often treated surgically with the implantation of glaucoma drainage devices (GDDs) to relieve eye pressure and prevent further damage to the optic nerve. This procedure requires tissue allografts to prevent GDD tube exposure; however, tube erosion and infection are persistent risks. The use of sterile irradiated eye tissue, such as Lions World Vision Institute's (LWVI's) OptiGraft® sterile tissue, is a cost-effective way to reduce these risks while also reducing the risk of infection and tissue rejection. In addition, sterile irradiated tissue such as OptiGraft has a long shelf life, can be stored at room temperature, and is ready to use, reducing waste due to tissue perishability and thus increasing the potential availability of high-quality tissue for implantation.


For high-quality corneal and scleral patch grafts for glaucoma surgery, surgeons have long turned to sterile irradiated corneal and scleral tissues.

## GLAUCOMA—A GROWING PROBLEM

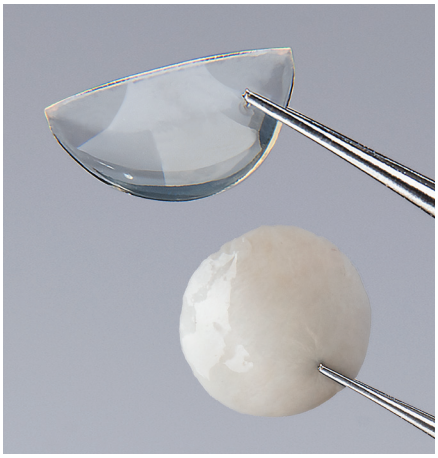
Glaucoma has become increasingly prevalent in the American population and is one of the leading causes of blindness worldwide.[1,2] Approximately 3 million Americans are affected by glaucoma, and The National Eye Institute has projected this number to increase to 4 million by the year 2030.[1-3] The major difficulty in treating glaucoma is that symptoms often go unnoticed, and it is estimated that 50% of patients are unaware they are affected by the disease.[2] Conventional medications such as eye drops and laser treatments are used to slow the progression of the disease, but when the condition worsens or becomes complex, physicians may opt for surgically implanted drainage devices.[4] These devices are referred to as glaucoma drainage devices (GDD) and serve to relieve pressure from inside the eye and prevent any further damage to the optic nerve. Several materials have been used as tissue allografts to prevent GDD tube exposure, including fresh cornea, glycerin-preserved cornea, sclera, amniotic membrane, dura mater, fascia lata, porcine intestinal submucosa, and pericardium.[5]

## THE RISKS OF GDD SURGERY— AND HOW IRRADIATED TISSUE CAN REDUCE THEM

GDD surgery is not without risk, however. Its most common complications are tube erosion and infections. Although scleral allografts are commonly used in glaucoma surgeries, post-operative follow-up studies have shown GDD tube erosion under the scleral patches.[6] Another complication of this surgery is endophthalmitis, which is caused by infection and is estimated to occur in 1 out of 107 transplants.[5,7] With the use of these materials, not much can be done to prevent infection because antimetabolites such as mitomycin C and 5FU are often required post-surgery to prevent excess cell and tissue growth, which can reduce the benefit of the GDD surgery. This leads to an increased risk for post-operative infection.[8]

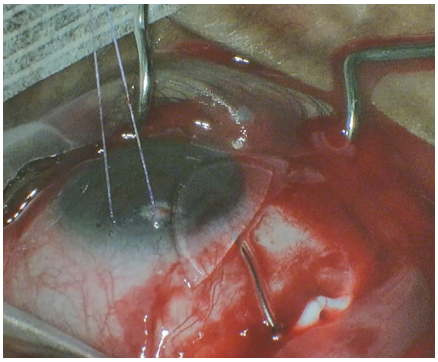
Ideally, the material used for glaucoma patches covering GDD tubes should not only be cosmetically acceptable, but more importantly, biocompatible and immunologically safe.[6] For high-quality corneal and scleral patch grafts for glaucoma surgery, surgeons have long turned to sterile irradiated corneal and scleral tissues. Irradiation has been used for over five decades as a verified, standard method of sterilization for medical products.[9,10] Several studies have found that sterilization by irradiation does not negatively affect the quality of the tissue integrity.[11-14] The use of sterile irradiated corneas has other important benefits as well: It can increase the amount of transplantable corneal tissues, decrease donor immunogenicity and risk of infection, improve clinical outcomes, and increase long-term tissue storage.[11,12]

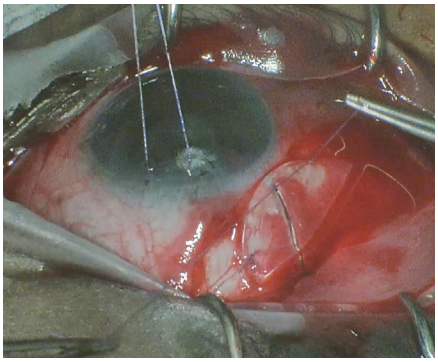
Despite its many advantages, irradiated corneal tissue has traditionally been costly, making it a premium option rather than a standard option for surgeons. However, new technology for preparation and packaging, such as that used in LWVI's new OptiGraft line of irradiated tissue products, significantly reduces its cost of production—and consequently, its cost to users.



*Sterile Patch Grafts:*

- *Clear Cornea Half-Moon, split thickness*
- *Scleral Disk (10mm)*





*Sterile, clear cornea half-moon graft shown above tube (photo 1) and covering tube (photo 2)*

## IRRADIATION STERILIZATION INCREASES TISSUE AVAILABILITY AND USABILITY

All too often, donor corneal tissue can't be transplanted due to poor tissue quality, specifically low endothelial cell count.[12] Irradiation sterilization, however, allows such tissues to be used for non-endothelial purposes such as patch grafts for GDD surgery.[6,15] This is because the mechanism of action of irradiation targets the cells' DNA bonds, killing epithelial and endothelial cells without affecting the integrity of the tissue. Ultine et al reported pull-through testing of irradiated corneas was as strong as fresh (Optisol-stored) corneas.[16] In another study, Chae et al. compared the biological and physical characteristics of gamma-irradiated corneas to fresh corneas and concluded that the elastic modulus, hydration, and light transmittance were of similar quality between fresh and irradiated corneas.[11] Furthermore, in a short-term study of irradiated sterile corneas, Daoud et al. found that the macroscopic quality and clarity of the transplanted tissues were not affected by the tissue irradiation.[12] And while Tran et. al found a slight increase in the light scattering of e-beam irradiated corneas, this increase was ultimately deemed insignificant for the quality of the tissue.[15] Eliminating the endothelial cell count constriction would thus increase the available supply of quality, transplantable-ready tissues for patch and lamellar surgeries.

## IRRADIATED TISSUE PREVENTS IMMUNE REJECTION

Another consideration for surgeons performing fresh tissue corneal transplants is the imminent risk of graft failure due to recipient immune rejection.[11] The immunosuppressive effect of irradiation sterilization eliminates this risk.[14] Irradiation sterilization decreases donor immunogenicity by killing the antigen-presenting cells and keratocytes that trigger immune responses in transplant recipients.[11,12] When antigen-presenting cells are depleted, direct sensitization is avoided, consequently decreasing the possibility of graft rejection.[16] Stevenson et al. found that T-cells isolated from irradiated allografts exhibited no secondary alloimmune response.[14] Additionally, Pan et al showed that irradiated corneas used for glaucoma patch graft demonstrated good biocompatibility.[6] The reduced immune rejection risk of sterile corneas is especially beneficial for patients who have had multiple transplantations or may already be immunocompromised.

## IRRADIATED TISSUE REDUCES THE RISK OF INFECTION

A potential complication of GDD surgery is endophthalmitis due to post-operative infection.[8] Currently, the standard method of fresh cornea storage is in Optisol; however, corneal grafts may also be preserved in glycerin. But, neither preservation method eliminates the risk of infection.[12] Irradiation sterilization, on the other hand, may reduce the risk of transplant infections by eliminating any microbes in the donor tissue.[15] This is especially relevant to the eye bank industry now because of the strict regulations for the procurement, storage, and handling of donor tissues currently being implemented to reduce the risk of infection.[15] It's possible that some of these regulations could be revised to reflect the decrease risk of infection from sterile corneas.

## IRRADIATED TISSUE IMPROVES CLINICAL OUTCOMES FOR GDD PATIENTS

While GDD implantation can be an effective treatment method for glaucoma, it presents the risk of a potentially serious complication: the erosion of the GDD tube through the patch graft and conjunctiva.[6] In a retrospective study, Pan et al found that graft thinning / melting only occurred in about 0.6% of the cases (2 out of 319 cases).[6] Similarly, Passo et al found that although e-beam irradiated corneas were used 3.8 times more often than scleral grafts, no erosion was noted in any of the sterile corneal grafts.[5] Furthermore, the transparency of sterile irradiated corneal grafts allows the surgeon to better monitor the implanted tube.[6]

New technology for preparation and packaging, such as that used in LWVI's new OptiGraft line of irradiated tissue products, significantly reduces its cost of production—and consequently, its cost to users.

## READY TO USE WITH A LONG SHELF LIFE, IRRADIATED TISSUE IS A PRACTICAL SOLUTION

Fresh, Optisol-stored corneas must be transplanted within 14 days of preservation, which restricts opportunities for their use.[12] Moreover, the tissue must be preserved in solution and refrigerated in temperatures between 2 - 8°C, requirements that pose challenges for tissue transport and storage. Another option for tissue storage is glycerin, which can last much longer. However, glycerin-preserved corneas have a noticeably rubbery feel and may be difficult to handle during surgery.[12] Even more problematically, glycerin-preserved corneas must be allowed to rehydrate prior to transplantation and are not sterile.[16]

Tissue irradiation eliminates these problems. It has been found to extend the shelf life of the tissue for up to 2 years without affecting its texture or readiness for use.[11] Because irradiated tissues are stored in human albumin, they do not require rehydration and can be stored at room temperature, making them ready for anytime use.[11] These characteristics are particularly beneficial for surgery centers lacking refrigerated storage and remote communities that can benefit from storing these tissues in large quantities. Additionally, studies have found no noticeable difference between the visualization of text through irradiated, long-term stored corneas (20 months) and through fresh corneas.[15] The tolerance of irradiated corneas to long-term storage make them ideal for emergency, trauma, and tumor resection cases. Moreover, in a mission trip to Lebanon, Fadlallah et al. found visual acuity improvement in 94.1% of their cases using irradiated corneas with no incidence of stromal necrosis or infectious keratitis.[10]

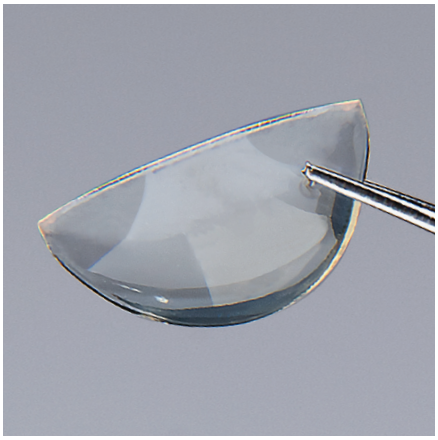

*OptiGraft sterile corneal tissue has an extended shelf life for up to two years and can be stored at room temperature.*

## E-BEAM VS. GAMMA RADIATION: WHAT YOU SHOULD KNOW

While many studies have focused on evaluating the effects of gamma irradiation on corneal donor tissues, electron beam (e-beam) irradiation has risen in popularity in the past several years, particularly for use with corneal patches for GDDs.[5,6] Both methods are valid sterilization techniques. However, the biggest difference between them is tissue exposure times. Gamma-irradiated tissues are subject to greater exposure times than e-beam radiation because gamma irradiation dose rates are much lower than those used for e-beam irradiation, thus requiring longer exposure times.[17] In contrast, e-beam irradiation exposes tissues to high dose rates of irradiation at a low penetration for a much shorter exposure time, making the e-beam process more effective and efficient. A disadvantage of the longer exposure periods of gamma-irradiated tissues is the formation of minor changes in corneal collagen matrix.[15] E-beam irradiation has not been found to cause noticeable differences in the collagen matrix of corneas, thereby leaving important clinical properties such as clarity and light scattering unaffected.[15] In fact, when surgeons examined long-term stored corneas for intact stroma, opacities, and overall structural integrity prior to surgery, they found no difference between sterile and fresh corneas.[12]

## OPTIGRAFT: THE PREMIUM CHOICE FOR GDD GRAFTS

Sterile irradiated corneas and scleras, such as those in LWVI's new OptiGraft line, provide a more flexible approach to glaucoma surgery patch grafts by permitting a longer shelf life and decreased immunogenicity at a much lower cost than fresh corneal tissues or other sterile tissue available. Their longer shelf life makes them a practical option for remote communities and mission trips. Unlike glycerin-preserved and Optisol-stored corneas, irradiated corneas do not require re-hydration or special handling techniques for transplantation. Because they're ready to use, sterile irradiated cornea and sclera are ideal for emergency and trauma surgeries.[10] And in addition to these benefits, OptiGraft products also offer ease of use through specially designed packaging. Additionally, the ability of irradiation sterilization to remove antigens can potentially increase the corneal tissue supply by allowing a wider range tissue to be made suitable for transplantation. Ideally, all tissue donated should be used for transplant, honoring and maximizing the donor's gift.



*Premium Sterile Patch Graft:*

- *Clear Cornea Half-Moon, split thickness*

## REFERENCES


1. Flaxman SR, Bourne RRA, Resnikoff S, et al. Global causes of blindness and distance vision impairment 1990-2020: a systematic review and meta-analysis. *Lancet Glob Health.* 2017;5(12): e1221–e1234. doi:10.1016/S2214-109X(17)30393-5
2. Glaucoma Facts and Stats. Glaucoma Research Foundation. https://www.glaucoma.org/glaucoma/glaucoma-facts-and-stats.php. Accessed March 9, 2020.
3. Glaucoma Data and Statistics. National Eye Institute. https://www.nei.nih.gov/learn-about-eye-health/resources-for-health-educators/eye-health-data-and-statistics/glaucoma-data-and-statistics. Published July 17, 2019. Accessed February 18, 2020.
4. Glaucoma. National Eye Institute. https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/glaucoma. Published July 29, 2019. Accessed March 10, 2020.
5. Passo RM, Hoskins ZB, Tran KD, et al. Electron Beam Irradiated Corneal Versus Gamma-Irradiated Scleral Patch Graft Erosion Rates in Glaucoma Drainage Device Surgery. *Ophthalmol Ther.* 2019;8(3):421–426. doi:10.1007/s40123-019-0190-x
6. Pan Q, Jampel HD, Ramulu P, et al. Clinical outcomes of gamma-irradiated sterile cornea in aqueous drainage device surgery: a multicenter retrospective study. *Eye (Lond).* 2017;31(3):430–436. doi:10.1038/eye.2016.230
7. Gedde SJ, Herndon LW, Brandt JD, et al. Postoperative complications in the Tube Versus Trabeculectomy (TVT) study during five years of follow-up. *Am J Ophthalmol.* 2012;153(5):804–814.e1. doi:10.1016/j.ajo.2011.10.024
8. Farber N, Muir K. Endophthalmitis After Glaucoma Surgery. American Academy of Ophthalmology. https://www.aao.org/eyenet/article/endophthalmitis-after-glaucoma-surgery. Published March 1, 2020. Accessed March 10, 2020.
9. Singh R, Singh D, Singh A. Radiation sterilization of tissue allografts: A review. *World J Radiol.* 2016;8(4):355–369. doi:10.4329/wjr.v8.i4.355
10. Fadlallah A, Atallah M, Cherfan G, Awwad ST, Syed ZA, Melki SA. Gamma-irradiated corneas as carriers for the Boston type 1 keratoprosthesis: advantages and outcomes in a surgical mission setting. *Cornea.* 2014;33(3):235–239. doi:10.1097/ICO.0000000000000065
11. Chae JJ, Choi JS, Lee JD, et al. Physical and Biological Characterization of the Gamma-Irradiated Human Cornea. *Cornea.* 2015;34(10):1287–1294. doi:10.1097/ICO.0000000000000555
12. Daoud YJ, Smith R, Smith T, Akpek EK, Ward DE, Stark WJ. The intraoperative impression and postoperative outcomes of gamma-irradiated corneas in corneal and glaucoma patch surgery. *Cornea.* 2011;30(12):1387–1391. doi:10.1097/ICO.0b013e31821c9c09
13. Sikder S, McCally RL, Engler C, Ward D, Jun AS. Evaluation of Irradiated Corneas Using Scatterometry and Light and Electron Microscopy. *Cornea.* 2011;30(5):503–507. doi:10.1097/ICO.0b013e3181eadd0f
14. Stevenson W, Cheng SF, Emami-Naeini P, et al. Gamma-irradiation reduces the allogenicity of donor corneas. *Invest Ophthalmol Vis Sci.* 2012;53(11):7151–7158. Published 2012 Oct 1. doi:10.1167/iovs.12-9609
15. Tran KD, Li Y, Holiman JD, et al. Light scattering measurements in electron-beam sterilized corneas stored in recombinant human serum albumin. *Cell Tissue Bank.* 2018;19(1):19–25. doi:10.1007/s10561-017-9666-x
16. Utine CA, Tzu JH, Akpek EK. Lamellar keratoplasty using gamma-irradiated corneal lenticules. *Am J Ophthalmol.* 2011;151(1):170–174.e1. doi:10.1016/j.ajo.2010.08.007
17. Odland TL.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