



Anatomopathological Aspects and Clinical Correlation of Conjunctival Bleb Fibrosis Following Encapsulation of a Biodegradable Collagen Matrix Implant in Glaucoma Surgery

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Abstract

This study reports a case series of glaucoma patients in whom a biodegradable collagen-glycosaminoglycan implant (Ologen®) failed to prevent fibrosis after non-penetrating deep sclerectomy (NPDS) and describes the associated histopathological findings. This single-centre retrospective study included four patients with progressive glaucoma and inadequate intraocular pressure (IOP) control despite maximal medical therapy. All underwent NPDS with implantation of a collagen-glycosaminoglycan matrix and adjunctive mitomycin C. Postoperative follow-up included IOP monitoring, slit-lamp examination, and photographic documentation. Patients with bleb failure required surgical revision, and excised tissue, including the implant and surrounding Tenon's capsule, was analysed histologically. All cases developed progressive bleb fibrosis. The implants remained intact, encapsulated by dense fibrotic tissue ("ring-of-steel" appearance), with minimal fibroblast infiltration, extensive collagen deposition, and no significant degradation

for up to three years. These findings highlight variability in tissue response and suggest a potential role of patient-specific fibrotic predisposition in surgical outcomes.

Keywords: Biodegradable collagen-glycosaminoglycan implant, glaucoma surgery, fibrosis, wound modulation, biodegradation

Introduction

Filtering surgery remains the most widely used surgical intervention for glaucoma.¹ These procedures aim to create a fistulous tract between the anterior chamber and the subconjunctival space to facilitate the drainage of aqueous humour and reduce intraocular pressure (IOP). As a result, aqueous humour accumulates in a subconjunctival reservoir known as the filtration bleb. The primary cause of surgical failure is excessive formation of fibrotic tissue around the new drainage pathway,^{2,3} which compromises proper functioning of the bleb.

Glaucoma surgery is intrinsically pro-fibrotic² due to a chronic pro-inflammatory conjunctival environment that often results from prolonged use of topical medications, preservative agents in eye drops, hypersensitivity to active compounds, and a high prevalence of dry eye disease. Furthermore, postoperative tissue exposure to aqueous humour, which is rich in pro-inflammatory cytokines, promotes fibroblast activation.⁴

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Fibrotic scarring involves the excessive synthesis of extracellular matrix (mainly consisting of dense, organised collagen fibres³) and the persistence of myofibroblasts that should normally undergo apoptosis.² Effectively modulating this fibrotic response is crucial for improving surgical outcomes.

Advances in tissue engineering have provided alternative strategies to modulate wound healing and reduce scar formation after glaucoma surgery, such as biodegradable implants. Unlike antimetabolites, whose non-specific inhibition of cell proliferation may lead to significant ocular toxicity, these implants promote the formation of functionally effective filtering blebs while degrading into non-toxic byproducts, thereby eliminating the need for surgical removal.⁵

Ologen® (Aeon Astron Europe B.V., Leiden, the Netherlands) is a biocompatible, biodegradable implant composed of collagen (90%) and glycosaminoglycan (10%).^{5,6} These components are organised in a three-dimensional system, creating a 95% porous structure that acts as a biological scaffold for the healing process,^{7,8,9} facilitating fibroblast growth inside the implant and guiding their migration to create a loose, randomly organised deposition of connective tissue similar to physiological conditions.^{6,7,8,9} This is the mechanism underlying the implant's modulation of wound healing.^{8,10,11,12} However, it is important to highlight that the implant itself does not have antifibrotic properties and could therefore hypothetically cause a secondary tissue reaction in the subconjunctival space.¹³ To avoid this reaction and modulate its immunogenicity, the collagen is purified with pepsins that eliminate telopeptides, which are the N- and C-terminal amino acid sequences responsible for the antigenicity of the collagen molecule.^{10,11,14,15}

Various published surgical series comparing patients undergoing surgery with and without the implant have yielded inconclusive results regarding its potential to enhance the antifibrotic effect of other techniques (summarised in [Tables 1](#)^{3,7,8,9,16-27} and [2](#)^{12,13,14,15,28-41}). In this case series, we present four cases of glaucoma surgery in which this biodegradable collagen-glycosaminoglycan implant failed to prevent fibrosis and was associated with an encapsulating fibrotic response surrounding the implant, which ultimately compromised surgical success.

Case Reports

Case 1

A 56-year-old female patient with moderate primary open-angle glaucoma (POAG) underwent non-penetrating deep sclerectomy (NPDS) with an intrascleral Esnoper V

Clip implant, subconjunctival Ologen® implantation (6 mm×2 mm), and a subconjunctival injection of 0.1 mL 0.01% mitomycin C (MMC). The patient exhibited progressive bleb flattening during the postoperative follow-up, causing a rise in IOP and requiring additional hypotensive medical therapy. One year after the initial surgery, the patient underwent surgical bleb revision. Intraoperatively, fibrotic conjunctiva and Tenon's capsule were observed encasing the intact Ologen® implant. Histopathological analysis revealed focal areas of dense fibrosis within the collagen matrix ([Figure 1](#)), with disorganised collagen bundles and scattered inflammatory cell infiltration, indicating a chronic foreign body reaction. Additionally, no significant degradation of the implant was observed.

Case 2

An 85-year-old female patient diagnosed with advanced POAG presented with inadequately controlled IOP despite maximally tolerated topical treatment. She underwent NPDS with a subconjunctival MMC injection and Ologen® implantation (6 mm×2 mm). During the postoperative course, the bleb developed an avascular appearance with cystic spaces and fluorescein leakage ([Figure 2A](#)). The patient was therefore scheduled for surgical bleb revision. Intraoperatively, the Ologen® implant was found to be intact 18 months after implantation, surrounded by a dense fibrotic capsule resembling a “ring-of-steel” reaction. This caused retraction of Tenon's capsule, leaving an area of thin, avascular limbal conjunctiva. Histopathological analysis ([Figure 2B](#)) confirmed the absence of Ologen® degradation,

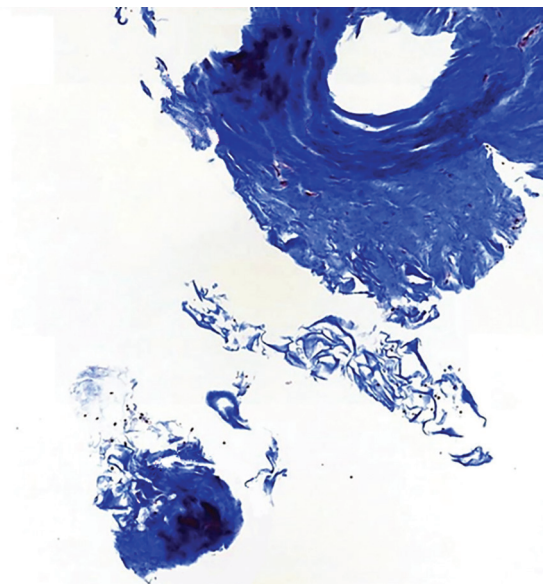


Figure 1. Masson's trichrome-stained sections showing fibrosis associated with exogenous mesh-like material (Ologen®)

Table 1. Published studies evaluating the safety and efficacy of Ologen® and MMC as adjuvants in trabeculectomy surgery for glaucoma									
Study	Type of study	Groups	N	Follow-up (months)	Outcomes	MMC dose	Complications	Compared to MMC-enhanced trabeculectomy	
Yuan et al. 2015 ¹⁶	Prospective randomised	Trab + OLO Trab + MMC	31 32	60	Higher success rates (complete and qualified) in OLO group Lower IOP in OLO group	0.2 mg/ mL 2 min	No significant differences between groups		
El-Sayyad et al. 2017 ¹⁷	Prospective randomised (IOAG)	Trab + OLO Trab + MMC	20 20	12	Lower IOP at end point in OLO group Better MBGS scoring of blebs in OLO group	0.4 mg/ mL 2 min	Higher rate of hypotony in MMC group Less needling and suture lysis in OLO		
Cillino et al. 2011 ¹⁸	Prospective randomised	Trab + OLO Trab + MMC	20 20	24	No differences in mean IOP and IOP reduction at end point. No differences in complete and qualified success at any target IOP Higher bleb height in OLO group	0.2 mg/ mL 2 min	Higher incidence of early hypotony in MMC, although not statistically significant Higher incidence of early bleb leak in OLO group		
Chelkerkar et al. 2021 ¹⁹	Prospective non-randomised	Phaco + Trab + OLO Phaco + Trab + MMC	40 53	12	No statistically significant differences in IOP or bleb height, area, and vascularity	0.2 mg/ mL 2 min	No significant differences between groups	OLO = MMC	
Glandorf et al. 2020 ²⁰	Retrospective	Trab + MMC Trab + MMC + OLO + BVZ Trab + MMC + OLO + intracameral BVZ	43 46 41	12	No differences in IOP reduction, complications, or need for additional medical treatment Greater success with MMC alone, although not statistically significant	0.2 mg/ mL 1 min	No significant differences between groups		
Paul et al. 2022 ²¹	Prospective non-randomised	Phaco + Trab + OLO Phaco + Trab + MMC	18 16	12	No differences in IOP reduction or need for additional medical treatment Better bleb morphology in OLO group	0.2 mg/ mL 1 min	No significant differences between groups		
Navero-Rodriguez et al. 2024 ²²	Retrospective non-randomised	Trab + MMC Trab + OLO Trab + OLO + MMC	44 34 41	36	No differences in IOP reduction, use of topical medications, or complete and qualified success rates More suture release and bleb needling with MMC alone	0.2 mg/ mL 2 min	No significant differences between groups		

Table 1. Continued									
	Study	Type of study	Groups	N	Follow-up (months)	Outcomes	MMC dose	Complications	
Compared to MMC-enhanced trabeculectomy	Rosentreter et al. 2010 ²³	Prospective randomised	Trab + OLO	10	12	Lower IOP at end point in MMC group Higher complete success rate in MMC group	0.2 mg/ mL 3 min	No significant differences between groups	
			Trab + MMC	10		More avascularity in MMC group			
	Senthil et al. 2013 ⁷	Prospective randomised	Trab + OLO	19	24	Lower mean IOP reduction at 6 months in OLO group	0.4 mg/ mL 2 min	More hyphaema in OLO group	
			Trab + MMC	20		No differences at 12 and 24 months			
	Rosentreter et al. 2014 ²⁴	Prospective randomised	Trab + OLO	15	12	Lower IOP at end point in MMC group Higher success rate in MMC group	0.2 mg/ mL 3 min	No significant differences between groups	
			Trab + MMC	15		Higher success rate in MMC group			
Compared to stand-alone Trab	Narayanaswamy et al. 2013 ⁸	Prospective non-randomised	Phaco + Trab + OLO	33		Lower IOP in MMC group Greater bleb area in MMC group		No significant differences between groups	
			Phaco + Trab + MMC	33	12	Needling required more frequently in OLO group	0.4 mg/ mL 2 min	No significant differences between groups	
	Sen et al. 2018 ²⁵	Prospective randomised	Trab + MMC	25	12	Greater IOP reduction in MMC group Blebs more diffuse in MMC group	0.1 mg/ mL 1 min	More hypotony in MMC group	
			Trab + MMC + OLO	25		More avascular blebs in MMC group			
Compared to stand-alone and enhanced Trab	Papaconstantinou et al. 2010 ³	Prospective randomised	Trab + OLO	20	6	No significant differences between groups in IOP or topical medication use	-	No significant differences between groups	
			Trab stand-alone	20					
	Khairy et al. 2023 ²⁶	Prospective randomised (PCG)	CTT without augmentation	21		No differences in IOP at end point		No significant differences between groups	
CTT + MMC			21	12	No differences in success rates, failure rates, or survival rates between groups	0.2 mg/ mL 3 min	No report of hypotony or shallow AC in OLO group		
CTT + OLO			21						
Non-comparative	Angmo et al. 2017 ²⁷	Retrospective	Trab + OLO + MMC	23	24	Significant reduction in IOP and use of hypotensive medications Complete success in 92.6% Failure in 3.7%	0.1 mg/ mL 1 min	Shallow AC in 14.8% Encapsulated blebs requiring needling in 11.1%	
	Dada et al. 2013 ⁹	Retrospective	Trab + OLO+MMC	33	12	Significant reduction in IOP and use of hypotensive medications	0.1 mg/ mL 1 min	2 cases of shallow AC 2 cases of encapsulated blebs requiring needling	
MMC: Mitomycin C, OLO: Ologen, Trab: Trabeculectomy, IOP: Intraocular pressure, JOAG: Juvenile open-angle glaucoma, MBGS: Moorfields Bleb Grading System, CTT: Combined trabeculectomy and trabeculectomy, Phaco: Phacoemulsification, BVZ: Bevacizumab, PCG: Primary congenital glaucoma, AC: Anterior chamber									

Surgery	Study	Type of study	Groups	N	Follow-up (months)	Outcomes	MMC dose	Complications
GDD	Rosentreter et al. 2010 ²⁸	Retrospective	Excision of GDD capsule + MMC + OLO	10	8-12	Adding OLO to capsule excision + MMC yielded higher success rate when revising GDD No significant differences in IOP	0.2 mg/mL 2 min	-
			Excision of GDD capsule + MMC	9				
	Salimi et al. 2019 ²⁹	Retrospective	Excision of GDD capsule + MMC + OLO	12	36	No significant differences between groups in IOP reduction, hypotensive medications or success rate Valid strategy for GDD revision, successful in reducing IOP in both groups	0.5 mg/mL 2 min	Significantly lower rate of complications in OLO group – no report of erosion of GDD, although MMC group had an erosion rate of 25%
			Excision of GDD capsule + MMC	11				
	Song et al. 2017 ³⁰	Retrospective	Conventional GDD	24	6	Same IOP reduction, no differences in success. Enzymatic degradation rate of OLO-7 was slower	-	Lower hypotony rates in OLO groups than in conventional surgery, and less hyphaema or choroidal effusion.
			GDD + OLO-6	20				
	Stephens et al. 2016 ¹²	Retrospective	Report of erosion rates when using OLO over GDD tube	43	12-45	95.4% required no intervention for tube erosion	-	-
			GDD + OLO over plate	8				
	Kim et al. 2018 ³¹	Retrospective	Conventional GDD	12	12	No differences between groups in overall IOP reduction, complete or qualified success. Number of IOP-lowering medications was significantly lower in OLO group during the early hypertensive phase	-	No differences in complication rates.
			GDD + OLO over plate	12				
	Sastre-Ibáñez et al. 2019 ³²	Prospective randomised	GDD + OLO over plate	27	12	No differences between groups in IOP reduction, complete or qualified success or survival rates.	-	No differences in complication rates.
			Conventional GDD	31				
	Suzuki Junior et al. 2023 ³³	Retrospective multicentre case-control	GDD + OLO over plate	25	6	No significant differences between groups in IOP reduction, hypotensive medication use, or complete success rate Better outcomes in OLO group for qualified success	-	No differences in complication rates.
			Conventional GDD	100				

Table 2. Continued

Surgery	Study	Type of study	Groups	N	Follow-up (months)	Outcomes	MMC dose	Complications
NPDS	Guedes et al. 2019 ³⁴	Retrospective	Phaco-NPDS + MMC + OLO	51	12	Significantly lower IOP and greater IOP reduction in OLO group Lower rate of medication use in OLO group	0.2 mg/mL subconjunctival injection	Higher rate of needling in group without OLO
			Phaco-NPDS + MMC	49				
	Aptel et al. 2009 ³⁵	Prospective	NPDS enhanced with OLO in scleral bed	15	3	Significant reduction in IOP Large fluid-filled spaces on AS-OCT, lower reflectivity in OLO group	-	-
	Elmekawey et al. 2020 ³⁶	Retrospective	NPDS + OLO NPDS	20 20	6	Significant reduction in IOP and better bleb morphology in OLO group	-	-
XEN	Park et al. 2022 ³⁷	Retrospective	XEN (± Phaco) + OLO	61	6	No significant differences in IOP reduction or antiglaucoma medication	0.4 mg/mL 2 min	Hypotony reported in OLO-augmented group, possibly related to increased filtration facilitated by aqueous humour absorption by OLO No significant differences between groups
			XEN (± Phaco)	42				
	Navero-Rodríguez et al. 2020 ³⁸	Case-control	XEN + OLO + MMC	74	Not reported	No differences between groups in IOP reduction or glaucoma medication use	0.1 mg/mL subconjunctival injection	More late bleb fibrosis with XEN standalone - more needling or 5-FU needed in this group
			XEN + MMC	75				
PRESERFLO	Jin et al. 2025 ³⁹	Retrospective	XEN ab externo + OLO + MMC	47	12	Significantly lower rate of medication use and bleb revisions in OLO group Greater cumulative surgical success in OLO group	0.2-0.4 mg/mL subconjunctival injection	Lower rate of complications in OLO group
			XEN ab interno + MMC	29				
	Vastardis et al. 2021 ⁴⁰	Retrospective	PRESERFLO + MMC + OLO	25	6	Comparable results in terms of IOP reduction and medication usage	0.2 mg/mL 3 min	Bleb fibrosis more frequent in OLO group
			PRESERFLO + MMC	25				

Table 2. Continued								
Surgery	Study	Type of study	Groups	N	Follow-up (months)	Outcomes	MMC dose	Complications
Ex-PRESS	Johnson & Sarkisian 2014 ¹⁵	Retrospective	Ex-PRESS + OLO	49	12	Significant reduction with no differences between groups. OLO is an effective alternative, but not superior to MMC	0.4 mg/mL 2 min	Similar rate of complications in both groups
			Ex-PRESS + MMC	50				
	Menda et al. 2015 ⁴¹	Retrospective	Ex-PRESS + OLO	7	12	Higher IOP and reoperation rate in OLO-only group	0.5 mg/mL 3-4 min	Higher rate of bleb leak in OLO-only group
			Ex-PRESS + MMC	34				
			Ex-PRESS + OLO + 5-FU	14				
MMC: Mitomycin C, GDD: Glaucoma drainage device, OLO: Ologen, IOP: Intraocular pressure, NPDS: Non-penetrating deep sclerectomy, Phaco: Phacoemulsification of cataract, AS-OCT: Anterior segment optical coherence tomography, 5-FU: 5-fluorouracil								

minimal fibroblast migration into the scaffold, and a thick wall of organised collagen deposition surrounding the implant.

Case 3

A 56-year-old female patient with a history of diabetic retinopathy was referred for primary angle-closure glaucoma. The patient developed toxicity associated with hypotensive treatment, and glaucoma progression was noted in the left eye. Therefore, NPDS with MMC injection and Ologen[®] implantation (6 mm×2 mm) was performed. Postoperatively, the bleb progressively became fibrotic, necessitating an escalation in hypotensive treatment. Bleb revision was performed three years after the initial procedure. Intraoperative findings revealed a highly retracted Tenon's capsule that had contracted the bleb around the Ologen[®] matrix, which had remained intact for three years ([Figure 3A](#)). Histopathological assessment

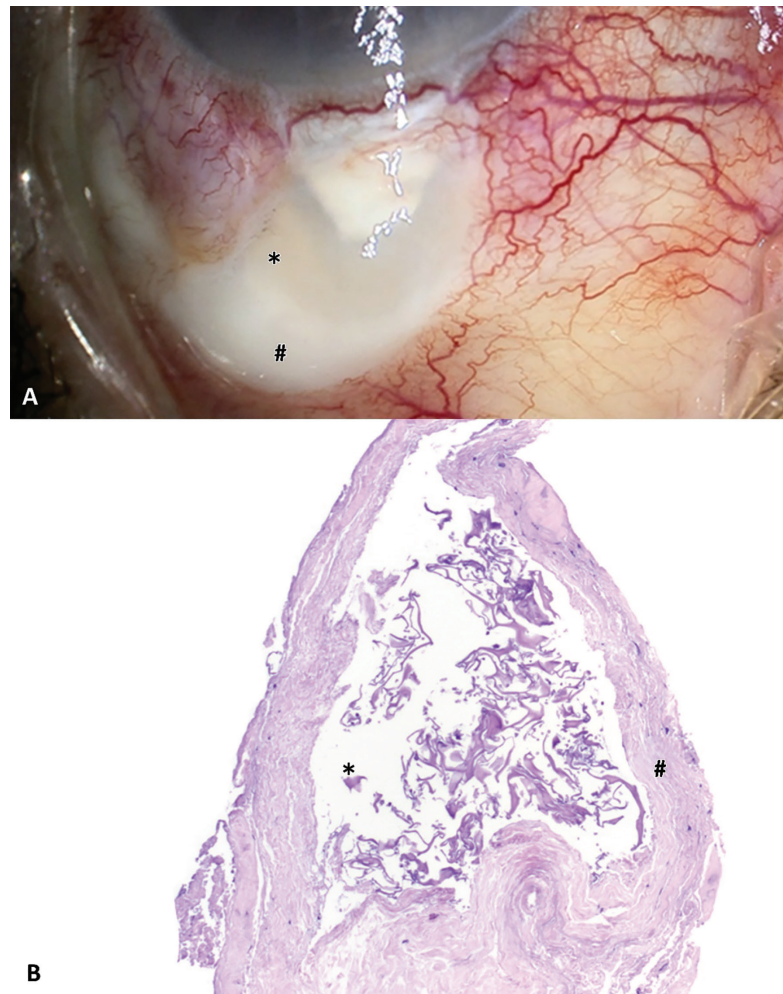


Figure 2. A) Intraoperative image showing the presence of Ologen[®] (*) surrounded by a fibrotic wall (#). B) Histopathological examination of haematoxylin- and eosin-stained sections of the resected bleb demonstrated that the Ologen[®] matrix (*) remained intact with very little fibroblast migration and a fibrotic wall encapsulating it (#)

(Figure 3B) revealed dense fibrotic tissue surrounding exogenous mesh-like material (Ologen®).

Case 4

A 53-year-old female patient diagnosed with pigmentary glaucoma presented with a long history of topical antiglaucoma therapy. Visual field progression warranted a combined phacoemulsification and NPDS procedure enhanced with MMC and Ologen® implantation (6 mm×2 mm). IOP control remained inadequate a year after the procedure, with a fibrotic bleb that required needling on two separate occasions to reach target IOP. During surgical bleb revision, an intense scarring reaction was observed around the scleral flap and Ologen® implant. The implant was encapsulated in a manner similar to a foreign body reaction. After debridement of the fibrous tissue and removal of the residual Ologen® matrix, a single-layer pericardial graft was placed to reinforce the scleral flap. Histological examination revealed the Ologen® material embedded within a hyalinised collagenous matrix with minimal fibroblast presence (Figure 4).

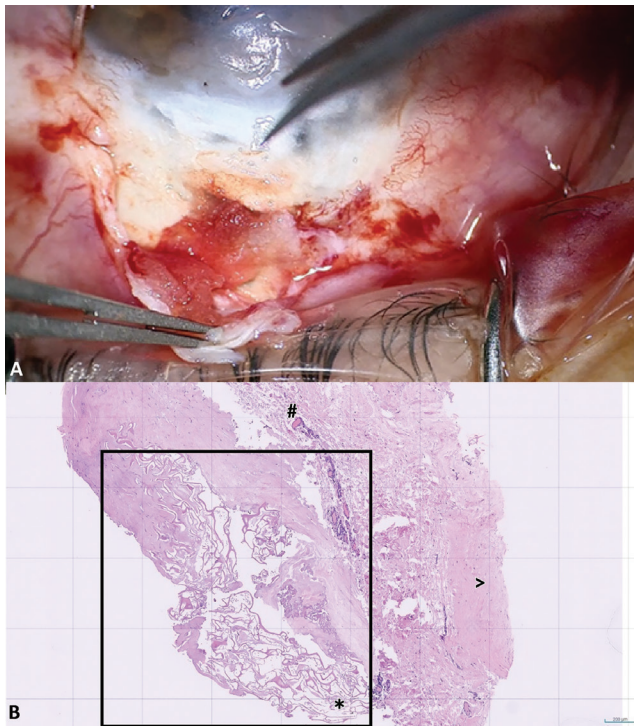


Figure 3. A) Intraoperative image of intact Ologen® trapped in fibrotic tissue. B) Severe fibrosis and dense collagen deposition in a haematoxylin and eosin-stained sample from Case 3. Exogenous mesh-like material (Ologen) is surrounded by dense fibrotic tissue (*), fibroblasts (#) and blood vessels (>)

Following bleb revision, all patients demonstrated improved bleb function and better IOP control. No additional surgical procedures were required during follow-up, and IOP remained stable with or without adjunctive medical therapy depending on the case.

Discussion

Numerous studies have examined the effectiveness of Ologen® across several types of glaucoma surgery (summarised in Tables 1^{3,7,8,9,16-27} and 2^{12,15,28-41}). However, interpretation is challenging due to variability in study design, limited sample sizes, and differences in surgical technique, including MMC timing and dosage. The heterogeneity of methodologies, from randomised trials to retrospective studies, further limits generalisability, resulting in inconsistent and sometimes contradictory findings.

Most literature focuses on comparisons with MMC in trabeculectomy. Meta-analyses report no significant differences in IOP control or success rates at 12-24 months.^{6,13} This implant is generally considered a safe and viable alternative to MMC; the absence of avascular blebs in the treatment groups, alongside a low incidence of postoperative complications, has been consistently reported.^{18,25} Additionally, this matrix promotes physiological bleb vascularisation²³ and serves as a mechanical buffer that mitigates overfiltration during the early postoperative period, potentially reducing the risk of hypotony.³⁵ In contrast, MMC is often associated with diffuse bleb formation, which may contribute to sustained long-term IOP reduction,²⁵ albeit at the cost of an increased risk of early hypotony and avascular bleb development.^{18,25}

Beyond trabeculectomy, studies on Ologen® use with glaucoma drainage devices (GDD) indicate that the implant may improve success rates when used as a patch graft over the tube.^{28,29} While no significant differences in IOP reduction were observed,^{29,30,31,32,33} it appears to lower the risk of tube exposure.²⁸

The biodegradable collagen-glycosaminoglycan implant modulates the deposition of connective tissue in a manner that more closely replicates physiological wound healing. It prevents direct contact between the conjunctiva and sclera, thereby acting as a biological spacer.^{12,42} Regarding the physical characteristics of filtering blebs, studies have reported mixed findings on the height and volume occupied by the collagen matrix. Some investigations indicate that the matrix can fill the entire subconjunctival space of the bleb, whereas others suggest that it occupies only a limited volume and gradually resorbs. Early postoperative observations consistently show that blebs in eyes receiving this implant appear more prominent than those in eyes

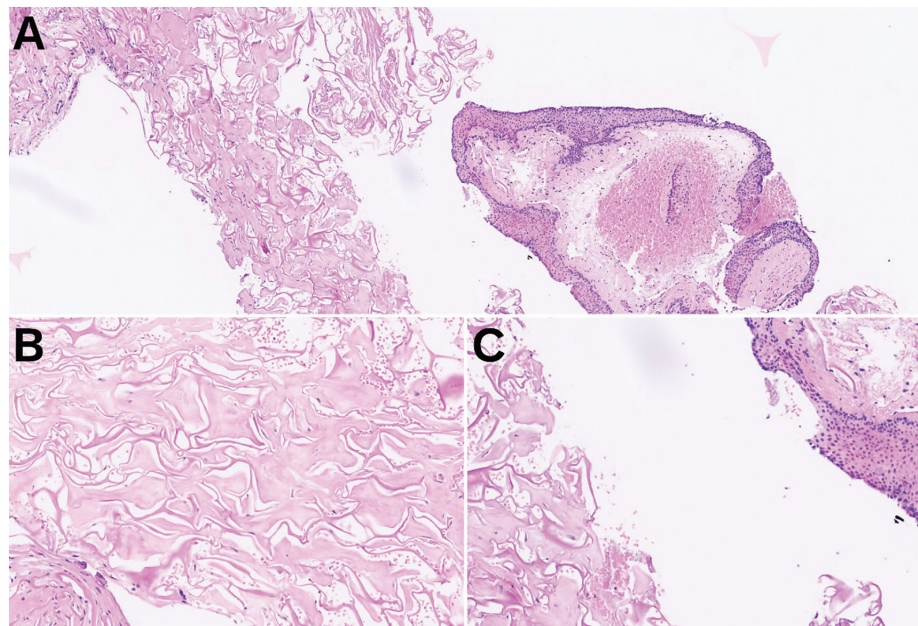


Figure 4. Histological sections of a surgical sample from Case 4, stained with haematoxylin and eosin. A) Fibrotic scar tissue around the Ologen® material (left) alongside a fragment of normal conjunctival mucosa. B) Detail of the fibrotic tissue showing sparse fibroblasts in a hyalinised collagenous matrix with entrapped mesh-like exogenous material. C) Close-up of the normal-appearing conjunctival mucosa (right) adjacent to the scar tissue (left)

treated with MMC, likely reflecting the immediate space-occupying effect of the subconjunctival implant.

Nevertheless, several studies report a higher incidence of encapsulated blebs and an increased need for postoperative needling.^{8,9,27} In a study by Min et al.⁴³, encapsulated blebs developed more frequently and more rapidly in eyes receiving this matrix compared to those undergoing conventional trabeculectomy. Most encapsulated blebs were observed between the second week and the first month postoperatively. The authors proposed that non-contractile, collagen-producing fibroblasts play a key role in this process. Because this implant is biodegradable, it may facilitate migration of fibroblasts into the bleb, contributing to early encapsulation. To mitigate this, the authors suggested strategies such as soaking it in relatively high concentrations of antimetabolites, applying antimetabolite eye drops in the early postoperative period, or injecting antimetabolites directly into the bleb during the first one to two weeks after surgery.

In a case reported by Voykov and Rohrbach¹¹, the implant remained in place one month after surgery, but no filtering bleb was observed. Histopathology showed no foreign body reaction or inflammatory infiltrate, with early fibrosis and vascularisation confined to the implant margins. These findings align with those of Rosentreter et al.²³, who reported fibroblast infiltration of the Ologen implant,

encasement by a collagenous pseudocapsule, accumulation of α -smooth muscle actin-positive myofibroblasts, collagen III deposition at the implant borders and within the pseudocapsule, strong fibronectin expression, and positive prolyl-4-hydroxylase staining in both the implant and overlying epithelium.

Studies on NPDS have demonstrated substantial reductions in IOP and the need for glaucoma medications.^{34,35,36} These observations are consistent with our own clinical findings. Similarly, subconjunctival devices such as XEN, PRESERFLO, and Ex-PRESS demonstrate comparable IOP reductions and medication usage between eyes treated with antimetabolites and those receiving this biodegradable collagen-glycosaminoglycan implant.^{15,37,38,40,41} Although late bleb fibrosis requiring subsequent needling or 5-fluorouracil was more frequently reported in the XEN group without Ologen,³⁸ the incidence of fibrosis was higher in the PRESERFLO group when Ologen was used.⁴⁰ In fact, individual genetic predisposition to a fibrotic response may also contribute to surgical outcomes. A hyper-fibrotic gene expression profile has recently been identified in patients experiencing surgical failure (with conjunctival overexpression of genes such as *VEGFA* or *CXCL8*).⁴⁴ We hypothesise that patients with this hyper-fibrotic profile may be inherently more prone to exaggerated scarring responses in general,

and specifically to Ologen[®], undermining its intended modulatory function.

This collagen matrix is designed for complete degradation within 90 to 180 days.^{19,35} However, factors such as the degree of cross-linking, type of collagen preparation, and enzymatic processing can influence this timeline.³⁰ In our clinical experience, degradation timelines deviated markedly from expectations: in Case 2, Ologen[®] remained intact for 18 months after implantation, and in Case 3, it persisted for 3 years. This phenomenon may be attributable to an encapsulating immunological reaction surrounding the implant, which prevents enzymatic degradation by tissue proteases. Similar histopathological findings have been reported by Selvan et al.⁴⁵, who described a “ring-of-steel” reaction encasing the intact implant in both eyes of the same patient. This phenomenon was observed following the use of MMC-soaked Ologen[®] and was thought to result from the prolonged localised effect of MMC and the resultant excessive fibroblast proliferation in the surrounding tissue. The observations with GDD and NPDS support the hypothesis of Stephens and Sarkisian¹² that this implant could become encapsulated when not directly exposed to aqueous humour, potentially hindering its biodegradation. In addition, other possible complications associated with Ologen[®] include implant migration and the development of symptomatic blebs, which may reflect an altered subconjunctival wound-healing response. These potential adverse events should be considered when interpreting the overall clinical performance of the implant.⁴⁶

In summary, Ologen[®] and MMC demonstrate comparable efficacy across various glaucoma surgical modalities. Although MMC may achieve marginally lower IOP in selected contexts, it carries an increased risk profile. Our findings do not challenge the overall safety of this biodegradable collagen-glycosaminoglycan implant but rather highlight that its biological behaviour may be unpredictable in selected patients. The matrix appears to reduce severe complications such as hypotony and tube erosion. However, as observed in our series, it may also be associated with encapsulation, delayed degradation, and bleb fibrosis, even when used in conjunction with MMC. These findings highlight the considerable variability in tissue response to biodegradable implants and suggest a potential role of patient-specific fibrotic predisposition. Emerging evidence indicating distinct conjunctival gene expression profiles associated with early surgical failure supports the concept that a hyper-fibrotic molecular phenotype may influence wound-healing responses to collagen-based implants. Consequently, careful patient selection, meticulous ocular surface preparation, and the future integration of genetic or molecular profiling of

hyper-fibrotic phenotypes may help to optimise surgical outcomes and refine the role of collagen-based implants in glaucoma surgery.

Ethics

Informed Consent: Informed consent was obtained from the patients included in the study.

Declarations

Authorship Contributions

Surgical and Medical Practices: E.M., Concept: E.M., Design: E.M., Data Collection or Processing: X.S., J.L.G., Analysis or Interpretation: L.C-R., S.L-T., X.S., J.L.G., E.M., Literature Search: L.C-R., S.L-T., Writing: L.C-R., S.L-T., E.M.

Conflict of Interest: No conflict of interest was declared by the authors.

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