INTRODUCTION

Trabeculectomy has become the golden standard for filtering surgery of glaucoma since its introduction by ***Cairns*** in ***1968***[1]**.**

It is believed that proliferation of fibroblasts plays an important role in bleb failure. Histological studies have shown that such proliferation occurs during the third to fifth postoperative day[2]**.**

Adjunctive anti-fibrotics such as 5-fluorouracil (5-FU) and mitomycin C (MMC) are commonly used to enhance the success of trabeculectomy. These agents, however, can cause many complications[3]**.**

5-FU is a pyrimidine analogue anti-metabolite which blocks DNA synthesis thereby inhibits fibroblast proliferation. The problem with 5-FU is that numerous postoperative injections had to be given to the patients. On top of this difficulty is the incidence of major complications like wound leakage and corneal epithelial defects[4]**.**

The medicine that came along next was MMC. It is somehow similar to 5-FU in that it is an anti-metabolite. In addition to affecting DNA, it also affects RNA and protein synthesis. It thereby inhibits fibroblast proliferation and is toxic to endothelial cells. MMC also has a more profound

effect than 5-FU and hence it can be given intra-operatively rather than postoperatively [5].

MMC has introduced new complications of its own, including chronic hypotony with maculopathy, cystic avascular blebs, bleb leakage, bleb infections and endophthalmitis[3].

Glaucoma drainage devices create an alternative aqueous pathway by channeling aqueous from the anterior chamber through a long tube promoting bleb formation[6]. However, the tube-shunt surgery has its complications which include excessive aqueous outflow, tube obstruction, corneal damage, strabismus, tube migration and long-term foreign body reaction[7].

Studies in animal models reported that the use of a bioengineered, biodegradable, porous collagen-glycosaminoglycan matrix implant in the subconjunctival space offers an alternative method for controlling the wound-healing process following filtration surgery, avoiding the complications of the administration of antifibrotic agents and offering the potential for maintaining long term IOP control[8-10].

A new collagen matrix implant for wound modulation following filtration surgery called Ologen was approved by the Food and Drug Administration in August 2009. Ologen is an artificial porcine extracellular matrix[11].

Ologen is made of atelocollagen cross-linked with glycosaminoglycan. Atelocollagen, which is obtained by pepsin treatment, is low in immunogenicity because it is free from telopeptides[12].

Ologen is a biodegradable scaffolding matrix that induces a regenerative wound healing process without the need for antifibrotic agents. It is designed to prevent episcleral fibrosis and subconjunctival scarring. Specifically configured to facilitate the repair of connective and epithelial ocular tissue, the implant is designed to minimize the random growth of fibroblasts and instead promote their growth through the pores in the matrix[11].

The surgeon places the device over the scleral flap during the filtering procedure. No suture is required to secure the implant, and as soon as it touches the sclera, it absorbs aqueous and molds to cover the scleral tissue. Collagen matrix therefore doesn't need to be presoaked or prepared in any way. After the collagen matrix's placement, the surgeon closes the conjunctiva in his or her usual meticulous fashion to ensure that the wound is watertight[13].

This implant is found to be biodegradable in 90 to 180 days[11,14]. After degradation, the implant leaves behind a loose alignment of collagen fibers inside the bleb that are remarkably similar to normal tissues[15].

The implant offers the potential for a new mean of providing controlled resistance between the anterior chamber and the subjconjuctival space in the early postoperative period, as well as maintaining long-term IOP control by avoiding early scar formation and creating a loosely structured filtering bleb[8,9].

It can be used in patients with a history of hypotony in the fellow eye following MMC-augmented trabeculectomy, and also has a place for patients with active blepharitis where the use of antimetabolites might further predispose the eye to infection[16].

The clinical applications of Ologen have been presented at conferences; ***European Congress of Ophthalmology, Vienna, June 2007 and World Glaucoma Congress, Singapore, July 2007***[17]. It can be used in ophthalmology in pterygium and strabismus surgeries[11].

Aim of the Study

The aim of this study is to compare between the efficacy of collagen biodegradable matrix and mitomycin C in subscleral trabeculectomy in cases of primary open angle glaucoma.

Anatomy of the Anterior Chamber Angle and Physiology of Aqueous Humor outflow

ANATOMY OF AQUEOUS HUMOR OUTFLOW

There are two main routes responsible for aqueous humor outflow which are the conventional pathway and the unconventional (uveoscleral) pathway[18].

1- Conventional (Canalicular, Trabecular) Aqueous Outflow

The conventional pathway consists of the trabecular meshwork (TM) and Schlemm's canal (SC). The TM is a filter made up of extracellular matrix (ECM), most of which is organized into a network of beams covered by endothelial-like trabecular cells[19].

The TM has three components ***(figure 1)***[20]***:***

- The uveal meshwork,
- The corneoscleral meshwork,
- The juxtacanalicular meshwork.

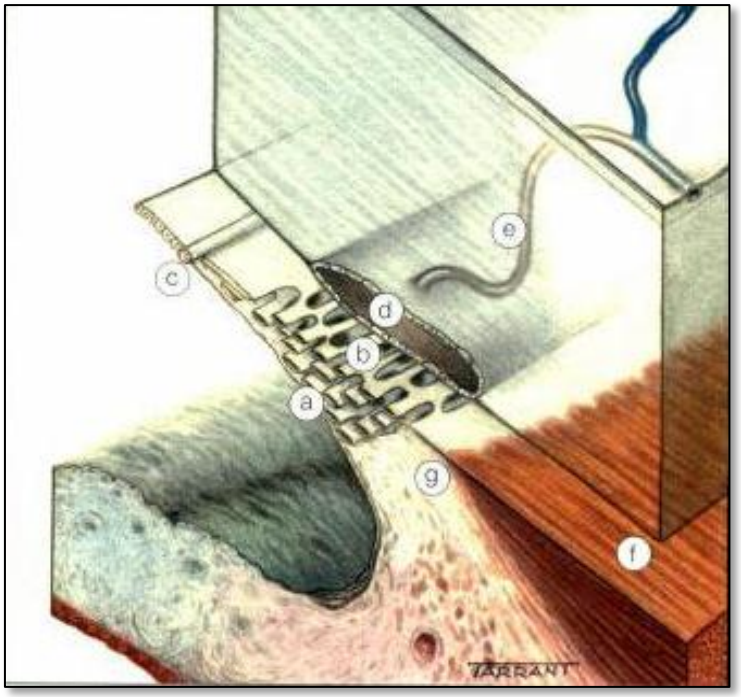


Figure 1: Anatomy of outflow channels.

a) uveal meshwork,

b) corneoscleral meshwork, c) Schwalbe's line, d) Schlemm's canal, e) collector channels, f) longitudinal muscle of the ciliary body,

g) scleral spur[21].

Uveal Meshwork

The uveal meshwork lies most internal. It is formed by prolongations of connective tissue arising from the iris and ciliary body. This layer does not offer much resistance to aqueous humor outflow because intercellular spaces are large[22].

Corneoscleral Meshwork

The corneoscleral meshwork contains a large amount of elastin, forming a series of thin, flat, perforated sheets arranged in a laminar pattern[23].

It makes up the larger middle portion that extends from the scleral spur to the Schwalbe's line. The meshes are sheet-like and the inter-trabecular spaces are smaller than in the uveal meshwork[21].

Endothelial cells lining these structures rest upon a basement membrane and are interconnected by desmosomes and gap junctions[24].

Tight junctions do not exist between these cells. These endothelial cells also have been shown to contain intermediate, actin–like filaments that may be important for cell motility and phagocytosis[25].

Juxtacanalicular (Endothelial) Meshwork

The outermost, or juxtacanalicular, region of the TM is thought to provide much of the resistance to aqueous humor outflow. This consists of a single, amorphous layer of tissue that borders the SC[26].

The outermost portion of this meshwork consists of a layer of endothelial cells that form the inner wall of SC. This area of tissue is approximately 2-20 μm thick[27].

These cells, which also contain actin filaments, possess variable numbers of large, or giant, vacuoles that project into SC, and small pores[28,29].

Intercellular junctions have been demonstrated between these endothelial cells, and these restrict, to some degree, aqueous flow from the TM into SC [24,30].

2- Unconventional (Extracanalicular, Uveoscleral) Aqueous Outflow

In this route, aqueous humor enters the ciliary muscle and exits through the supraciliary space and across the anterior or posterior sclera, through the emissarial canals around the vortex veins, or into the choroidal vessels[31].

However, small quantities of aqueous humor probably diffuse anteriorly through the cornea, and posteriorly into the vitreous and out of the eye through the retina or optic nerve head[26].

This outflow was first demonstrated by showing that a large portion of radiolabeled albumen injected into the anterior chamber of monkey eyes later appeared in the uvea and sclera[32].

As there is no epithelial barrier between the anterior chamber and the ciliary muscle, aqueous humor may freely pass between the ciliary muscle bundles[33].

Aqueous probably flows within the loose connective tissue that exists between the fibers of the longitudinal portion of the ciliary muscle. These fibers insert posteriorly into the connective tissue of the suprachoroidal space[26].

Tracer studies using different size materials have confirmed these pathways. Small molecules, such as fluorescein, readily pass from the anterior chamber (AC) into the suprachoroidal space[34].

These can also penetrate into the vessels of the iris and ciliary body, leading to the vortex veins. This forms another potential outflow pathway, termed the uveovortex pathway, the relative importance of which is poorly understood[35].

In primates, larger particles, including latex spheres, can rapidly pass from the AC into the suprachoroidal space, even to the posterior region of the eye. These have been shown to exit the sclera through the perforating emissary canals around the ciliary vessels and nerves[36].

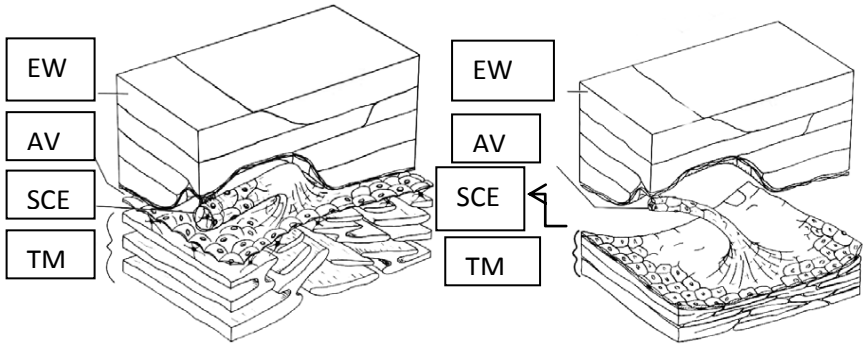
Physiology of Aqueous humor outflow

Intraocular pressure (IOP) is determined by the balance between aqueous humor production and outflow. Most alterations in IOP result from a change in the resistance to aqueous outflow[26].

The initial reports by both ***Ascher***[37] and ***Goldmann***[38] of the presence of aqueous veins pointed out that a mechanism is present to transmit the intraocular pulse across the TM to SC and the aqueous veins.

Ascher[39] had provided exquisitely detailed descriptions of the effect of the pumping mechanism that moves aqueous from SC into the episcleral veins.

Flexible trabecular tissue movement pumps aqueous from the AC to SC through a series of valves spanning SC ***(figure 2)***[40].



IOP Normal ***IOP decreased***

Figure 2: Aqueous outflow anatomy when IOP is normal or decreased. *TM trabecular* meshwork, *SCE* Schlemm's canal endothelium, *EW* Schlemm's canal external wall, *AV* aqueous valve[41]**.**

The aqueous outflow pump receives its power from transient IOP increases such as during systole of the cardiac cycle, respiration, blinking, and eye movement. These IOP transients cause deformation of the elastic structural elements of the trabecular tissues. During systole, the pressure increase moves the TM outwards ***(figure 3).*** This narrows SC, forcing aqueous into collector channels and aqueous veins. Pressure decay causes the elastic tissues to respond by recoiling and this causes a pressure reduction in SC that induces aqueous to flow from the aqueous collector vessels or valves into SC ***(figure 4)[40].***

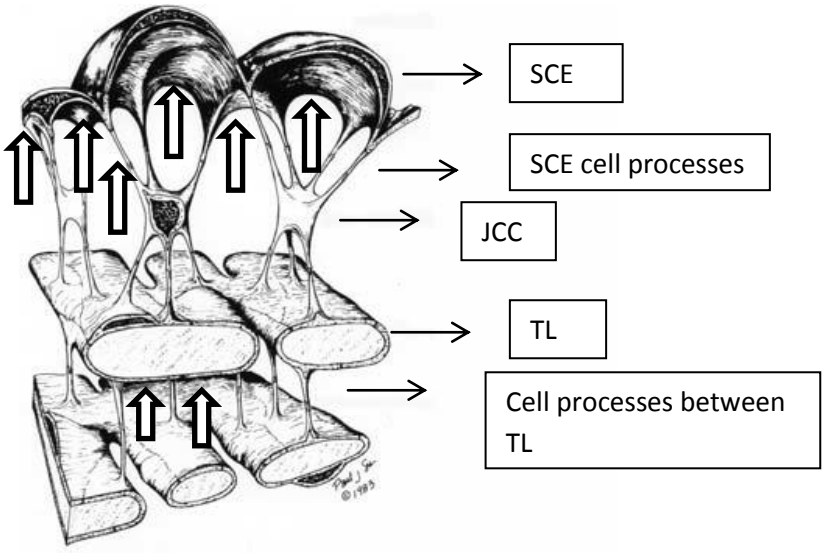


Figure 3: Appearance of aqueous outflow system at physiologic IOP. *Arrows* depict deforming forces of pressure that act on Schlemm's canal endothelium. The IOP forces transmit through cellular processes to the trabecular meshwork. SCE Schlemm's canal endothelium, *JCC* Juxtacanalicular cells, TL trabecular lamellae[42].

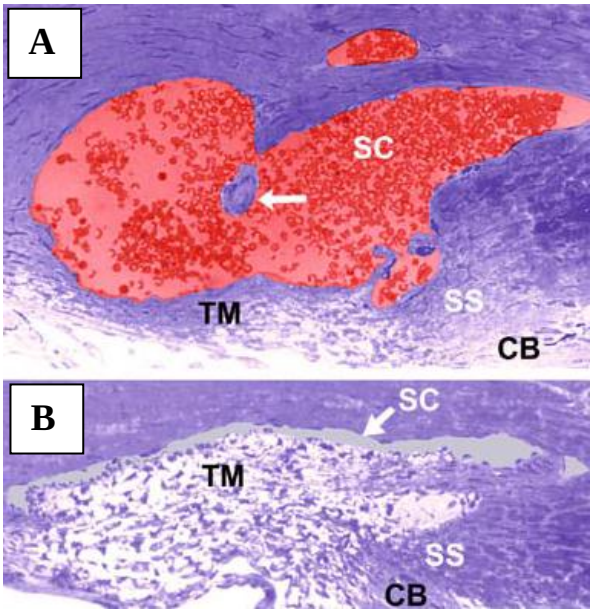


Figure 4: Trabecular meshwork (*TM*) movement following IOP reduction allows TM collapse, Schlemm's canal (*SC*) expansion, and blood reflux. **A:** Intraocular pressure zero, episcleral venous pressure (EVP) ~8 mm Hg. The higher pressure in SC causes the highly flexible trabecular TM to collapse. The pressure on the collapsed TM forces it inward and posteriorly carrying the scleral spur (*SS*) and ciliary body (*CB*) attachment with the TM, thus greatly enlarging SC. **B:** Intraocular pressure 25 mm Hg, EVP ~8 mm Hg. The IOP causes SC endothelium to distend outward carrying the TM with it. TM movement toward SC also forces the attached SS and CB toward SC causing closure of SC lumen[40].

The relative proportion of aqueous humor entering each site is controversial. The uveoscleral outflow pathway was largely considered a passive and minor route for aqueous humor outflow[43]. In humans, reports range from 4% to 60% [44].

Although increased ciliary muscle tone improves conventional outflow, it diminishes uveoscleral outflow. However, in both pathways, ECM appears to contribute to aqueous humor outflow resistance[26].

Intraocular pressure

In enucleated human and monkey eyes, increased IOP appears to immediately diminish aqueous humor outflow facility[45,46].

This appears to be due primarily to collapse of the TM at the higher pressure[45,47].

Uveoscleral outflow, by contrast, is relatively independent of IOP in normal eyes[48].

This homeostatic IOP regulatory mechanism suggests that trabecular cells can sense the juxtacanalicular ECM distortion produced by elevated IOP and they can respond by increasing ECM turnover in this region[49].