

Cryopreserved Amnion Grafts and Tenonplasty for Scleral Melt due to Ischemia

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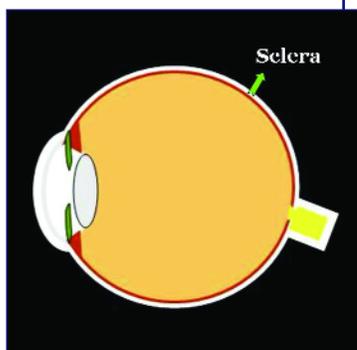


Fig. 1

Overview

The sclera serves as a protective coat and a stable support for the intraocular tissues (Fig. 1). Its thickness is not uniform, being the thickest at the posterior pole (1-1.35 mm), gradually decreasing to be the thinnest immediately posterior to the rectus muscle insertion (0.3 mm), and increasing again towards the limbus (0.8 mm). The scleral matrix is compact and made of collagen fibers and interfibrillar proteoglycans. In a normal healthy eye, the scleral stroma is avascular, receiving its nutrition from choroidal blood vessels and the vascular plexus in the Tenon's capsule and on the episcleral surface.

Scleral melt is a serious and challenging clinical problem as it threatens the integrity of the eye. Clinically, scleral melt is almost always the result of ischemia which interrupts the blood flow of episcleral blood vessels. Therefore, scleral ischemia and melt can be caused by a number of diseases that interrupt the blood circulation. Acutely, scleral ischemia can occur in chemical or thermal burns. When such ischemia extends near the limbus, it further compromises the limbal epithelial stem cells. Chronically, scleral ischemia can happen when excessive, beta irradiation or mitomycin C are used to treat pterygia or develop after systemic vasculitis and connective tissue disorders.

This Guide demonstrates how Tenonplasty can be used to restore the blood supply. Once the blood supply is established on the ischemic sclera, lamellar corneal graft and/or amniotic membrane transplantation can be used as a tectonic substitute for the missing scleral tissue depending on the depth of the scleral defect. Furthermore, the overlying conjunctival surface healing is facilitated by the transplantation of a cryopreserved amnion graft. As illustrated in this Guide, lamellar corneal tissue and amniotic membrane transplantation can be accomplished without sutures by using fibrin glue. As a result, the surgical time is shortened (allowing topical anesthesia), the patient's recovery time is reduced, and the postoperative care is simplified.

Key Pre-operative Points:

- If the patient does not have a clear underlying etiology such as acute chemical burn or use of beta irradiation or MMC for pterygium, known to cause scleral ischemia, and if the scleral melt is limited to the limbal and peripheral corneal regions (like peripheral ulcerative corneal diseases), it is advised to rule out whether there is a systemic collagen vascular disease caused by autoimmune dysregulation. An appropriate diagnostic work-up and consultation are needed. If verified, systemic immunosuppression should also be initiated. Mooren's ulcer is a disease diagnosed after exclusion of these diseases.

Key Pre-operative Points:

- Dellen formation due to insufficient tear flow or spread can cause scleral thinning or aggravate a scleral melt. Therefore, it is also important to determine whether there is neurotrophic keratopathy, aqueous tear deficiency (dry eye) or surface exposure due to infrequent blink and incomplete closure by checking corneal sensitivity, performing Schirmer test without anesthetics, and checking the blink rate. If noted, these problems should be managed first by punctal occlusion (to both upper and lower) with punctal plugs or even with permanent cauterization, followed by large scleral lens protection, pressure patch (temporarily), or tarsorrhaphy.

Supplies:

- Donor corneal tissue from any eye bank: Both epithelial and endothelial qualities do not matter as the main purpose is tectonic but not optical.
- Cryopreserved amniotic membrane: AMNIOGRAFT® purchased from Bio-Tissue, Inc. by calling their toll free phone number, 1-888-296-8858. Four sizes are available as shown. The graft size is chosen according to the area that needs to be covered. For more information visit www.biotissue.com

Catalog #	AMNIOGRAFT® Sizes	Actual Size
AG-2520	A	2.5 x 2.0 cm
AG-2015	B	2.0 x 1.5 cm
AG-3535	C	3.5 x 3.5 cm
AG-1510	D	1.5 x 1.0 cm

- Traction Sutures: Use 7-O Vicryl sutures
- For sutureless surgery, use fibrin glue: TISSEEL VH (Vapor Heated) fibrin glue (1.0 mL, part # 921028) purchased from Baxter Biologics by calling their toll free phone number, 877-TISSEEL (877-847-7335). For product information, visit www.advancingbiosurgery.com/us/products/tisseel/. We prefer to use the two components separately, each with a special needle provided without dilution, instead of combining them via the provided DUPLOJECT.

NOTE: The ophthalmic use of Fibrin Glue is considered “off label”.

- For surgery with sutures, 10-O nylon is used for the bulbar area and 8-O Vicryl is used for the forniceal area.

Key Surgical Steps

It is recommended that you view OSREF DVD Vol. 11 “Scleral Ischemia and Melt” and call Dr. Tseng at 305-274-1299 for any questions BEFORE your first procedure.

Anesthesia: Topical anesthesia is preferred. After prep and drape of the eye and insertion of a lid speculum, drops of non-preserved epinephrine 1/1000 (Hospira, Inc., Lakes Forest, IL) are instilled on the ocular surface to achieve vasoconstriction for hemostasis, and 2% lidocaine gel (AstraZeneca LP, Wilmington, DE) is applied for anesthesia.

Traction Suture and Exposure: A 7-0 double armed Vicryl suture is placed as a traction suture at 2 to 3 mm from the superior and inferior limbus with episcleral bites (Fig. 2). The eye is rotated by hanging a locking needle holder to allow adequate exposure of the bulbar sclera where the ischemia and melt is most pronounced.

Incision: Sharp Wescott scissors are used to release the healthy conjunctiva along the border of the scleral melt (Fig. 3A) and to create relaxing incisions radially from the edge of the scleral melt toward the healthy fornix. This allows for subsequent isolation of the Tenon's capsule located posterior to the melt and creates a pedicle graft (Fig. 3B).

Removal of Necrotic Tissue and Calcium Plaque: The scleral melt area is further debrided to remove all unhealthy necrotic tissue (Fig. 4A). If there is calcified plaque (e.g., in chronic scleral melt) it can simply be removed by superficial lamellar dissection using a #64 blade (Fig. 4B). The goal is to restore a clean host bed that may reveal the underlying uveal tissue.

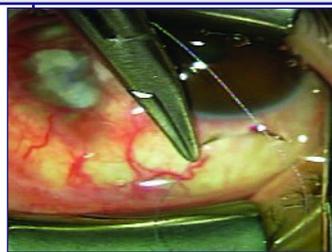


Fig. 2



Fig. 3A



Fig. 3B

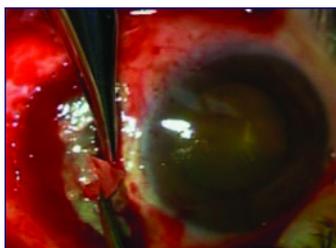


Fig. 4A



Fig. 4B

For Repair of Scleral Ischemia in Acute Chemical/Thermal Burns: After removal of necrotic tissue (Fig. 5A, 5B, 5C), the ischemic zone is first covered by a layer of cryopreserved amnion graft to protect the remaining sclera using 10-0 nylon interrupted sutures (Fig. 5D) or fibrin glue (see below).

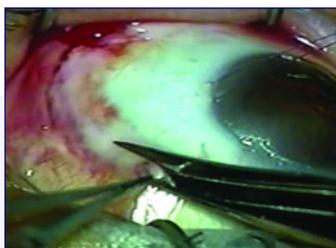


Fig. 5A

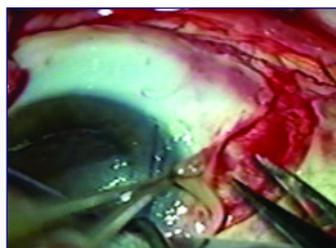


Fig. 5B



Fig. 5C

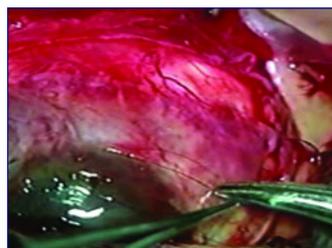


Fig. 5D

Key Surgical Steps

For Repair of Scleral Tissue Loss using a Lamellar Corneal Graft: For eyes showing scleral melt, a notable loss of scleral tissue can be supplanted by lamellar corneal tissue. After measuring the dimension of the scleral defect, the corneal graft is stripped off the endothelium and the epithelium using a Q-tip. A free-hand lamellar graft is created by using scissors and a super blade to match the scleral defect size (Fig. 6A). This lamellar corneal graft can be secured to the scleral bed without sutures using fibrin glue; it is hard to place sutures if the melt extends to the equator. This gluing is achieved by drying the scleral bed with a Weckcel, applying the thrombin (watery, colorless) solution to the bare sclera (Fig. 6B), and then by applying the fibrinogen (viscous, tawny) solution to the concave stromal surface of the lamellar corneal graft (Fig. 6C). The lamellar corneal graft is then flipped to cover the scleral defect, and attached to the sclera using a muscle hook to smooth and spread the fibrin glue evenly underneath (Fig. 6D).

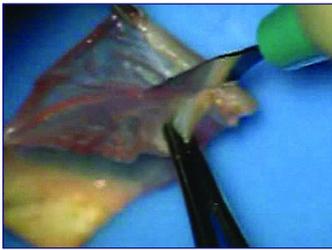


Fig. 6A

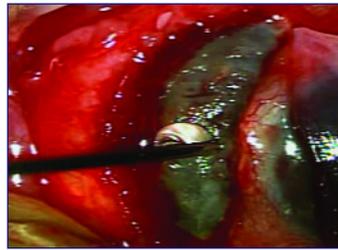


Fig. 6B

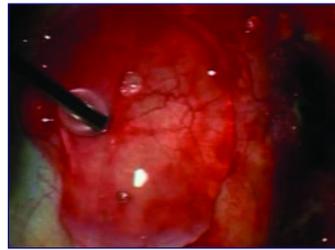


Fig. 6C

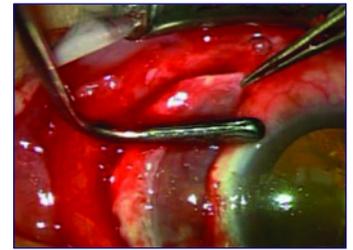


Fig. 6D

Tenoplasty: The subconjunctival Tenon tissue is carefully dissected from the episcleral space and from the overlying conjunctiva tissue, and prepared as a pedicle graft (Fig. 7A). Such a Tenon graft is easily stretched to cover a large area. The size of such a Tenon graft is contingent upon the size of the ischemic area to be covered. It is advisable to cover at least a part, if not all, of the defect by either using 10-O nylon sutures with solid episcleral bites to the healthy sclera (Fig. 7B) or fibrin glue. The thrombin (watery, clear) solution is applied on the top of the corneal graft (Fig. 7C) and the fibrinogen (viscous, tawny) solution is applied to the inner surface of Tenon's capsule. Using two 0.12 forceps, the Tenon is stretched to cover the scleral defect area, and held for at least 5 seconds (Fig. 7D). A muscle hook is then used to spread and smooth the fibrin glue underneath.

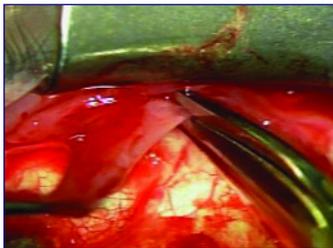


Fig. 7A

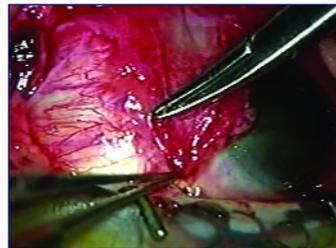


Fig. 7B

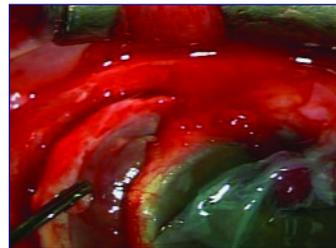


Fig. 7C

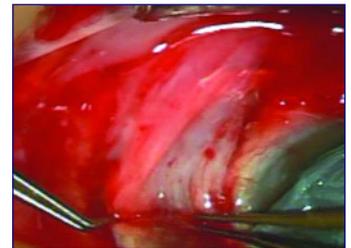


Fig. 7D

Key Surgical Steps

Transplantation of Amnion Graft: The cryopreserved amnion graft is peeled from the nitrocellulose filter paper using two 0.12 forceps and laid down onto the scleral melt area with the sticky, stromal surface facing down to cover the entire defect (Fig. 8A). The membrane is flipped in half so one half of the stromal surface will be facing up (Fig. 8B). The thrombin (watery, clear) solution is applied to the surgical bed/defect (now covered by Tenon's capsule) (Fig. 8C) and fibrinogen (viscous, tawny) solution is applied to the stromal side of folded membrane (Fig. 8D). Next the membrane is flipped back on the bed/defect and a muscle hook is used to spread the fibrin glue into an even and thin layer underneath the amnion graft (Fig. 8E). The above steps are repeated to secure the other half of the membrane. After a short time (less than 30 sec) of polymerization, check the strength of the adhesion by lifting each corner of the membrane with 0.12 forceps. If easily detached, apply the two fibrin glue components directly onto the bed/defect and spread the glue and smooth the membrane again using a muscle hook. Trim the excess membrane and fibrin glue from the edges (Fig. 8F).

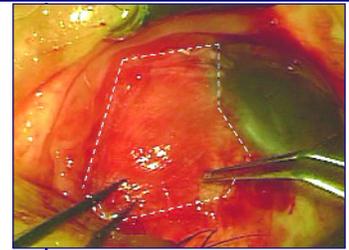


Fig. 8A

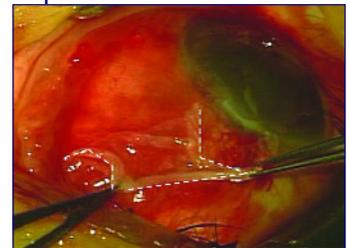


Fig. 8B

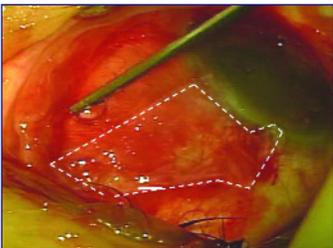


Fig. 8C

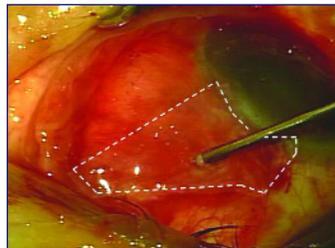


Fig. 8D

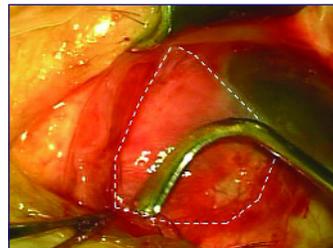


Fig. 8E

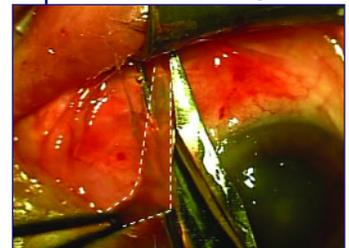


Fig. 8F

About Sutures:

If fibrin glue is not used, both lamellar corneal graft and Tenon's pedicle graft can be secured by interrupted 10-0 nylon sutures. The cryopreserved amnion graft can be secured using several interrupted 10-0 nylon sutures on peri-limbal bulbar conjunctiva and by 8-0 Vicryl sutures in a mattress fashion, parallel to the fornix, with solid episcleral bites to seal the fornix border.

Key Post-operative Points:

It is advised to see the patient POP 1 day, 1 week, 3 to 4 weeks and thereafter depending on the clinical outcomes. At POP day 1, instructions such as avoiding dirty water into the eye are given and medications such as Prednisolone acetate 1% (Pred Forte®) four times a day and Ofloxacin 0.3% (Ocuflox®) three times a day are started. At the 3 to 4 week visit, complete epithelialization over the cryopreserved amnion graft and restoration of the scleral integrity are expected. During this visit, Ocuflox® is stopped and PF is tapered off at a weekly schedule from four times a day. Additionally, if fibrin glue is not used, remove all sutures at this time. (Fig. 9A and 9B for acute chemical burn: Fig. 9C and 9D following pterygium surgery).



Fig. 9A



Fig. 9B



Fig. 9C

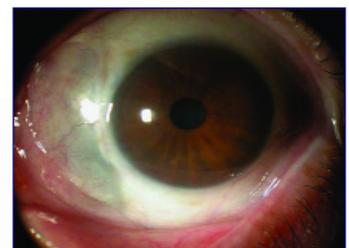


Fig. 9D

Literature Summary

Scleral ischemia, thinning and melt can occur in acute severe chemical or thermal burns and following ocular surgeries such as pterygium excision with a bare sclera technique,¹ especially if such adjuvant therapies as beta-irradiation and mitomycin C are used.² In addition, scleral melt has also been described after retinal detachment repair, glaucoma surgery, systemic vasculitis and connective tissue disorders.^{3,4}

Reim et al first described the use of Tenonplasty as an excellent alternative to treat limbal and scleral ischemia in patients with severe chemical and thermal eye burns in 1989 to facilitate conjunctival healing and to halt progressive scleral melt.^{5,6} Since then, several reports have been published reassuring the effectiveness of this surgical approach.⁷⁻⁹ Lin et al⁹ in 2002 reported the use of Tenonplasty and amniotic membrane transplantation in 6 patients with scleral perforation after pterygium surgery. There were no recurrences during a follow-up period of 12 to 24 months.

On the other hand, when severe scleral thinning or melt with impending globe perforation is evident, sclera reinforcement is necessary. Different types of tissue grafts have been proposed and/or actually used to fulfill this purpose. They include preserved sclera, cornea, pericardium, fascia lata, dura, conjunctiva, amniotic membrane, etc.^{9,10} None of the proposed grafts have been universally accepted. Lin et al¹¹ in 1996 described a method for scleral grafting using preserved sclera and tissue adhesive with an overlying conjunctival flap, and noted good results in 5/6 cases with infectious scleral ulcers. Rodriguez-Ares et al¹² successfully used scleral graft and amniotic membrane transplant to repair a large scleral perforation in a patient with Marfan's syndrome and a past history of various surgeries in both eyes. Hanada et al,¹³ used multilayered amniotic membrane transplantation for the treatment of 11 patients (11 eyes) with deep corneal ulcers (n=5), corneal perforations (n=4) and scleral ulcers (n=2). After surgery 8/11 eyes, including 2 cases with scleral defects did properly heal. Ma et al¹⁴ used cryopreserved amniotic membrane as a patch graft to reduce stromal melting and promote reepithelialization in four cases of infectious scleral ulcers with persistent scleral melting and three cases with corneoscleral ulcers with perforation. They noted that melting and inflammation at the lesion site decreased after the amniotic membrane grafting. It should be noted that in all their cases the causative microorganisms were identified and the appropriate topical and systemic antibiotics were given to all patients before the surgery. Oh et al¹⁵ performed a prospective study in 8 eyes (8 patients) using preserved sclera and amniotic membrane transplantation for the surgical repair of scleromalacia with impending perforation. All patients experienced loss of ocular pain and inflammation and rapid epithelialization. Ti et al¹⁰ reported the successful use of tectonic corneal lamellar grafting with overlying conjunctival flap in 95% of their cases (19/20 patients) with severe scleral melts after pterygium surgery with mitomycin C or beta irradiation. Golchin et al¹⁶ reported lamellar keratoplasty as an effective treatment option for scleral necrosis induced by beta irradiation, achieving tectonic restoration in all of their patients (30 eyes). Most recently Sangwan et al³ retrospectively evaluated the outcome of alcohol preserved scleral patch grafts in conjunction with overlying conjunctival flaps or amniotic membrane, in patients (n=13) with scleral defects of varying etiologies, and noted this approach was effective in preserving the globe integrity in 77% of these cases.

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- **Is it safe to use retrobulbar or peribulbar anesthesia?**
Both peribulbar and retrobulbar anesthesia, if not done properly, can induce orbital congestion and hemorrhage that will distort the tissue planes and make isolation of the Tenon's capsule difficult.
- **Could I retrieve the Tenon from the caruncle area?**
No. It is better not to do so because Tenon's capsule retrieved from the caruncle area might result in contracture, leading to motility restriction. Therefore, it is better to take Tenon from the superior or the inferior fornix.
- **Do I always need to perform lamellar corneal graft?**
No. If the scleral melt is not full thickness and large, multiple layers of cryopreserved amnion graft are sufficiently strong to restore the scleral integrity. That is why lamellar corneal graft is not used in acute chemical burns when there is scleral ischemia without melt. However, when the scleral melt is near full-thickness and large in size, it is necessary to reinforce the tectonic support. In addition to lamellar corneal graft, one can also consider scleral graft or pericardium graft (also see Literature Summary).
- **Should the amnion graft be trimmed while still on the paper or after being laid on the defect?**
As a personal preference, the entire amnion graft is best laid on the defect without trimming. The excessive graft and fibrin gel can be trimmed after the glue has set. This avoids the graft being cut too small to cover the defect.
- **What is the real value of using fibrin glue?**
The use of fibrin glue eliminates sutures, which can be very difficult to do especially if the melt is close to the equator. Due to the lack of sutures, the surgical time is shortened to the point topical anesthesia is feasible in most cases.
- **Should I perform tarsorrhaphy at the end of the surgery?**
For most cases, it is not necessary to do so. However, for severe chemical burn, especially if the lid margin is also involved and if there is a thermal component (e.g., firework injury), it is a good idea to bring the lid margin together with tarsorrhaphy, which will prevent exposure (due to lack of effective blink and closure) and wound contracture to the lid tissue.
- **Should I perform transplantation of limbal stem cells at the same time in acute chemical burns?**
No. It is better to wait until the limbal tissue has been fully vascularized by the aforementioned procedures before transplantation of autologous or allogeneic stem cells. Therefore, it is better not to do it at the same time.
- **Why is cryopreserved amnion graft (AMNIOGRAFT®) recommended?**
AMNIOGRAFT® is the only commercially available cryopreserved amnion graft in the U.S. The method of cryopreservation retains the biologic actions of the tissue *in utero* (anti-scarring, anti-inflammation, anti-angiogenesis, and promotion of healing).
- **What if the patient experiences pain after surgery?**
This complaint is infrequently observed using the surgical methods detailed above. If it is, use analgesics.
- **Is it necessary to use ointment and patch at the end of surgery?**
Application of an antibiotic/steroid ointment such as Tobradex® and a patch at the end of surgery maintained overnight, stabilizes and secures the graft.

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For additional clinical information, contact Scheffer C.G. Tseng, M.D., Ph.D. by phone at 305-274-1299 or by e-mail at stseng@ocularsurface.com

Financial interest disclosure: Dr Tseng and his family are >5% shareholders of TissueTech, Inc. and Bio-Tissue, Inc. which currently distributes AMNIOGRAFT® and PROKERA™.

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