The Current Situation in Non-penetrating Glaucoma Surgery

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The concept of non-penetrating glaucoma surgery (NPGS) originated in 1964 when Krasnov published his first report on sinusotomy. This operation consisted of removing a lamellar band of the sclera, opening the Schlemm’s canal over 120° from 10 to two o’clock. The inner wall of the Schlemm’s canal was untouched and the conjunctiva was closed. However, sinusotomy never became popular because it was a difficult operation, it needed a surgical microscope and the Schlemm’s canal had to be found, which is not easy.

In the late 1960s and for the next three decades, trabeculectomy, as described by Sugar in 1961 and Cairns in 1968, became the gold standard technique for filtering surgery. However, even with the numerous modifications proposed to the original trabeculectomy, several surgeons reconsidered Krasnov’s work because of the lack of a reproducible post-operative intraocular pressure (IOP) reduction and the early post-operative complications, which were mainly related to the penetration of the anterior chamber with sudden decompression of the eye.

Several techniques of non-penetrating filtering surgery based on sinusotomy have been described. As the main aqueous outflow resistance is located at the juxtacanalicular trabeculum and the inner wall of the Schlemm’s canal, these two anatomical structures were targeted. Non-penetrating trabeculectomy was proposed by Zimmerman in 1984 and Arenas first coined the term ab externo trabeculectomy in 1991. Fyodorov encouraged the removal of the corneal stroma behind the anterior trabeculum and the Descemet’s membrane, and called this deep sclerectomy (DS). This was also described by Kozlov and later by Stegmann. Currently, DS with ab externo trabeculectomy and viscoanalostomy (VCS) are the most commonly used non-penetrating procedures.

Principles of Non-penetrating Glaucoma Surgery – Deep Sclerectomy and Viscoanalostomy

The principal common concept of NPGS is to create filtration through a naturally occurring membrane that acts as an outflow resistance site, allowing a progressive decrease in IOP and avoiding post-operative ocular hypotony, without penetration into the anterior chamber. This membrane, the trabeculo-Descemet’s membrane (TDM), consists of the anterior trabecular meshwork and the peripheral Descemet’s membrane. To expose the membrane, a deep sclerokeratectomy should be performed, providing a post-operative intrascleral space; the juxtacanalicular trabeculum and Schlemm’s canal endothelium are then removed (see Figure 1). The intrascleral space may act as an aqueous reservoir and as a filtration site that may reduce the need for a large subconjunctival filtration bleb, therefore reducing the risk of late bleb-related complications. The main disadvantage of both DS and VCS is that they are associated with a long and demanding learning curve.
Surgery

**Figure 1: Deep Sclerectomy with Ab Externo Trabeculectomy**

Under the superficial scleral flap, a deep comeoplasty unroofing the Schlemm’s canal has been performed and the deep scleral flap has been removed. Now a clear membrane can be seen, consisting of the floor of the Schlemm’s canal (opaque band) and Descemet’s membrane (transparent segment). The juxtacanalicular trabeculum and inner wall of the Schlemm’s canal can be grabbed with a blunt forceps and peeled easily by pulling on them.

The Use of Implants

To avoid secondary collapse of the superficial flap, a space maintainer implant is placed in the scleral bed. The first to be used was the collagen Aquaflow implant (STAAR, Collagen Glaucoma Drainage Device, STAAR, Surgical AG Nidau, Switzerland), a highly purified porcine collagen dehydrated into a cylinder (4x1x1mm). It swells rapidly once exposed to the aqueous humour and is resorbed within six to nine months after surgery. Another device that has been proposed to maintain the intrascleral space is the reticulated hyaluronic acid implant (SK-GEL, Corneal Laboratories, Paris, France), which is an equilateral triangle 3.5mm long and 500μm thick or an isoceles triangle of 4.5x3mm at the same thickness. The advantage of this implant is that it occupies a large volume in the filtration area while allowing for sufficient circulation of the aqueous humour, and it does not need to be sutured at the sclera. More recently, a hydrophilic acrylic implant (T-flux implant, IOLTech Laboratories, La Rochelle, France) that is non-absorbable has been developed. It is a T-shaped implant that creates an evacuating canal along the foot and each arm of the T shape and is inserted into one of the surgically created openings of the Schlemm’s canal. New implants have been developed in the past few years with promising results, such as the 2-hydroxyethyl-hethacrylate (HEMA) implant (Esnoper, AJL Ophthalmics, La Rochelle, France) that is non-absorbable has been recently, a hydrophilic acrylic implant (T-flux implant, IOLTech Laboratories, Paris, France), which is an equilateral triangle 3.5mm long and 500μm thick or an isoceles triangle of 4.5x3mm at the same thickness. The advantage of this implant is that it occupies a large volume in the filtration area while allowing for sufficient circulation of the aqueous humour, and it does not need to be sutured at the sclera. More recently, a hydrophilic acrylic implant (T-flux implant, IOLTech Laboratories, La Rochelle, France) that is non-absorbable has been developed. It is a T-shaped implant that creates an evacuating canal along the foot and each arm of the T shape and is inserted into one of the surgically created openings of the Schlemm’s canal. New implants have been developed in the past few years with promising results, such as the 2-hydroxyethyl-hethacrylate (HEMA) implant (Esnoper, AJL Ophthalmics, SA, Milano, Alava, Spain) and a cross-shaped rigid non-absorbable implant made of poly-methyl-methacrylate (PMMA) (HOMDEC SA, Belmont, Switzerland). Other low-cost implants such as chronic suture material and autologous scleral implant have been used in deep sclerectomy. Amniotic membrane has also been tried as an implant. Further studies are needed to evaluate the role of these implants.

Neodymium-doped:Yttrium–Aluminium–Garnet Goniotuncture

When filtration through the TDM is considered to be insufficient because of elevated IOP, neodymium-doped (Nd):YAG goniotuncture can be performed. An insufficient surgical dissection can be the reason for elevated IOP in the first post-operative period or fibrosis of the TDM if it is required later than approximately nine months, and may lead to a flattened bleb. Using a gonioscopy contact lens, the aiming beam is focused in the semi-transparent TDM. Using the free-running Q switched mode with a power of 5–10mJ, two to 15 shots are applied, resulting in the formation of microscopic holes through the TDM and allowing the direct passage of aqueous from the anterior chamber to the intrascleral space. In their study results on DS, Shaarawy et al. performed goniotuncture in 42–46% of their patients who had undergone DS without implant and in 46–51% of those who had undergone DS with collagen implant (DSCI). The immediate success rate was 91.6%. In their study on results of VCS, 37% of their patients needed goniotuncture post-operatively to control raised IOP. Overall, the rate of goniotuncture after DS (with or without implant and/or antimetabolites) ranges between 4.6 and 81%, with an IOP reduction as high as 45%; the rate of goniotuncture after primary VCS varies ranges between 4.1 and 56%, with an IOP reduction as high as 38.2%.

Indications and Contraindications of Non-penetrating Glaucoma Surgery

NPGS targets the presumed site of pathology in primary open-angle glaucoma (OAG), namely the trabecular meshwork. The site of aqueous outflow resistance is presumed to be the juxtacanalicular trabeculum, the inner wall of the Schlemm’s canal and the endothelial lining. Scraping, thinning out and peeling the posterior trabeculum improve filtration. In NPGS, DS and ab externo trabeculectomy are both necessary to obtain an optimal decrease in outflow resistance. NPGS has the advantage of being less cataractogenic than trabeculectomy and ideally should be considered as a safer option in phakic patients with primary OAG. It is an efficient surgery in medically uncontrolled primary OAG. It appears to offer glaucoma patients with high myopia a safe filtering procedure, is a safe and valuable option in patients with pseudoxfoliative glaucoma and seems especially appropriate in these patients, given the increased permeability of the blood–aqueous barrier as well as the higher risk of complications with intraocular surgery. NPGS is a potential therapy for pigmentary glaucoma also. It targets the site of pathology – the pigment-loaded trabecular meshwork – which can be reconditioned to establish filtration. In uveitic glaucoma cases NPGS is associated with less post-operative inflammation. Moreover, NPGS may be indicated in some cases of congenital, juvenile and aphakic glaucoma when the irido-corneal angle is not severely distorted. If not sufficient, it can be associated with other ab externo procedures and/or with laser or medical treatment. Converting to penetrating surgery may be necessary in refractory cases. There are no published reports on NPGS in primary-angle closure glaucoma. This is not surprising considering the principles of function of NPGS. Likewise, secondary angle closure anatomical entities are a relative contraindication. However, the decision depends on the degree of angle closure. Neovascular glaucoma is an absolute contraindication because new blood vessels invade the iridoconal angle and the trabeculum loses its filtering function because of the neovascularisation, providing little chance of surgical success.

Complications of Non-penetrating Glaucoma Surgery

There is an agreement among published reports that NPGS offers a lower rate of complications compared with conventional trabeculectomy, with or without antimetabolites. This is largely due to the fact that the eye is not fully penetrated as with trabeculectomy, and that the aqueous is percolated through the remaining TDM, thus preventing a sudden intra- and post-operative hypotony. Moreover, visual acuity is generally preserved after NPGS and returns to the pre-operative level within the first post-operative week. Complications of NPGS can be intraoperative, e.g. rupture of the TDM, early post-operative or late post-operative. Long-standing hypotonia, hypotonic maculopathy, flat anterior chamber, choroidal detachment and
suprachoroidal haemorrhage are rare difficulties, whereas they are potentially sight-threatening complications following trabeculectomy. Similarly, blebitis is a well-known and potentially dangerous complication after trabeculectomy, and can lead to endophthalmitis. In NPGS, the TDM offers a barrier against the intracocular spread of bacteria. Blebitis and infectious keratitis are rare complications. Cataract progression is less influenced by DS compared with trabeculectomy. The Advanced Glaucoma Intervention Study (AGIS) estimated that the rate of cataract formation after the first trabeculectomy is 78% at five years. The risk of cataracts is doubled if there is a significant post-operative inflammation or a flat anterior chamber. Shaarawy et al. followed 105 patients for a mean of 64 months and showed progression of existing age-related cataracts in 25% of eyes, but no surgery-induced cataracts. Wound leaks or a positive Seidel test occur more often after trabeculectomy than after NPGS. In a two-year prospective study on bleb characteristics of 125 eyes that had mitomycin-C-augmented glaucoma surgery, bleb leaks were more frequently observed in the trabeculectomy group than in the DS group (24.6 versus 3.1%). Bleb fibrosis and encapsulation may occur after NPGS, and their incidence is comparable with that after trabeculectomy. The rate of post-operative S-fluorouracil (S-FU) injection for uncontrolled IOP after DS (with or without implant and/or antimetabolites) ranges between 4.6 and 56%, and may be as high as 35% following VCS.

Efficacy of Non-penetrating Glaucoma Surgery
The last years have witnessed numerous publications on NPGS. If the safety margin of glaucoma surgery could be increased significantly without sacrificing efficacy, surgical intervention for glaucoma could be considered earlier.

Deep Sclerectomy
Prospective studies of DSCI report complete success rates of 45–69%, with qualified success rates (IOP <21 mmHg with medication) being much higher. In addition, the use of a collagen implant enhances success rates and reduces the need for post-operative medications. Shaarawy et al. reported their long-term results of a randomised prospective trial of 104 eyes comparing DS with and without an implant. The complete success rate (IOP ≤21 mmHg without medication) was 34.6% at 48 months for the DS group and 63.4% for the DSCI group. The qualified success rate was 78.8% at 48 months and 94% for the DSCI group. The mean number of medications was reduced in the latter group and no significant operative complications were observed in either group. These results were confirmed by a subsequent study of 26 eyes reported by the same author, who randomly assigned a collagen implant to one eye of each patient with the contralateral eye of the same patient having DS without implant. The complete success rate (IOP ≤21 mmHg without medication) was 38% at 48 months for the DS-treated eyes and 69% for the DSCI-treated eyes, with the qualified success rate being 69 and 100%, respectively.

Viscocanalostomy
The largest study of VCS, reported by Stegmann et al. in 1999, was a prospective study of 214 eyes of 157 African patients with OAG with an average follow-up of 35 months. They reported a complete success rate (IOP ≤22 mmHg without medication) in 82.7% of eyes. The qualified success rate (IOP ≤22 mmHg with topical beta-blocker and/or alpha-blocker) was achieved in 89% of eyes. Shaarawy et al. presented their long-term results of VCS in a prospective trial in which 57 eyes of 57 Caucasian patients were consecutively enrolled. The complete success rate (IOP ≤21 mmHg without medication) was 60%, whereas the qualified success rate (IOP ≤21 mmHg with or without medication) was 90% at 60 months. Both studies concluded that VCS provides reasonable long-term IOP control with few post-operative complications. Several other studies have been published, reporting results on the safety and efficacy of both DS and VCS. A recent meta-analysis based on 35 studies published between 2000 and 2005 reported that the mean percentage of cases achieving ≤21 mmHg was 48.6% after primary DS, 68.7% after DS with implant, 67.1% after DS with antimetabolite, 51.1% after primary VSC, and 36.8% after VSC with antimetabolite or implant. Lower IOP targets, the rates of success varied between 35 and 86% for DS and between 10 and 67% for VSC. The mean follow-up of the studies was in the three-year range.

Comparative Studies Between Trabeculectomy and Non-penetrating Glaucoma Surgery
One of the most intriguing questions regarding NPGS is how well it fares compared with trabeculectomy, which was regarded for many decades as the gold standard against which all novel glaucoma procedures were tested. Randomised controlled trials comparing NPGS with trabeculectomy have a consensus on the superior safety profile of NPGS, but are not in agreement when it comes to efficacy, where we find conflicting results in terms of how low NPGS affects IOP compared with trabeculectomy. This is attributed to a number of factors, including the fundamental differences between NPGS and penetrating filtering techniques, the long learning curve of NPGS and the need to use gonio-puncture to achieve target IOPs. El Sayyad et al. prospectively compared the efficacy and safety of DS without implant against trabeculectomy in a randomised study, and showed the latter to be more effective at lowering IOP at 18 months, but with a higher complication rate. However, it should be noted that the authors did not perform gonio-puncture during the follow-up and their non-penetrating technique differed in that only the external wall of the Schlemm’s canal was removed, without peeling its inner part and the adjacent trabecular meshwork. In our judgement, considering gonio-puncture to be a failure criterion could be comparable to considering suture lysis and capsulotomy as failure criteria of glaucoma and cataract surgeries, which is mostly uncommon.

El Sayyad et al. prospectively compared the efficacy and safety of DS without implant with trabeculectomy in bilateral primary OAG. At 12-month follow-up there was no statistical significance between the two groups regarding both the complete and qualified success rates. However, there was a significantly lower incidence of complications for the DS group compared with the trabeculectomy group. Chiou et al. also considered DS without collagen implant against trabeculectomy in a randomised study, and showed the latter to be more effective at lowering IOP at 18 months, but with a higher complication rate. However, it should be noted that the authors did not perform gonio-puncture during the follow-up and their non-penetrating technique differed in that only the external wall of the Schlemm’s canal was removed, without peeling its inner part and the adjacent trabecular meshwork. In our judgement, considering gonio-puncture to be a failure criterion could be comparable to considering suture lysis and capsulotomy as failure criteria of glaucoma and cataract surgeries, which is mostly uncommon.

Mermod et al. prospectively compared two groups: DSCI (44 eyes) versus trabeculectomy (44 eyes). The complete success rate (IOP ≤21 mmHg without medication) were 57% for the trabeculectomy group versus 69% for the DSCI group. The number of post-operative medications was significantly lower in the DSCI group. The authors concluded that
success rates of both DSCI and trabeculectomy were comparable; however, a lower rate of complications was observed in the DSCI group.

Conclusions

NPGs continues to evolve as a technique. It is certainly safer than trabeculectomy and thus may have a worthwhile role earlier in the treatment process. Its superior safety profile makes it a first choice in many cases. The major controversy that arises is the success rates of NPGs compared with trabeculectomy, with trabeculectomy being perceived by many to lower IOP to a greater degree. The learning curve of NPGs and the need to consider goniopuncture as an adjuvant to the procedure and not as a failure criterion cannot be overstated. The use of implants in NPGs offers better IOP control for longer periods, thus enhancing success rates. Variable definitions of success, different follow-up times and various study designs make direct comparisons between reported results challenging. A prospective, randomised multicentre study is needed to draw final conclusions on how NPGs fares compared with trabeculectomy and to examine the different techniques.