Core Concepts

- In the last 15 years, glaucoma filtration surgery (GFS) success and complication rates have improved due to a better understanding of functional components of the surgery as well as management of wound healing.
- The best-organized and best-known modern approach to trabeculectomy is the Moorfields Safe Surgery System (MSSS).
- Mitomycin-C (MMC) improves post-trabeculectomy IOP control significantly, but is also associated with bleb leaks or long-term hypotony. The latter issues may be minimized with appropriate surgical technique.
- Despite development of glaucoma filtration surgery (GFS) into modern trabeculectomy over the last 40 years, current methods still cannot simultaneously achieve all of low cost, high efficiency, low complication rates and high long term success rates.
- The Express implant effectively stents the sclerostomy, but adds cost without proven benefits in long-term efficacy and safety.
- Non-penetrating glaucoma surgery (NPGS) approaches have decreased complication rates, but also yield less IOP-lowering effects. YAG laser goniodoplasty may be needed to create a sclerostomy.
- Bleb morphology needs to be optimized, diffuse blebs are desirable. Considering how vital bleb outcomes are in trabeculectomy, there is minimal reporting on bleb outcomes from procedure variants.
- The Moorfields Bleb Grading system is excellent for grading blebs if detailed analysis is required.

1) Introduction

Since this topic last appeared in Glaucoma Now, Glaucma Filtration Surgery (GFS) has become more refined, and the short and medium term effects of these refinements on outcomes have started to be described. At the same time, longer term results of the Tube versus Trabeculectomy (TtT) study imply that we should consider changing our threshold for tube implant surgery, with probable inroads into the role of trabeculectomy - which remains the most commonly performed glaucoma procedure. And there are new Minimally Invasive Glaucoma Surgery (MIGS) contenders which are being promoted and tested.

GFS still lacks the high efficiency, excellent success rates, and long-term stability that we expect from cataract surgery. There are many new options for glaucoma surgery, particularly implants and machines, actively being promoted. All of these hold some hope of a better safety profile or easier or faster procedure than traditional filtering surgery.

Despite all of these new options, when faced with the need to subject their patient to an operation for glaucoma, most surgeons continue to opt for trabeculectomy most of the time. That decision is partly due to the excellent IOP control for many years that results from successful GFS. But getting to that endpoint is never guaranteed and often is not easy.

2. Technical Advances In Trabeceuctomy

Readers of glaucoma surgery articles are so accustomed to that prototypical first sentence referencing Watson and Cairns’ publications that it is easy to forget their fundamental message. Modern trabeculectomy is different enough from the original early 1970s description of even the name itself is a misnomer; usually no trabeculum is excised. But the core advance of trabeculectomy, the message of ‘control outflow to improve the safety of the procedure’, became neglected frequently enough that postoperative flat anterior chambers, choroidal detachments, and hypotony complications came to be expected, and many authors published results showing that the control of IOP after surgery was poor and complications very common.

The subtle and yet substantial changes to trabeculectomy technique developed in the late 1990s, epitomized by the Moorfields Safer Surgery System (MSSS), remain the state of the art for trabeculectomy. These modifications have been adapted to fit with each surgeon’s preferred approach to surgery; even those trained in the epicentres of the MSSS have ended up developing a variety of surgical techniques while adopting the underlying principles. The MSSS emphasizes fornix-based conjunctival flap to avoid a scar tissue demarcation, large area of subTenons dissection and antimetabolite treatment, careful construction of the scleral flaps, maintaining IOP and the anterior chamber throughout surgery via preplaced sutures with BSS infusion (especially in high-risk cases), and understanding the use and mechanism of adjustable scleral flap sutures. Recent MSSS updates include closing the conjunctiva with interrupted sutures buried in peripheral corneal grooves, and injecting local anaesthetic into the bleb area at the end of surgery to minimise inflammation and scarring along with pain. The innovation of staining MMC with dyes has made handling and applying antimetabolites more effective and safer.

But we are still quite a long way from the ideal; the 10-10-10 target as recently proposed by Professor Sir Peng Khaw: an IOP of 10 mmHg, for 10 years, done in 10 minutes.

Speed, Economy, Quality: Pick Any Two

Trabeculectomy requires mastery; performing it well and consistently requires fastidious attention to detail and a...
Fig 1. Indocyanine green (or trypan blue) can be mixed with Mitomycin C to show exactly where the MMC has gone, how large the treatment area is, and the location of any split antimetabolite; making the procedure safer for the patient and operating theatre staff. Trypan blue stain lasts for several hours, ICG is visible on for a day or two after surgery.

Fig 2. Full thickness drainage at the edge of the scleral flap results from the edge of the sclerostomy being too close to the edge of the scleral flap. The appearance of an avascular (‘cystic’) area overlying the full-thickness defect is characteristic, sometimes referred to as an ‘aqueous jet’, and was the typical appearance following the full-thickness glaucoma procedures that preceded guarded filtration surgery. Blebs like this typically weep and are associated with late hypotony and bleb-related endophthalmitis. It is important to ensure that the width of the scleral flap is much greater than that of the sclerostomy.

The trade-off for this greater control is time and effort. To get trabeculectomy right requires attention to detail and a fast procedure is less likely to be a good one. Trabeculectomy with some kind of implant (e.g. Ex-Press), may shorten the procedure slightly, but at additional cost and possibly little long-term benefit.

3. Safety And Efficacy Of Modern Trabeculectomy

While some authors still refer to trabeculectomy as having a “very high risk profile”, with “moderate long-term results at best”\(^7\), modern publications of results suggest that trabeculectomy has made major advances\(^8\). Publications of small series of Moorfields SSS trabeculectomy have shown very low complication rates and good short and intermediate-term success rates, with typical figures for flat anterior chambers, hyphema, and choroidal detachments of well under 5% and IOP below 18mmHg in approximately 90% of cases at 3 years\(^9\)\(^,\)\(^10\).

Recently, Kirwan et al\(^1\) published a series of 428 procedures with more than 2 years of follow up, sourced from 9 glaucoma units with fellowship-trained glaucoma consultants. These surgeons followed a broadly similar surgical approach, including a fornix based conjunctival flap, adjustable or releasable sutures, most with antimetabolites. A subgroup analysis used inclusion and assessment criteria based on the TVT study; the unqualified success rate was 85%, with qualified success rates of 92%. In 3 patients there was vision loss of 3 or more Snellen lines (one patient declined treatment for hypotony maculopathy), 31% had cataract surgery subsequently, bleb leaks were identified in 13.6%, with 95% of these in the first weeks after surgery. Between 6 months and the final post-surgery visit, 7.2% of cases had an IOP reading of less than 5mmHg.

The most interesting aspect of the Kirwan et al study is that post-trabeculectomy complications related to scleral flap construction and suturing were impressively low: shallow anterior chamber (AC) in 0.9%, flat AC in 0%, and choroidal detachment at any time in 5%. Both CIGTS and AGIS reported 13-15% AC after trabeculectomy.

In the TVT study\(^4\), a large multi-center trial which published 3-year results in 2009\(^5\), the trabeculectomy group had an average of 1 +/- 1.5 medications, a 31% chance of failure, 60% complications, and 27% chance of complications severe enough to warrant reoperation or result in 2 lines or more of visual loss. This study is one of the best surgical glaucoma studies ever published, but one reservation held about interpreting the results is that the outcomes and complications for the trabeculectomy group were not as good as expected. As a counterpoint, the reporting standards of randomized clinical trials (RCTs) are usually higher than that of retrospective audits, so it is possible that the TVT study better represents contemporary trabeculectomy results. Despite this, the difference in success rates compared with Kirwan’s data is substantial.

Scleral flap, Sclerostomy, and Sutures

It is the combination of the scleral flap and sutures that controls the early post-operative IOP. Using relatively simple measures and attention to detail, understanding scleral flap function, and carefully utilized adjustable sutures, early postoperative hypotony and trabeculectomy complications can be prevented.

Important factors in scleral flap construction and suture placement\(^3\)\(^-\)\(^14\):

- Apposition of the scleral flap over the scleral bed that contains the sclerostomy (not apposition of the edges of the flap to the edges of the scleral bed), created by suture tension, provides resistance to flow and therefore the all-important control of perioperative IOP. Get this right and most complications can be avoided.
- If the sclerostomy is located between, or posterior to, the cut sides of the scleral flap, it can be difficult to generate enough appositional force for IOP control, and posteriorly directed flow may be harder to encourage. It is best to locate the sclerostomy anterior to a line connecting the anterior extent of the side cuts.
- If the sclerostomy is very close to the scleral flap sides, a full thickness fistula around the edge of the flap may result (Figure 2). A punch (Khaw punch or Kelly punch) makes a more discrete and controllable sclerostomy than a blade-cut sclerostomy and minimizes this risk. Ideally there would be at least 0.5mm between the flap edge and the sclerostomy edge.
- For most surgeons, depth is more controllable and it is therefore easier to produce consistent scleral flaps by starting with a scleral tunnel made with a crescent blade. In our wet-lab studies, we found that keeping the antero-posterior deep understanding of how components of the procedure interact. The single most important recent refinement to trabeculectomy technique is making the scleral flap and sutures work as intended: an adjustable pressure-sensitive flow restrictor. While the scleral flap location and dimensions, and its relationship with the underlying sclerostomy, do affect long term bleb morphology – cystic blebs overlying full thickness sclerostomies being a great example (Figure 2) – it is the scleral flap and suture complex that avoids the vast majority of oft-quoted periooperative complications\(^5\).

Getting the scleral flap and sutures right, and testing that they are right before the patient leaves the operating room, can give results that match the best minimally invasive procedures\(^2\) for early postoperative complications.
extent of the central trapdoor less than 2.5mm decreased the chance of accidentally making a flap that was irregular or lacked sufficient rigidity.

- Our recently developed understanding of the mechanisms of scleral flap function and technical aspects of flap construction has led us to a W-shaped or modified trapezoidal flap (Figure 3). This maximizes posterior flow by making resistance to posterior flow less than lateral, meets the objectives discussed above, and the <2.5mm anterior dissection distance lessens the risk of mistakes in scleral flap creation.

- Full thickness flow through the scleral flap will negate the desired effect, so choose location carefully to avoid perforating blood vessels, and avoid suture holes in the flap except near the flap edges.

- A suture that is both releasable and adjustable (Figure 4) gives the best possible control of postoperative IOP with the best range of options for manipulation. Lysis misses an opportunity for adjustability, and non-removable sutures have no option but to stay as a foreign body in the surgical site. Four throws of 10-0 Ethilon have proved to be dependable and robust, and yet remain adjustable.

- The single most important step to avoid loss of IOP control: via a paracentesis if no AC maintainer, or by turning off the AC maintainer, test the sutured scleral flap for the ability to maintain IOP before conjunctival closure - and don’t start closing the conjunctiva until adequate flow resistance and IOP control is achieved. Place more sutures if necessary, then test again. Aiming for a day 1 IOP of approximately 20 via appropriate suture tightness gives the option to lower the IOP by using adjustable sutures.

- Once the flap-suture complex controls flow adequately, use a very light touch in the area while completing the operation to avoid loosening the adjustable sutures.

Suture adjustment:

Once healing and eventual remodeling of the surgical site has occurred, adjustability of the scleral flap is lost. But prior to that, maybe extended by many weeks by antimetabolites, it is the tension of the sutures translated to scleral flap tension over the sclerostomy that controls IOP. It is easy to lower this tension, and therefore the IOP, with a high degree of fidelity in laboratory models\textsuperscript{14} and it is just as effective in the clinic (Figure 5)\textsuperscript{7,13}.

Adjustment of these sutures is not only straightforward, it is more reliable and safer than suture lysis/release/removal, more effective than focal massage of the trapdoor region, and both more effective and immediate than digital massage by the patient\textsuperscript{13}. Suture adjustment can be done safely with forceps, e.g Khaw Suture Adjustment Forceps (Duckworth and Kent, http://duckworth-and-kent.com), or with a modified contact lens such as Wells Suture Adjustment Lens (Ocular Instruments, http://www.oculinarinc.com).

Producing an aqueous gush, also known as ‘burping the bleb’, is likely to falsely reassure the patient and surgeon because it may take more than 30 minutes to re-establish equilibrium IOP\textsuperscript{13}. IOP measured in the first few minutes after aqueous release will always be low, but if the sutures have not been loosened then the IOP will return to pre-massage levels within an hour.

Sclerostomy:

The commonly available punch models are more than big enough. To cope with aqueous flow rates of up to 3.5µL/minute, even with slightly turbid aque-
ous, a sclerostomy only needs to be over 50µ wide which is 1/5th the diameter, and 1/25th of the area, of the smallest available punch. Some surgeons express concern that iris or vitreous might plug the sclerostomy, and that larger might be better in this circumstance. In fact, plugging is associated with loss of anterior chamber and bulk outflow of aqueous, which is more likely if the sclerosotomy is too large and there is loss of posterior chamber and bulk outflow of aqueous, which is more likely if the sclerostomy is too large and there is loss of effective scleral flap control of flow. The sclerostomy should be just anterior to the trabeculectomy meshwork, in peripheral cornea, to avoid intraoperative hemorrhage and possible ciliary body incarceration.

Stenting the Sclerostomy

Originally the Ex-Press glaucoma implant was intended to drain directly under the conjunctiva: predictably results included 91% hypotony, 30% choroidal detachment, and 18% suprachoroidal hemorrhage. The Ex-Press lumen size does not restrict flow to any significant degree in clinical practice. A flow restrictor based on diameter would need to be about 30 microns at normal aqueous flow rates (~2.5µL/min). Issues with tube diameter based flow restriction arise when flow rate and viscosity vary, which of course they do, and the dependence of such flow restriction on radius of the tube to the 4th power mean that small flow or radius variations have dramatic effects on outflow resistance.

The obvious modification to Ex-Press implantation, placing it under a scleral flap, was widely adopted quickly. This approach is effectively a stent to the sclerostomy, which is usually not thought of as a high-risk failure site. Several comparative studies and an excellent review comparing trabeculectomy with trabeculectomy with Ex-Press implanted beneath a scleral flap have shown possible short term advantages, especially better early anterior chamber and IOP control, but no benefit in long term outcomes. Implant exposure can occur even if the Ex-Press is implanted beneath a scleral flap and suprachoroidal hemorrhage and blebitis remain a risk. Kirwan et al’s results suggest that with due care to flap construction and adjustable/releasable sutures, the addition of this expensive implant may only bring minimal benefit, although we may yet see further refinement of technique, just as we have with trabeculectomy and GDD surgery.

Weighted against the variable but possibly improved perioperative risk profile are cost, and the device-specific risks of pain from malposition, erosion through conjunctiva and subsequent exposure, or, of greater concern, a free metal object in the anterior chamber from which endothelial cell loss could follow. Ex-Press implants may not be stable in high-power (more than 3T) magnetic fields, as found in some MRI machines.

4. Aggressive Bleb Management

A likely true maxim is that half of a successful trabeculectomy outcome is due to the operation itself and half is from the perioperative management; especially with regard to managing scarring the first months after surgery. The results reported by Kirwan et al depended on relatively intensive postsurgical management, with 27% having sub-conjunctival 5FU injections, 16% requiring bleb needling, and 5% having additional sutures placed. Management of bleb healing, using anti-metabolites and needling procedures as well as the routine frequent steroid eye drops, are now standard practice in many units and while extra interventions are undesirable the approach is widely accepted.

Anti-VEGF agents have been trialed and, anecdotally, in some places used as a routine adjunct for management of bleb vascularity. Although few blebologists doubt the role of vascularization in bleb failure, results from the studies of anti-VEGFs in glaucoma surgery have been mixed.

5. Interaction With Cataract Surgery

Cataract surgery results in breakdown in the blood-aqueous barrier that persists for some months. This is most apparent when a cataract procedure precipitates bleb failure after a successful trabeculectomy. Decisions regarding cataract and a need for better IOP control should be undertaken with this, and the resulting possible compromise in trabeculectomy success rates, in mind. The optimal sequence of events usually is to have the cataract surgery at least 6 months prior to trabeculectomy, if there is time to arrange this option.

6. Beyond IOP Control: Optimizing Blebs

As the safety of trabeculectomy has improved, so the next target for glaucoma surgeons and researchers should be optimization of bleb morphology, with important implications for long-term surgical success and late compli-
cations such as blebitis and bleb-related endophthalmitis. Diffuse blebs without significant avascular areas are desirable (Figure 6); surgical technique as well as antimetabolites influence bleb outcomes. Thin-walled or cystic blebs are of most concern since they predispose to bleb-related endophthalmitis and late hypotony. Nowadays it is common to blame MMC for these complications; they were common after full-thickness surgical procedures that predated antimetabolite use and may be significantly minimized with changes in surgical technique.

In some centres, an alternate method of MMC application is being trialed. Instead of applying 0.2-0.4 mg/ml MMC on sponges, 10-20 micrograms of MMC is injected into the superior subconjunctival space or sub-conjunctivally before the peritomy. MMC is injected into the superior subconjunctival space before the peritomy. This should deliver the antimetabolite to where it is needed while eliminating wound edge contamination with MMC, avoids the risks of lost sponges and of spillage of an open MMC container with exposure of the surgeon and the theatre staff to MMC. Applying MMC in this way might also contribute to more diffuse bleb formation.

Modern bleb grading systems for clinical studies, such as the Moorfields Bleb Grading System (MBGS) (www.blebs.net) carry important clinical clues to bleb complications and failure that older grading systems can’t capture. While it is probably not necessary to use the MBGS or similar systems in routine clinical practice, it is valuable for glaucoma surgeons to understand the parameters and implications. Given the maxim that half the success of a trabeculectomy is due to what is done in theatre, and half from post-surgical care, there is relatively little high quality data for post-trabeculectomy manipulation of bleb morphology using tools such as anti-metabolites, needling procedures, medication regimens for the wide variety of bleb morphologies that can appear after trabeculectomy.

Microstructural imaging of the bleb using confocal or OCT technology is available, but is a tool that currently lacks a solid application. It may turn out to be useful when we better understand the images these instruments produce.

7. Non-Penetrating Surgery

Non-penetrating glaucoma surgery (NPGS), for example ‘deep sclerectomy’, has been a popular procedure in parts of Europe since the late 1990s. The principle of NPGS is to filter aqueous and to avoid loss of IOP control with aqueous egress though a trabeculo-Descemetic window rather than a sclerostomy, preferably without a bleb. This window is created by unroofing Schlemm’s canal, with aqueous percolating into the space beneath a scleral flap. It is typically an attempt to create an intra-scleral space, or ‘lake’, to function as the location of aqueous absorption to a variable combination of the supra-choroidal space or sub-conjunctivally. There are multiple described variants, many with implants of a variety of materials, with most of these commonly collagen-based, but the Ex-Press implant has also been trialed in deep sclerectomy, in what is apparently a complete reversal of the NPGS ethos.

Proponents of NPGS refer to laudable postoperative complication rates, but acknowledge that the IOP-lowering effect of NPGS may be less than with trabeculectomy. As NPGS evolves, it may become equivalent to trabeculectomy. YAG laser gono-puncture is used to open a sclerostomy in much the same way as suture adjustment for initial intraocular pressure egress though a trabeculectomy. Mitomycin can avoid hypotony and manage wound healing with attendant decreases in complication rates and improved success. Remaining challenges include unpredictable wound healing responses between individuals and, despite 5FU and MMC, suboptimal tools for modulating the wound healing response.

8. Newer Approaches To Surgical Control Of Iop

Ab interno approaches, discussed in detail elsewhere in this publication, have been given a great deal of attention recently; they range from adult goniotomy to laser, surgical and stented opening of Schlemm’s canal, to micro-implants, to aqueous shunts both into the subconjunctival space made in gel with no plate and also into the supra-choroidal space. So far, the highly desirable approach of a minimally traumatic and possibly blebless alternative to trabeculectomy, with the same success rates and reliability, range from promising but unconfirmed at best to elusive at worst.

9. Conclusion

Recently trabeculectomy success and complication rates have improved significantly, not as a result of redesigning the procedure, but as a result of understanding mechanisms and meticulous attention to detail. We know that we can avoid hypotony and manage wound healing with attendant decreases in complication rates and improved success. Remaining challenges include unpredictable wound healing responses between individuals and, despite 5FU and MMC, suboptimal tools for modulating the wound healing response.

References

7. Ashraff NN, Wells AP. Transconjunctival suture adjustment for initial intraocular pressure

Fig 6. An ideal bleb, 3 years after W-flap trabeculectomy with 0.3mg/ml Mitomycin C applied intraoperatively for 3 minutes. Bleb is diffuse and lightly vascular, asymptomatic and IOP has ranged between 9 and 12 mmHg between 2 weeks and 3 years follow-up.