



ologenTM

Collagen Matrix for Tissue Repair

Surgical Techniques Glaucoma Surgery

English version





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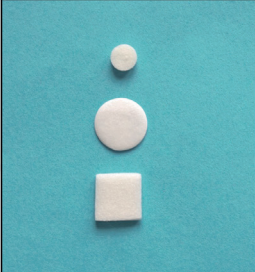
1. The application of ologen™ Collagen Matrix in ophthalmic and glaucoma surgery for eye tissue repair

ologen™ Collagen Matrix (ologen™ CM) may be used as an adjuvant to anti-fibrotic agents in various ophthalmic surgeries. The ologen™ CM is highly porous and biodegradable. It can modulate ocular tissue repair via wound modulation and randomization of the collagen deposition to facilitate scar-free physiological wound healing.

In glaucoma surgery, you may consider using the ologen™ CM for the patient population in which the use of anti-metabolites is not recommended or is prohibited:

- Elderly patients
- Patients with thin or weak scleral tissue: myopia/ history of scleral thinning/ buphthalmos/ Ehlers Danlos
- Patients with thin or weak conjunctival tissue
- Bleb in non-superior position
- History of MMC-associated complications

ologen™ CM is available in various sizes:

Product shape	Model number	Size
	830601	6 mm (D) x 2 mm (H)
	862051	12 mm (D) x 1 mm (H)
	870051	10 mm (W) x 10 mm (L) x 2 mm (H)

ologen™ CM is biocompatible; its biosafety is proven by more than 50,000 cases of eye surgery worldwide. Communication with the patients is essential to help them understand that the collagen matrix may harmlessly remain in the eye for a reasonable time range.

2. When and how do I use ologen™ Collagen Matrix with other anti-scarring adjuvants such as antimetabolites?

In patients with high risk of scarring, you may consider using the ologen™ CM with other anti-scarring adjuvants, such as MMC. In this case the MMC concentration and application time may be adjusted, by less exposure time or lower concentration, and can be as low as, for example: 0.1 mg/ml for 1 minute^[1, 2]. Do not soak the ologen™ CM in MMC, as it will prolong antimetabolite exposure.

According to the Moorfields Safe Surgery System's high risk definition and feedback from surgeons, patients who are liable to encounter post-operative super scarring and for whom the combination regimen, ologen™ CM and low dose MMC, may be considered are:

- Neovascular glaucoma
- Uveitis; chronic conjunctival inflammation
- Secondary glaucoma
- Previously failed trabeculectomy/ tubes
- Thick Tenon's capsule
- Multiple risk factors

Post-operative digital massage combined with 5-FU or MMC injection may be used when the ologen™ CM is initially implanted but is still unable to satisfactorily reduce unexpected post-operative scarring. The post-operative IOP reduction is a direct result of the surgery, not of the ologen™ CM itself and may be adjusted by the techniques in the next section.

3. How can Trabeculectomy be optimized with ologen™ Collagen Matrix?

When in your standard surgery antimetabolites are used, the combination with the ologen™ CM allows you to either reduce the concentration or exposure time or both to obtain optimal results. Position of surgical site: the superior half of the globe is recommended, as this position may minimize the incident of complications with the protection of eyelid.

Conjunctival flap:

- Limbus-based flap: you may use ologen™ CM Model 830601 (6x2 mm) or Model 862051 (12x1 mm) according to your preference.
- Fornix-based flap: if you choose Model 862051 (12x1 mm), you may need to trim or temporarily fold the ologen™ CM for ease of the insertion into the subconjunctival space.

Scleral flap:

- With side incisions cut right to the limbus: the anterior flow of aqueous humor may be more prominent and may lead to more anterior focal bleb. You may consider placing ologen™ CM slightly to the anterior on the top of the closed scleral flap (please also refer to section “The closure of scleral flap” for surgical techniques).
- With side incisions limited to 1-2mm posterior to the limbus: the posterior flow of aqueous humor may be more prominent and may lead to more posterior diffuse bleb. You may consider placing ologen™ CM slightly to the posterior on the top of the closed scleral flap.
- The scleral flap should be created with moderate thickness. However, ologen™ CM itself is a good patch graft to reinforce a thin or weak scleral flap, and may prevent scleral flap dehiscence or shrinkage, if a thin or weak sclera was found intra-operatively.

Sclerostomy:

- Sclerostomy is recommended to be done perpendicularly to the surface at the sclerolimbal junction through the anterior part of the trabecular meshwork. This may help avoid choroidal detachment (when sclerostomy is done too posteriorly) and Descemet's membrane detachment (when sclerostomy is done too anteriorly).

The closure of the scleral flap:

It is recommended that the scleral flap is closed with moderate or releasable sutures (that allow some flow of aqueous humor). This technique is critical to optimize the glaucoma surgery, because the ologen™ CM will exhibit a tamponing effect with additional pressure. Do not tie the flap with further and tighter sutures as you would do when using MMC only.

- The aggressiveness of the surgical manipulation should be in accordance with the target IOP that you would like to achieve for each individual patient. The tighter and the additional scleral flap sutures you use, the higher the post-operative IOP and the chances of post-operative scarring.

The placement of ologen™ CM on top of the scleral flap:

- ologen™ CM does not have to directly cover the whole of the scleral flap's incisions. Fibroblasts would be guided into the ologen™ CM to achieve the effects of wound modulation and randomization of the collagen formation.
- It is not necessary to suture the ologen™ CM onto the sclera. However, it is possible*.

*The suturing of the ologen™ CM is practiced in repair of scleral thinning and oculo-plastic surgeries.

The release of the scleral flap sutures:

- We recommend to monitor post-operative IOP and consider releasing the sutures within 2 weeks, in case of tight sutures. Do not wait until a few months as with MMC.
- The use of releasable sutures is an alternative option.
- The use of a suture lysis lens, such as the Blumenthal lens^[3] and digital massage may help with a better visualization for laser suture lysis.
- The use of an extended stitch or long suture may also facilitate visualization enabling suture lysis.

4. Is hypotony a concern if moderate sutures are used to close the scleral flap with ologen™ Collagen Matrix on top?

When ologen™ CM is placed on the top of the scleral flap, it may exhibit minor additional pressure^[4].

- Never place ologen™ CM under the flap in penetrating surgery such as Trabeculectomy.

Transient early hypotony:

- If transient early hypotony occurs, it usually resolves in 5-10 days.
- Simply monitor IOP if a flat anterior chamber (flat AC) does not develop and VA is not affected. For cases with grade II flat AC, you may use lenses, viscoelastic injection into AC, and/or compression sutures to manage the wound, whilst avoiding suturing over the ologen™ CM.

5. Can ologen™ Collagen Matrix be used when buttonholes develop?

Never use toothed forceps.

When buttonholes develop, we recommended you do not use antimetabolites (alkylating agent) such as MMC, or that you avoid it coming into contact with the buttonholes.

ologen™ CM itself is a good option to reinforce the repair of buttonholes as it does not interfere with tissue healing. However, it is recommended you do not expose the ologen™ CM through unclosed buttonholes or suture over the ologen™ CM with transconjunctival compression sutures in order to prevent infections.

While in harmony with the use of the ologen™ CM, buttonholes may be excised or closed with adjacent conjunctiva onto the cornea or sclera, or further sealed with the covering of Tenon's, if present.

6. The application of ologen™ Collagen Matrix in non-penetrating surgery

There are many options for application of the ologen™ CM in non-penetrating surgery involving deep scleral excision, including non-penetrating deep sclerectomy (NPDS):

- Single placement posterior of the scleral flap (as in trabeculectomy).
- Single placement in the deep scleral excision space (scleral lake); you may trim the ologen™ CM to fit into the space.
- Double placement as follows: one larger piece placed under the conjunctiva and Tenon's flap and a smaller piece placed under the superficial scleral flap ^[5]. This may prevent both subconjunctival and subscleral scarring.

7. The application of ologen™ Collagen Matrix in revision surgery

You can use the ologen™ CM in various types of bleb revision:

- For revision cases with hypotony ologen™ CM is a good revision surgery solution as it exhibits a tamponing effect with some pressure. When using transconjunctival compression sutures, avoid suturing over the collagen matrix.
- For revision cases with **subconjunctival fibrosis** where buttonholes are likely to develop due to a weakened tissue, the collagen matrix is a good patch graft to reinforce and protect the weakened conjunctiva.
- For revision cases with **encapsulation** or the closure of the transscleral fistula, the scleral tissue is sometimes weakened due to the extensive revision manipulation required. ologen™ CM is a good option to reinforce the scleral tissue as applied in the repair of scleral thinning, and may prevent scleral flap dehiscence or shrinkage in these cases.
- Please refer to the section “How can I optimize my trabeculectomy with ologen™ Collagen Matrix?” for related surgical techniques if a bleb is to be created at the original revision site.

8. Alternative applications of ologen™ Collagen Matrix

ologen™ CM has been used in combination with **Glaucoma Drainage Devices** such as the Ahmed Glaucoma Valve (AGV):

- The ologen™ CM is positioned on top of the plate of the AGV. By mediating the formation of a dense and porous fibrous tissue, minimizes the formation of a thick capsule around the AGV. In this way, the intra-ocular pressure during the early post-operative period is significantly reduced.
- In patients undergoing capsule excision for revision after Glaucoma Drainage Device surgery^[6].

ologen™ CM has also been used in other indications:

- The ologen™ CM may be applied during the repair of **scleral thinning**^[7, 8] in primary cases, or in the secondary cases associated with the use of MMC.
- The ologen™ CM can also be applied in **pterygium excision** as an alternative to conjunctival autograft transplantation^[9].
- Please do not use surgical glue in combination with ologen™ CM. The glue will fill the pores of the ologen™ CM, rendering it ineffective.
- The ologen™ CM can also be applied in **strabismus surgery**^[10].

Note: These alternative applications of ologen™ CM are case studies. The degree of success may vary. Please use with caution.

9. What affects the degradation time of ologen™ Collagen Matrix?

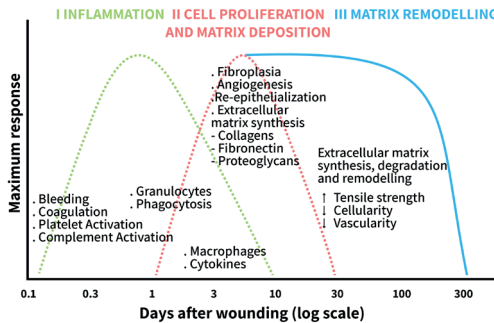
Collagen metabolism is a complex and highly regulated process. The factors contributing to a shorter degradation time include: inflammation, the degree of filtration (for filtering surgeries), and the presence and activity of matrix metalloproteinases (MMP's). Many cells in the human body synthesize and release MMP's, including neutrophils, macrophages and tumor cells.

For example:

- Inflammation: the ologen™ CM may degrade faster in cases such as revision surgery, neovascular glaucoma, uveitic glaucoma, or where clinically significant postoperative inflammation is involved. In such cases, the ologen™ CM could dissolve within 90 days.
- The degree of filtration: it is proposed that overfiltration may lead to a shorter degradation time, while under-filtration and the use of steroid/ MMC may lead to a longer degradation time.
- The ologen™ CM may last longer in indications where no filtration of aqueous humor is involved, eg. strabismus surgery, leaving in its wake the patient's own connective tissue to repair and protect the intended area.
- In general, the ologen™ CM is bio-degraded between 3 and 6 months. Patient per patient variation does occur.

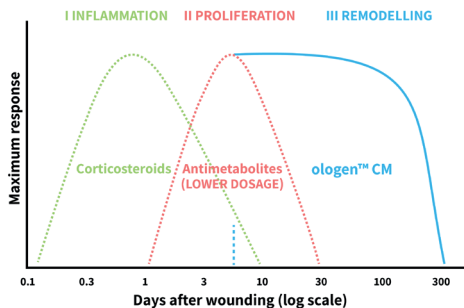
10. Mechanism of action in glaucoma surgery in combination with low dose anti-metabolites.

Phases of repair in acute (normal) wound healing



Adapted from S. Enoch, P. Price. World Wide Wounds, 2004

Wound healing process modulation



By using ologen™ CM in combination with low dose anti-metabolites, the proliferation and remodelling phases of the wound healing process are modulated:

II. Proliferation phase

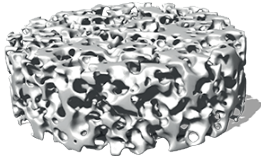
Fibroblast proliferation is controlled by the use of anti-metabolites in a low dose.

III. Remodelling Phase

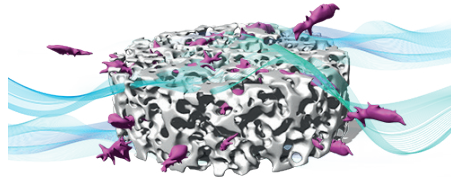
ologen™ CM guides fibroblast ingrowth and collagen deposition in a random way thus avoiding scar formation.

The combined use of low dose anti-metabolites and ologen™ CM reduces the formation of scarring tissue by controlling fibroblast proliferation and creating a random and relatively loose re-organization of the myofibroblasts and collagen extracellular matrix.

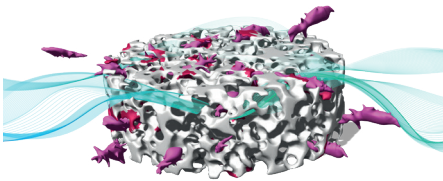
11. Modulation of scar formation process



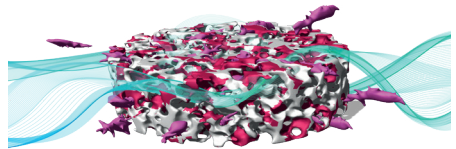
ologen™ collagen matrix (ologen™ CM) is a collagen based porous biodegradable scaffold.



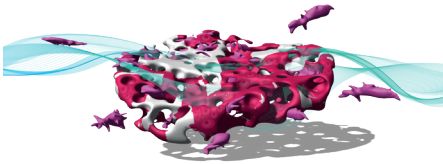
Myofibroblasts that are involved in the remodelling phase of wound healing migrate inside the ologen™ CM, settle and adhere.



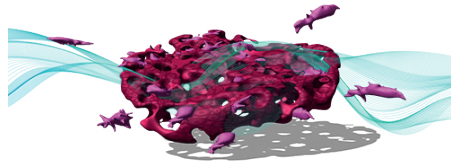
Myofibroblasts start to proliferate and the process of matrix synthesis starts.



While a new collagen matrix is being produced by the myofibroblasts, ologen™ CM starts to degrade.



ologen™ CM degradation process continues and the scaffold is replaced by myofibroblast-produced matrix.



After 3-6 months the ologen™ CM is completely degraded and replaced by a scaffold-like matrix structure produced by the myofibroblasts.

Appendix I References

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Appendix II Studies of ologen™ Collagen Matrix used in patients with 24 months follow-up or more.

- I. *Cillino S. et al.* Biodegradable collagen matrix implant vs mitomycin-C as an adjuvant in trabeculectomy: a 24-month, randomized clinical trial. *Eye* (2011), 1–9.
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- IV. *Fan K.C. et al.* Ologen versus Mitomycin-C for Trabeculectomy in a Predominantly African American Population. *Glaucoma Open Access* 2016, 1:1.
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- VII. *Yuan F. et al.* Biodegradable 3D-Porous Collagen Matrix (Ologen) Compared with Mitomycin C for Treatment of Primary Open-Angle Glaucoma: Results at 5 Years. *Journal of Ophthalmology* Vol. 2015, Article ID 637537.





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