

## Advanced Glaucoma Surgery with a Focus on Schlemm's Canal

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### Abstract

New surgical strategies for open-angle glaucoma aim to re-establish the physiological aqueous outflow by directly targeting the site of maximal resistance, i.e. the juxtacanalicular meshwork and inner wall of Schlemm's canal. Canaloplasty uses an *ab externo* approach, whereas Trabectome (trabeculotomy) and trabecular micro-bypass (iStent) use an *ab interno* approach. They all work independently of a filtering bleb and have an inherently lower complication rate than trabeculectomy. Preliminary data suggest that they lower intraocular pressure (IOP) to the mid-teens and are more efficient in combination with phacoemulsification. However, their ability to lower IOP is limited by the level of the episcleral venous pressure. Its good safety profile means that Schlemm's canal surgery may become more popular in the near future, but the outcome of these procedures still needs to be validated in long-term randomised, controlled studies.

### Keywords

*Ab interno* trabeculotomy, bleb-independent, canaloplasty, iStent, micro-bypass, Schlemm's canal surgery, Trabectome

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Glaucoma surgery has been considered the last resort for glaucoma therapy as surgeons prefer to delay surgery for the potentially vision-threatening complications of classic trabeculectomy despite or because of the use of antimetabolites.<sup>1-3</sup> Complications are often related to filtering bleb, such as leaks and infections, or to overfiltration, such as flat anterior chamber, choroidal effusion and cataract and hypotony maculopathy.

Some authors have proposed that if the safety margin of glaucoma surgery could be increased without sacrificing the efficacy, surgical intervention for glaucoma might be considered earlier. Over the past few years there has been increasing interest in non-penetrating glaucoma surgery, which goes back to the pioneering work of Krasnov, who externalised aqueous from Schlemm's canal, originally called 'sinusotomy'.<sup>4</sup> Later, Fyodorov and Kozlov continued this approach by excising sclero-corneal stroma over Descemet's membrane and anterior trabeculum, which results in a thin trabeculo-Descemet's membrane (TDM) that provides some resistance to aqueous outflow. This strategy is known as 'deep sclerectomy'.<sup>5,6</sup>

Stegmann described a bleb-independent procedure<sup>7</sup> with 'visco-canalostomy' in which the narrowed or (presumed) collapsed Schlemm's canal is expanded with viscoelastic material. Today, there are numerous modifications of non- or minimally penetrating techniques with and without implants (see *Table 1*). Some are established methods, whereas others are under investigation. Some methods use implants that are designed to avoid the collapse of the created scleral space, whereas others use implants that work as shunts or stents. It is relevant, not only from a pathophysiological

perspective but also for the safety and risk profile, whether aqueous is redirected into the subconjunctival space or flows out through the physiological pathway of the eye.

This article covers the principles of advanced glaucoma surgery, with an emphasis on Schlemm's canal. It distinguishes between bleb-dependent and bleb-independent procedures.

### Bleb-dependent Deep Sclerectomy

The main advantage of deep sclerectomy over trabeculectomy is the ability to avoid entering the anterior chamber during surgery, thereby controlling the rate of aqueous egress at the level of the TDM, possibly providing a steadier outflow in contrast to the scleral flap resistance in trabeculectomy.

Hypotony-related complications such as flat anterior chamber, maculopathy and cataract formation – particularly cumbersome in the young glaucoma patient – are rarely seen after deep sclerectomy. Also, complications such as bleb dysesthesia or blebitis are largely avoided by the typically diffuse and shallower bleb. Nevertheless, scarring is still the main cause of failure in deep sclerectomy that very much depends on a filtering bleb. Hence, various modifications including the use of implants and application of antimetabolites have been implemented to improve the longevity of the filtration (see *Table 1*).

Whereas some studies showed a higher success rate when mitomycin-C was applied during surgery,<sup>8-10</sup> others reported on the benefit of 5-fluorouracil in post-operative management.<sup>11,12</sup> Due to

inconsistent data on concentrations and application time, as well as the definition of success, comparative analysis should be carried out with caution.

To increase the success rate, some surgeons have combined the use of antimetabolites with collagen implants.<sup>9,10</sup> Such implants are thought to keep the intrascleral lake patent (space maintainer) during the healing process.<sup>13-15</sup> In a randomised study, complete success of lowering intraocular pressure (IOP) to less than 21mmHg was significantly higher (69.2%) in eyes with a collagen implant than in eyes without (38.5%).<sup>16</sup>

Neodymium:yttrium–aluminium–garnet (Nd:YAG) laser goniopuncture has been performed in 4.6–81% of patients after deep sclerectomy.<sup>10,17,18</sup> Currently available data suggest that goniopuncture not only reduces IOP by enhancing permeability but also increases the success rate by providing continuing aqueous outflow that may inhibit subconjunctival healing. Studies with a high rate of goniopuncture achieved lower mean IOPs.<sup>10,18,19</sup> The need for early goniopuncture after surgery is probably due to an inadequate dissection, whereas late goniopuncture is more likely to be due to a decrease in permeability at the level of TDM due to fibrosis evolving over time.<sup>20</sup> The lack of goniopuncture may result in poor IOP control despite the use of mitomycin-C, as has been demonstrated in high-risk patients.<sup>21</sup> This exemplifies the importance of goniopuncture being integral to success in deep sclerectomy. However, patho-physiologically goniopuncture converts deep sclerectomy into a penetrating procedure; strictly speaking the term 'non-penetrating' is no longer correct in this instance and may even be a misnomer.

### Bleb-independent Schlemm's Canal Surgery

Eliminating the dependence of surgical success on the healing properties of the conjunctiva and sclera would be a great advantage for 'non-penetrating' strategies. This section deals with newer procedures conceived as bleb-independent, namely viscocanalostomy and canaloplasty, *ab interno* trabeculotomy (Trabectome) and trabecular micro-bypass (iStent). They all have one intention in common: to restore the physiological outflow system while exclusively targeting the site of maximal resistance to aqueous, i.e. the juxtacanalicular meshwork and inner wall of Schlemm's canal.

### Viscocanalostomy

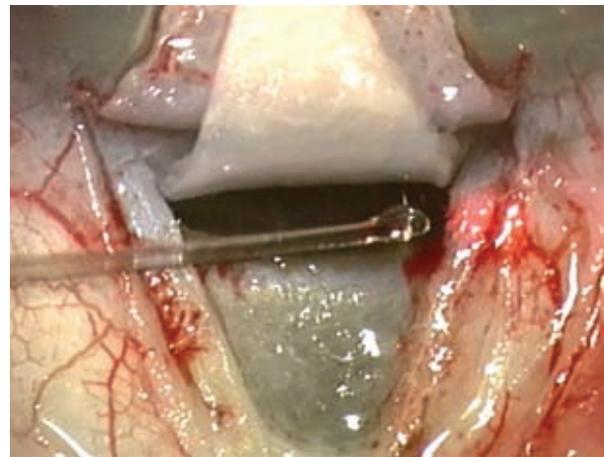
This procedure aims to enhance internal outflow by expanding Schlemm's canal with viscoelastic material through a specific microcannula (Alcon-Grieshaber).<sup>7</sup> In studies on human eyes at autopsy and monkey eyes,<sup>22-24</sup> injection of viscoelastic material into Schlemm's canal resulted in a marked dilation of the canal and adjacent collector channels. It also led to focal disruption of the inner and outer wall, allowing communication between the lumen of the canal and the juxtacanalicular space and the tissues of the ciliary body.

A meta-analysis showed that viscocanalostomy lowers IOP overall to the mid-teens.<sup>15</sup> Large differences in the success rate (IOP 21mmHg or less) in Caucasian patients ranging from 0<sup>25</sup> to 93%<sup>26</sup> may also very much reflect the surgeon's skills and dexterity. The majority of randomised controlled trials suggest that pressure reduction is not as marked in viscocanalostomy as in trabeculectomy, but the complication rate is much lower.<sup>19,27,28</sup> Re-collapse of the canal and closure of the ostia of the collector channels are among the main causes of failure in viscocanalostomy (Dr Stegmann, personal communication).

**Table 1: 'Non-' and Minimally Penetrating Procedures and Implants for Glaucoma Management**

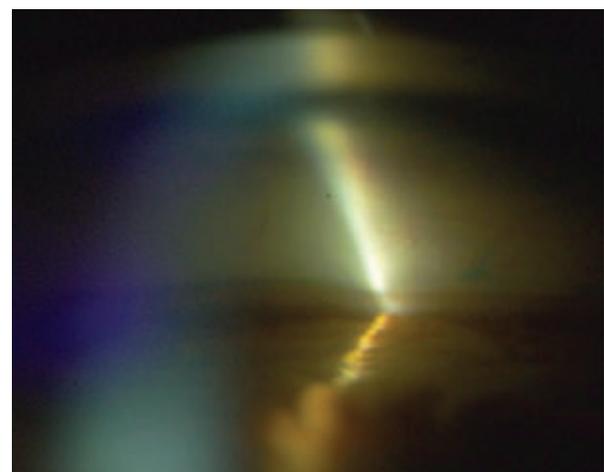
'Non-penetrating'	Implants
Deep sclerectomy	High-molecular-weight hyaluronic acid (Healon GV®) Reticulated hyaluronic acid implant (SkGel®) Collagen–glycosaminoglycan (OculusGen®) Collagen (porcine scleral collagen – Aquaflow®) Highly hydrophilic acrylic (T Flux®)
Viscocanalostomy	High-molecular-weight hyaluronic acid (Healon GV®)
Canaloplasty	High-molecular-weight hyaluronic acid (Healon GV®) and 10-0 polypropylene suture (Prolene®)
Minimally penetrating	Stainless steel (Ex-Press™) Gold (DeepLight Gold MicroShunt®) Silicon tube (EyePass®) Titanium (iStent™)

**Figure 1: Introduction of a Flexible Microcatheter into the Lumen of Schlemm's Canal**



Note the laser light, which allows transscleral visualisation of the catheter's tip as it traverses the canal.

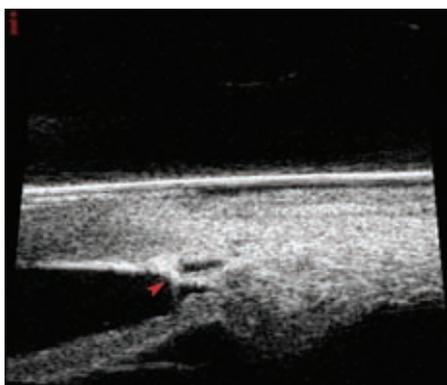
**Figure 2: Suture in Place of Schlemm's Canal**



Note the indentation of the inner wall.

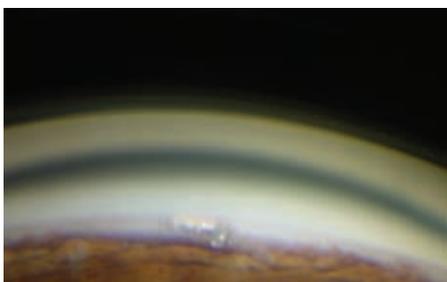
Expansion of a greater part of the canal may give aqueous access to collector channels remote from the site of the TDM window and may increase the chance of a more consistent canal patency and circumferential flow.<sup>23</sup> The fact that the largest number of collector channels is located inferiorly and nasally<sup>29,30</sup> has meant that the

**Figure 3: Ultrasound Biomicroscopy (80MHz) of the Chamber Angle**



Note the widely opened canal and the reflectivity of the suture stent below the area of Schwalbe's line.

**Figure 4: Gonioscopic View of the iStent in Schlemm's Canal**



Courtesy of Glaukos Corporation.

concept of circumferential dilation of the canal has existed for many years. However, it could not be translated into clinical practice for technical reasons until the recent development of a flexible microcatheter (iTrack-250A). In a study on human perfused cadaver eyes, 180° expansion of the canal showed a significant increase in outflow facility; likewise, the amount of dilation correlated with the relative increase in outflow facility.<sup>31</sup> More recently, a clinical pilot study investigating the viscodilation of the entire canal ('enhanced' viscodilation) demonstrated a promising reduction in IOP with few post-operative complications.<sup>32</sup> A circumferential tensioning suture placed in the canal completes this procedure, which is known as canaloplasty.

## Canaloplasty

Canaloplasty combines viscodilation with a circumferential distention of the canal.<sup>33</sup> After dissecting the scleral flaps and dilating the ostia of the canal, a flexible microcatheter is introduced into the canal and advanced 360° to dilate the lumen stepwise by injecting microvolumes of sodium hyaluronidate 1.4% (Healon GV®). The microcatheter has a 200µm-diameter shaft and incorporates an optical fibre to provide an illuminated beacon tip to assist in guidance. The illuminated tip is observed through the sclera during the catheterisation to identify the location of the distal tip of the catheter in the canal (see *Figure 1*).

Following viscodilation of the entire length of canal, a 10–0 polypropylene suture (Prolene®, Ethicon Inc.) is affixed to the distal tip of the microcatheter and looped through the canal. The suture is tightened to the extent that it stretches the Schlemm's canal and

trabecular meshwork circumferentially (see *Figure 2*). This manoeuvre can be monitored with the help of ultrasound biomicroscopy (see *Figure 3*).

In the two-year interim report of a multicentre study on 127 eyes, the mean post-operative IOP was 16.3mmHg in eyes with canaloplasty alone and 13.4mmHg in combination with phacoemulsification.<sup>34</sup> The major IOP drop occurred early after surgery and mean pressures remained stable after three months. The frequency of serious complications was low and included suture extrusion through the trabecular meshwork, gross hyphema and Descemet membrane detachment, each in two eyes, and hypotony in one eye.

Canaloplasty is claimed to be a safe and effective alternative to filtering procedure; however, its IOP-reducing mechanism is not yet known. It has been suggested that suture distension increases the permeability of the inner wall region, ensures circumferential flow and reduces the risk of canal collapse.<sup>33</sup> A pilocarpin-like effect has also been postulated. The drawback of this technically challenging procedure is the lack of knowledge of adequate suture tension.

## Ab Interno Trabeculotomy (Trabectome)

The Trabectome is a device that employs microcautery to ablate and remove the meshwork and inner wall of Schlemm's canal. The surgical approach is *ab interno*, typically via a clear corneal incision from the temporal side. The procedure has been described in detail earlier.<sup>35,36</sup> In brief, the anterior chamber is filled with viscoelastic material and the tip of the hand-held device simultaneously irrigates and aspirates the ablated strip of trabecular meshwork and inner wall of Schlemm's canal under direct visualisation with a modified Swan–Jacob gonioscopy lens (Trabectome gonioprism). Commonly, up to 120° of tissue is removed from the nasal angle.

Similar to canaloplasty, the rationale behind this procedure is to create a direct flow of aqueous into the canal and collector channels. To date, two large studies have been published, one in combination with cataract surgery and one without.<sup>37,38</sup> In Trabectome-alone cases, the IOP reduction was around 40% at three years and 32% at five years to a mean level of 16.4mmHg.<sup>37</sup> About one in seven eyes (14%) were failures, defined as the requirement for additional glaucoma surgery (repeat Trabectome, trabeculectomy, aqueous shunt, etc.). In conjunction with phacoemulsification, a further IOP reduction of about 2mmHg can be expected.<sup>38</sup>

Trabectome is regarded as a safe procedure with virtually no vision-threatening complications. Intraoperatively, damage to the iris, lens and corneal endothelium may all theoretically occur in the case of misguidance of the device, but have rarely been encountered.<sup>35</sup> A common feature after Trabectome is blood regurgitation into the anterior chamber causing transient hyphema. Larger or persistent hyphema have not been found, unlike in classic trabeculotomy or goniotomy. Post-operative inflammation appears to be minimal as the ablated tissue is aspirated.

A further advantage of this procedure is that the conjunctiva is not harmed and therefore subsequent filtering surgery will not be compromised. Notwithstanding any advantages, one has to keep in mind that this relatively straightforward procedure has a learning curve, particularly if one is not experienced in gonioscopic angle surgery and in working from the temporal position.

### Trabecular Micro-bypass (iStent)

The concept behind iStent is to bypass the trabecular meshwork and to re-route aqueous from the anterior chamber into the Schlemm's canal without disrupting the scleral surface. The iStent is a titanium L-shaped implant coated with heparin (see *Figure 4*). It is guided into Schlemm's canal by means of a Swan-Jacobs lens and a special inserter. The procedure is suitable for combined surgery as the same temporal corneal incision is used as for cataract surgery.

A multicentre study reported on 58 patients who underwent combined iStenting and cataract surgery.<sup>40</sup> The IOP and the number of medications was reduced from  $21.7 \pm 3.9$  to  $17.4 \pm 2.9$  mmHg ( $p < 0.001$ ) and from  $1.6 \pm 0.8$  to  $0.4 \pm 0.6$ , respectively. In some smaller case studies, IOPs in the mid-teens in iStent-alone procedures were achieved.<sup>39</sup>

Potential complications of the iStent may include chronic inflammation, clogging of the device's lumen and poor function in the case of malposition in the canal.

### Conclusions and Future Directions

In open-angle glaucoma, the bulk of the pathologically increased resistance to aqueous outflow is located in the juxtacanalicular tissue and inner wall. For this reason, bypassing or selective removal of the site of maximal outflow resistance without harming other structures of the eye has been the declared goal of glaucoma surgery for many years. Trabeculectomy was originally designed to restore the natural physiological system, but for more than 40 years the key to success in the standard glaucoma procedure has been subconjunctival filtration.

However, the ongoing struggle with complications has forced surgeons to search for safer alternatives. Owing to recent technical advances, the concept of re-establishing the physiological pathway has moved again into the centre of attention. Surgeries involving Schlemm's canal correct the pathological defect in the system and force aqueous into the collector channel system. Current data

suggest that these procedures are safe, whether performed *ab externo* or *ab interno*. They are designed to obviate the need for a filtering bleb and all the problems inherent with transscleral filtration. Moreover, hypotony is virtually eliminated due to the intrinsic resistance of the episcleral venous system.

However, this is the other side of the same coin. Schlemm's canal surgery is limited in its ability to lower IOP below 12 mmHg and may not be suitable for eyes in which a very low IOP goal is deemed necessary. Canaloplasty and Trabectome may be more promising than the micro-bypass iStent, simply for the fact that they target a larger area of diseased trabecular meshwork. Comparative, randomised studies and long-term results are awaited to draw final conclusions as all procedures remain subject to biological changes and repair mechanisms over the years.

In the near future, the significance of surgery in glaucoma therapy will be redefined and the time of intervention scrutinised owing to the good safety profiles of the newer techniques. There will be a trend towards earlier intervention with Schlemm's canal surgery. This is because many surgeons are concerned that eyes treated for years with topical antiglaucomatous drugs<sup>41</sup> may have a poorer surgical outcome, particularly if success depends largely on the integrity of the physiological outflow system, as in Schlemm's canal surgery. ■



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