ologen® Collagen Matrix- Surgical Techniques

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(1) The application of ologen® Collagen Matrix in ophthalmic and glaucoma surgery for eye tissue repair

- ologen® collagen matrix may be used as an antifibrotic agent in many different ophthalmic surgeries. The collagen matrix is highly porous and biodegradable. It can modulate ocular tissue repair via wound modulation and randomization of the collagen formation to promote wound healing.

- In glaucoma surgery, you may consider using the collagen matrix for the patient population in which the use of anti-metabolites is not recommended or is prohibited:
  - Elderly patients
  - Children or expectant mothers (MMC and 5FU are prohibited)
  - 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
(2) When and how do I use ologen® Collagen Matrix with other anti-scarring adjuvants such as antimetabolites?

- With high risk patients, you may consider using the collagen matrix with other anti-scarring adjuvants (separate procedures), such as MMC. In this case the MMC concentration and application time may be adjusted to eq. 0.1 mg/ml for 1 minute\(^1\). Do not soak the collagen matrix in MMC, as it will affect the functionality of the collagen matrix.

- According to the Moorfields Safe Surgery System’s high risk definition and feedback from surgeons, the high risk patients who are liable to encounter post-operative super scarring and for whom the combination regimen 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 collagen matrix 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 the collagen matrix itself and may be adjusted by the techniques in the next section.

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(3) How can I optimize my trabeculectomy with ologen® Collagen Matrix?

- 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® Collagen Matrix Model 830601 (6*2 mm) or Model 862051 (12*1 mm) according to your preference.
  - Fornix-based flap: if you choose Model 862051 (12*1 mm), you may need to trim or temporarily fold the collagen matrix 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® Collagen Matrix 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® Collagen Matrix slightly to the posterior on the top of the closed scleral flap.
  - The scleral flap should be created with moderate thickness. However, ologen® Collagen Matrix 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 scelrostomy is done too anteriorly).

- **The closure of the scleral flap:**
  - It is recommended that the scleral flap is closed with 1-2 loose-to-moderate/ releasable sutures. This technique is critical to optimize the glaucoma surgery, because the collagen matrix will exhibit a tamponading effect with an additional pressure of 0.5-5 mmHg. Do not tie the flap with further and tighter sutures as you would with MMC.
  - 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® Collagen Matrix on the top of the scleral flap:**
  - Collagen matrix does not have to directly cover the whole of the scleral flap’s incisions. Fibroblasts would be guided into the collagen matrix to achieve the effects of wound modulation and randomization of the collagen formation.
It is not necessary to suture the collagen matrix onto the sclera. However, it is possible*. This is intended for the ease of post-operative manipulation when digital massage may be used to push the collagen matrix temporarily aside for a better visualization for suture lysis. (*The suturing of the collagen matrix is practiced in repair of scleral thinning and oculoplastic surgeries.)

The release of the scleral flap sutures:

- We recommend removing/releasing the sutures within 2 weeks. Do not wait until a few months as with MMC.
- When using tighter and additional scleral flap sutures, you should lyse or release the sutures earlier than you normally would. The rationale is to reduce the time and chances of wound adhesion that may close up the transscleral fistula, if indeed more or tighter scleral sutures are used instead of the recommended 1-2 loose to moderate sutures.
- Suture lysis lens² and digital massage may help with a better visualization for suture lysis

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(4) Is hypotony a concern if I use 1-2 loose sutures to close the scleral flap with ologen® Collagen Matrix on top?

- When ologen® Collagen Matrix is placed on the top of the scleral flap, it will exhibit a tamponading effect with an additional pressure of 0.5-5 mmHg. The collagen matrix can act as a dynamic buffering system to prevent clinically significant hypotony\(^3\).

- 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 collagen matrix.

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\(^3\) TS Dietlein et al: Brit. J. Ophthalmol, June 12, as 10.1136/bjophthalmol-2013-303357
(5) Can I use ologen® Collagen Matrix when buttonholes develop?

- Never use toothed forceps.
- When buttonholes develop, we recommended you do not use antimetabolite (alkylating agent) such as MMC, or that you avoid it coming into contact with the buttonholes.
- ologen® Collagen Matrix itself is a good patch graft to reinforce the repair of buttonholes as it does not interfere with tissue healing. However, it is recommended you do not expose the collagen matrix through unclosed buttonholes or suture over the collagen matrix with transconjunctival compression sutures in order to prevent infections.
- While in harmony with the use of the collagen matrix, 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 collagen matrix in non-penetrating surgery involving deep scleral excision, including NPDS (non-penetrating deep sclerectomy) and canaloplasty:
  - Single placement on the top of the scleral flap (as in trabeculectomy). Follow your routine device implantation/canaloplasty procedure or viscoelastic injection in the deep scleral excision space.
  - Single placement in the deep scleral excision space\(^4\); you may trim the collagen matrix to fit into the space.
  - Double placement in the above two compartments\(^5\). This may prevent both subconjunctival and subscleral scarring.

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(7) The application of ologen® Collagen Matrix in bleb revision

- You can use the collagen matrix in various types of bleb/tube revision:
  - For revision cases with antimetabolite related hypotony\(^3\) or leak\(^6\), ologen® CM is a good revision surgery solution as it exhibits a tamponading effect with an additional pressure of 0.5-5 mmHg. The collagen matrix acts as a dynamic buffer system to resolve the conditions. 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. The collagen matrix is superior to other donor grafts due to its pliancy and flexibility and is less likely to cause irritation or bulky stress to conjunctiva.
  - For revision cases with encapsulation or the closure of transscleral fistula, the scleral tissue is sometimes weakened due to the extensive revision manipulation required. ologen® Collagen Matrix is a good patch graft 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.

\(^6\) Oluwatosin Smith, David Godfrey, Davinder Grover, Michelle Butler, Ronald Fellman. Surgical Outcomes Following the Use of a Biodegradable Subconjunctival Collagen-Glycosaminoglycan Matrix in Revisions of Late-Onset Glaucoma Filtering Bleb Leaks. Poster 40 at the 2014 AGS Annual Meeting, Washington DC.
(8) The patch graft application of ologen® Collagen Matrix in ophthalmic surgery

- You can use ologen® Collagen Matrix as patch graft with the following indication:
  - It is proposed that the collagen matrix can be used as patch graft to cover the tube of various glaucoma drainage devices\(^7\), in combination with, or as an alternative to donor grafts for tube exposure repair\(^8,9\). The collagen matrix is more flexible, is pliable, and is less likely to cause irritation or bulky stress to conjunctiva.
  - The collagen matrix may be applied during the repair of scleral thinning\(^10,11\) in primary cases, or in the secondary cases associated with the use of MMC.
  - The collagen matrix can also be applied in pterygium excision to prevent pterygium recurrence when the use of MMC/irradiation is not recommended.
  - ologen® Collagen Matrix is synthesized from SPF (specific pathogen free) porcine origin. It does not have a stromal/epithelial side and may be applied both ways.

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(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 collagen matrix 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 collagen matrix 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. Also, the collagen matrix may last longer when applied as patch graft in indications where no filtration of aqueous humor is involved. Leaving in its wake the patient’s own connective tissue to repair and protect the intended area.

- **ologen® Collagen Matrix is biocompatible; its biosafety is proven by more than 20,000 cases of 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.**