Minimally Invasive Glaucoma Surgery

2

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2.1 Introduction

Minimally invasive glaucoma surgery (MIGS) interventions are intended to deliver reduction of intraocular pressure (IOP) with a better safety profile than conventional glaucoma surgery. There has been active development of novel MIGS devices and implants, and these continue to evolve.

The role of MIGS is the subject of some uncertainty. Although it is generally accepted that MIGS interventions are not as effective as conventional glaucoma drainage surgery, their better safety profiles may make them suitable for patients who do not require very low intraocular pressures to control their glaucoma. To resolve such debates, high-quality randomized controlled trial data are required. When MIGS is being combined with cataract surgery, trials need to disentangle the effect of phacoemulsification from that of MIGS because phacoemulsification itself is known to lower intraocular pressure (Chen et al. 2015; Mansberger et al. 2012). Moreover, the role of MIGS may not be fully established by studies that focus solely on efficacy and safety. Rather, patients' quality of life and cost-effectiveness in comparison to conventional medical and surgical treatments need to be taken into account.

Presently, MIGS techniques are designed to increase the outflow of aqueous in one of several ways. External drainage devices such as the XEN Gel Implant permit drainage of aqueous into the subconjunctival space. Trabecular bypass techniques

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such as iStent, Trabectome, and Hydrus aim to improve access of aqueous from the anterior chamber to Schlemm's canal and thence to functional collector channels. Choroidal shunts such as CyPass are designed to increase drainage of aqueous into the suprachoroidal space. This chapter will focus on the devices mentioned above. The principles that emerge are likely to be applicable to other MIGS techniques, both current and future.

2.2 Trans-trabecular Meshwork Surgeries

2.2.1 iStent

2.2.1.1 Safety and Efficacy

Randomized controlled trials on the first-generation version of the iStent (Glaukos, Laguna Hills, USA) focused on its use with concomitant phacoemulsification (Craven et al. 2012; Fea 2010; Samuelson et al. 2011).

In an industry-funded open-label trial involving 240 patients with open-angle glaucoma controlled with topical medications, implantation of iStent in conjunction with cataract surgery was compared to cataract surgery alone (Samuelson et al. 2011). Seventy-two percent of eyes treated with iStent versus 50 % of control eyes achieved IOP of 21 mmHg or lower without use of medication at 12 months. Stent obstruction was observed in 4 % of subjects and 4 % required stent-related secondary surgery in the form of repositioning or replacement. At 15 months postoperatively in a separate double-masked randomized controlled trial (Fea 2010), 67 % of eyes with primary open-angle glaucoma having iStent implantation at the time of cataract surgery did not require topical medication versus 24 % of eyes who had cataract surgery alone. At 24 months, patients with stents appear to be more likely than those without to achieve IOP of 21 mmHg or lower without medication, though there was no overall difference in ocular hypotensive medication between the two groups (Craven et al. 2012).

A second generation of device, called the iStent inject, has been developed. This has a conical shape and is provided on an injector preloaded with two devices.

In a prospective unmasked study (Voskanyan et al. 2014), two iStent inject devices were implanted in each of 99 patients who had open-angle glaucoma that was uncontrolled on two or more topical medications. Two-thirds of subjects achieved an IOP of 18 mmHg or lower without medication at 12 months. The commonest postoperative complications were elevated IOP (10 %) and stent obstruction (3 %). Secondary surgery was performed in 3 % of patients for elevated IOP. The stent was not visible gonioscopically in 13 % of patients.

An industry-sponsored prospective unmasked randomized trial enrolling 192 subjects (Fea et al. 2014) found that implantation of two iStent inject devices was at least as effective in terms of IOP control as medical therapy with the fixed combination of latanoprost and timolol (Xalacom, Pfizer) in patients who had open-angle glaucoma that was not controlled with a single topical medication. At 12 months, 95 % of eyes treated with stents and 92 % of eyes treated with Xalacom achieved

IOP reduction of at least 20 %. 93% of eyes achieved IOP of less than or equal to 18 mmHg in the stent group versus 90 % of eyes in the Xalacom group. One of the 94 patients in the stent group experienced "decompensation" of IOP to 48 mmHg.

2.2.1.2 Procedure

IStent surgery can be performed under topical anesthesia and intracameral anesthesia is recommended. The trabecular stent can be implanted through the clear corneal incision used for phacoemulsification in cases of combined surgery or through a 1.5 mm incision when the stent is implanted as an isolated operation. A wider incision facilitates surgical maneuvers and is recommended during the learning curve, as this facilitates a better implantation angle especially when more than one implantation attempt is required. The injection of acetylcholine into the anterior chamber is advisable in phakic patients as this minimizes risk of lens damage. In the majority of cases, the corneal incision should be temporal so allowing the stent to be implanted in the nasal region of the trabecular meshwork, where the number of collecting channels is greatest.

The G1 Glaukos® trabecular micro-bypass (GT100) is made of titanium and covered with a layer of heparin (Duraflo® powder). It is L-shaped, measures 1 × 0.4 mm with an external diameter of 180 μm and is designed to fit within the lumen of the canal. The end of the canal portion is pointed to allow penetration through the meshwork during insertion. Three retention ridges spaced along the half-pipe portion allow for secure placement of the micro-bypass. The stent is preloaded in a 26-gauge insertion device with a release button. The stent is usually implanted through a temporal approach in a nasal position. If two implants are used, one is placed inferonasally and the other superonasally.

Before starting the iStent procedure, the head of the patient must be repositioned at 45° to the opposite side of the eye undergoing surgery, while tilting the microscope 30° for a good view of the trabecular meshwork on the nasal side of the angle using a Swan–Jacob gonioscope. After filling the anterior chamber with viscoelastic and checking the visualization of the angle, the inserter is introduced into the anterior chamber. The tip of the iStent should approach the trabecular meshwork at an angle of 15° to facilitate penetration. The point of the trabecular micro-bypass must go through the trabecular meshwork and softly advance through the Schlemm's canal. Once the trabecular meshwork covers all of the implant, it is released by pressing the applicator button. Only the proximal end of the stent should remain visible in the anterior chamber. The stent can be seated in its final position by gently tapping the side of the snorkel with the inserter tip. The stent should be placed parallel to the plane of the iris with the inner part covered by the meshwork and the lumen away from the iris. A small reflux of blood from the Schlemm's canal is common and reflects adequate positioning of the stent. Excessive resistance indicates a path that is too perpendicular to the trabeculum. If difficulty is encountered with insertion at the primary location, it is recommended finding another location inferiorly or superiorly or try inserting 0.5 clock hours inferiorly, and continue to move inferiorly as needed for subsequent attempts. At the end of the procedure, the anterior chamber is flushed to eliminate any refluxed blood. This ensures good visualization to confirm that the implant is well

located at sufficient depth. The viscoelastic agent can then be removed and the anterior chamber filled with saline solution.

In combined surgery the same corneal incision can be used. When phacoemulsification has been completed acetylcholine can be injected, then the anterior chamber should be refilled with a cohesive viscoelastic and then proceed as previously described.

For iStent inject (GTS400) the procedure is similar. This implant is conic and smaller than the G1 and also made of titanium. The Stents are preloaded in the customized injector system designed to deliver the stents automatically into the Schlemm's canal. To do so the inserter should be positioned in the desired position in contact with the angle but not pushing the tissue. The injector features a release button on the housing so by pressing this button the stent is released into the Schlemm's canal.

2.2.1.3 Patient Selection and Indications

The best indications for the trabecular stent are cases with primary open-angle, pigmentary, or pseudoexfoliative glaucoma. In secondary open-angle glaucoma, this type of surgery may be indicated as long as the Schlemm's canal and collecting channels are found to be undamaged. A good indication is corticosteroid-induced glaucoma (Morales-Fernandez et al. 2012). The ideal candidate for this type of surgery is a patient with early or moderate stage glaucoma, also patients with compliance issues, low tolerance to medical treatment or simply patients reluctant to undergo a chronic daily treatment. Another indication could be high-risk OHT or early/mid-disease patients with high IOP or suboptimal IOP control but in which a conventional filtering surgery may be too aggressive.

Patients with advanced glaucoma or those who require very low target pressures to obtain stabilization of their disease are not suitable candidates. Nevertheless, iStent could be considered in some cases when a filtering procedure is not recommended or refused by the patient.

Candidates for combined surgery using the iStent are patients with cataract and open-angle glaucoma with early/mild disease, even if they are well controlled on two or three medications.

2.2.1.4 Complications

The published evidence shows that, when performed with care iStent implantation is safe and the complication rate is very low. Visualization and correct selection of the area of implantation are key for a successful and effective implantation.

Selecting the Area of Implantation Preoperative evaluation of the areas with more collector channels is difficult. However, with the decompression of the anterior chamber the blood reflux can help identify the areas with more blood reflux. This is an indirect sign to determine the areas with more favorable anatomy and is especially helpful when the blood column is fragmented. If these areas are not accessible through the initial incision, the surgeon should consider making a new incision.

Intraoperative Complications

Prevention of Complications. Angle Visualization The most common mistake when performing the surgery the first few times is failure to position the microscope and/or the patient adequately in order to obtain an adequate view of the trabeculum. This step is crucial for all the angular surgeries described in this chapter, and the surgeon should take some time to assure the correct visualization and identification of the angular structures. This is more difficult when trabecular meshwork pigmentation is poor. So before introducing the inserter in the anterior chamber the surgeon should check the positions of the patient's head and the microscope together with the angle visualization. If visualization is not good enough, position should be adjusted. By following these steps, most of the complications related to the insertion procedure can be minimized.

Incorrect Implantation. iStent Position The implant should be completely inserted in the Schlemms's canal as described above, so the iStent final position should be parallel to the iris root with the ridges located on the back wall of Schlemm's canal. If it is too superficial or not completely introduced, it may fall out. Implantation angle is important and iStent position must be checked before it is released from the applicator. If the implant is not completely introduced the inserter tip can be used to tap the iStent into place. If snagged in the tissue or the iStent is outside the canal, or even if it was released before firmly anchored in place and is loose in the anterior chamber, it can be recovered with the inserter or retinal forceps. Then it is possible to reload the iStent onto the inserter and try again. In the series by Arriola-Villalobos et al. (2012), in 33.3 % of cases two attempts were required to implant the iStent correctly, and in 6 % of the cases a third attempt was needed.

Trabecular Meshwork Tear Once the implant is correctly positioned inside the Schlemm's canal, the surgeon must cease all movement and release the implant. If the movement continues once the iStent is inside the Schlemm's canal, the iStent tip will tear the trabecular meshwork. While this might be considered a minor complication, it will increase the trauma to the outer wall of the canal and even damage the collector channels. Moreover, with the loosening of the trabecular meshwork inner wall the tissue required to support the implant is lost. This consideration is also important if more than one attempt is needed. If during successive implantation attempts, an adequate implantation angle is not obtainable using the initial incision a new corneal incision could be performed if necessary.

Cyclodialysis Cleft. Suprachoroidal Implantation If the implantation technique is inadequate or, more frequently, visualization of the angle structures poor, then there is a risk of tearing the iris root with the iStent tip and inserting the iStent in the ciliary band or even introducing the implant in the supraciliary/suprachoroidal space. This risk is higher when several attempts are required and blood prevents adequate angle visualization. This increases the risk of bleeding that could also be

more severe than usual. If the tear is limited and bleeding is not important the surgery can usually be completed. If the tear is longer and associated with a visible cleft or the bleeding becomes severe, the procedure should be cancelled.

If the angle structures are incorrectly identified and the ciliary band misidentified as the pigmented meshwork or if for any reason visualization is not good enough, there is a risk of implanting the device in the ciliary band or even deeper into the supraciliary/suprachoidal space. Even if intracameral anesthesia is used if the iStent touches the ciliary tissue or the iris root, the patient will feel some pain, so this is an important sign to recognize. In this case, the recommendation is to check the angle structures and positioning to be sure that the area of implantation has been correctly identified.

Iridectomy/Iridodialysis/Lens Damage Incorrect manipulation of the inserter in the anterior chamber may cause iris damage and even iridodialysis. This may also happen if the angle structures are not correctly identified or if the iris is caught on the tip of the iStent and the surgeon keeps moving the inserter. Moreover, these cases usually involve severe bleeding and this can make surgery more difficult. In phakic patients the surgeon may damage the lens with the inserter and even tear the anterior capsule of lens. To avoid this complication the use of acetylcholine is recommended in phakic eyes. Also introduce the inserter slightly up until the pupil is crossed instead of aiming directly at the angle.

Bleeding Some bleeding is common and usually indicates the blood reflux through the iStent. But it could be important in case of the complications described above. Ensuring a correct visualization of the angle is crucial. Also surgery should be carried out with gentle movements. In case of bleeding that prevents visualization the surgeon should wait until the bleeding decreases or stops completely. Then proceed to clean the anterior chamber and start the surgical procedure again. If bleeding is severe or visualization is not good enough the surgeon may have to consider cancelling or postponing the procedure.

Early Postoperative Complications

Malposition. Free Implant As mentioned above, it is important to verify the final implant position before the end of the surgery. If visualization was not good enough, it is important to check for the implant position postoperatively. If only the proximal part of the snorkel is outside the canal, no further intervention is usually needed and this will not interfere with the efficacy of the procedure. However, if it is just puncturing the tissue, outside the canal or positioned unattached in the angle or on the iris, the surgeon has to consider repositioning the implant to avoid possible future complications (and for the implant to be functional). However, even if the stents are detached from the trabecular meshwork they usually will settle on the angle and will not move (Arriola-Villalobos et al. 2012), since they are highly biocompatible and well tolerated they may also be left in the anterior chamber. In this case, adequate follow-up is needed and if inflammation or other problems are detected they should be removed (Fig. 2.1).

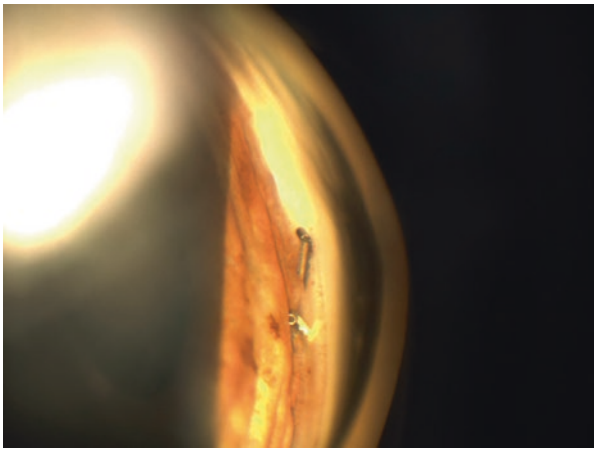

Fig. 2.1 Two malpositioned iStent implants

Superficial Implantation If the iStent is too superficial or incompletely inserted, there is a risk of detachment. In the case of superficial implantation, the iStent does not penetrate the trabecular meshwork completely and can be just engaged in the superficial layers of the trabecular meshwork. In this case there would be no communication between the anterior chamber and the Schlemm's canal so the implant would not be efficacious. Moreover, it could come loose over time. Repositioning should be considered, but as mentioned before, most of the time the implant will settle on the iris root and cause no problems.

Cyclodialysis Cleft/Suprachoroidal Implantation If IOP is very low during the first week a cyclodialysis cleft has to be ruled out. Also if the iStent is not seen in the angle and the iris root/ciliary tissue appear to have been damaged the area should be imaged with OCT or UBM to find the stent. Most of the cases can be managed conservatively as the cleft will close over time. If pressure remains too low or maculopathy develops, it may be necessary to suture the cleft. If the iStent is in the suprachoidal space but there is no inflammation removal is not necessary but close follow-up is required.

Late Postoperative Complications

A 5-year case series study by Arriola et al. showed no major complications regarding stent placement in the meshwork in a 19 patient study after 5 years (Arriola-Villalobos et al. 2012).

IStent obstruction If the Stent is rotated toward the iris, the anterior chamber is narrow and not very deep or the iris is floppy, the aqueous humor flow to the iStent could facilitate the blockage of the device with the iris. This situation can be resolved by lasering the iris in order to unblock the stent snorkel. This has been described for both implant types (Fernandez-Barrientos et al. 2010; Arriola-Villalobos et al. 2012; Arriola-Villalobos et al. 2013; Fea 2010; Samuelson et al. 2011).

Endothelial damage Arriola-Villalobos et al. (2013) analyzed prospectively the endothelial changes after combined surgery (Phaco + GTS400/Glaukos inject). At 2 years of follow-up the endothelial cell count decrease was 13.22 %, a reduction similar to that reported after phacoemulsification alone. However, if the implant was malpositioned and in contact with the corneal endothelium, it should be removed to avoid progressive endothelial damage.

2.2.2 Hydrus

2.2.2.1 Safety and Efficacy

The Hydrus Microstent (Ivantis, Irvine, USA) has been evaluated in an industry-funded randomized controlled trial in which 100 patients with open-angle glaucoma and cataract were randomized to receive either Hydrus implantation with concomitant phacoemulsification or phacoemulsification alone (Pfeiffer et al. 2015). Washed-out diurnal IOP was evaluated at baseline, 12 months and 24 months. IOP-lowering medications were allowed at other times if follow-up IOP exceeded 19 mmHg or there was evidence of progressive optic nerve damage or visual field loss. Mean diurnal IOP was calculated from measurements made using a two-person system (observer and reader), with at least two readings being made at each of three time points, spaced 4 h apart between 8 am and 4 pm.

At 24 months, the proportion of patients with 20 % reduction in washed-out diurnal IOP was 80 % in the treatment group compared to 46 % in the control group (p = 0.0008) assessed on an intention-to-treat basis. In a separate analysis that excluded patients who did not wash out medications for safety reasons, a 20 % reduction in washed-out diurnal IOP was achieved in 89 % of the treatment group versus 64 % of the control group (p = 0.0140). Washed-out mean diurnal IOP at 12 months was 16.6 mmHg in the treatment group versus 17.4 mmHg in the control group. At 24 months, washed-out mean diurnal IOP was 16.9 mmHg in the treatment group compared to 19.2 mmHg in the control group (p = 0.0093). The proportion of patients using no hypotensive medication at 24 months was 73 % in the treatment group compared to 38 % in the control group (p = 0.0008).

In terms of adverse events, peripheral anterior synechiae formation was noted in 19 % of treated patients versus 2 % of controls at 24 months (p = 0.0077). However, the presence of PAS was not thought to affect IOP or medication outcomes. Best-corrected visual acuity decreased by 2 lines in 2 patients in the treatment group, but resolved by 1 month. By month 3, best-corrected visual acuity was 20/40 or better in 96 % of subjects in the treatment group versus 90 % in the control group. Hypotony and stent migration were not found in the treatment group. Secondary glaucoma surgery was required in 2 % of the treatment group versus 4 % of the control group, and the difference was not statistically significant.

2.2.2.2 Patient Selection and Procedure

The Hydrus implant is an 8 mm crescent-shaped implantable device. The implant is very flexible, made from nitinol (a nickel/titanium alloy), and is preloaded onto a

handheld delivery system. The device not only bypasses the trabecular meshwork but scaffolds and dilates the Schlemm's canal. Due to its flexibility it easily sits in the Schlemm's canal and dilates it. As it scaffolds around one quarter of the canal it can provide access to multiple aqueous channels.

The surgery set-up is similar to the IStent surgical procedure described above, and a goniolens is needed to visualize the angle. Surgery can be performed under topical anesthesia or the technique of choice of the surgeon. Acetylcholine can be used in combined procedures; it can be implanted through the same corneal incision used for the phacoemulsification. For Hydrus alone procedures the implant can be inserted through a 1–1.5 mm corneal incision. If the target implantation site is not easily accessible/visible through the phaco incision, a secondary incision can be performed opposite to the desired implantation site.

After filling the anterior chamber with viscoelastic the delivery system is introduced in the anterior chamber and advanced until the inserter tip comes into contact with the trabecular meshwork. The trabecular meshwork is perforated using the beveled tip of the cannula. Once opened the device is implanted into the Schlemm's canal by rotating the advancement mechanism with one finger. The inserter terminal segment should be positioned parallel to the canal (flat angle) and with the bevel pointing slightly up. Otherwise, during the delivery the device could move down and out of the canal. Also if the angle between the angular surface and the inserter is excessive or the position is forced there could be problems with the delivery. The implant should advance with little or no resistance, if resistance is found the implant can be retracted and the position can be cautiously modified.

Once the implant is in place, the central core wire of the delivery system is retracted, allowing the complete detachment of the implant. The inlet segment (1–2 mm) should remain in the anterior chamber and the rest of the implant in the canal. On confirmation of the implant position, surgery is completed once the viscoelastic has been removed.

Conceptually the indications of the Hydrus implant are similar to the iStent. But, due to the dual action of the Hydrus implant, which bypasses the trabecular meshwork and expands the Schlemm's canal thus giving access to multiple collector channels, it is possible that the IOP reduction could be higher than after iStent implantation. However, this higher efficacy has still to be established.

2.2.2.3 Complications

Reported complication rate is very low, and when performed in combination with phacoemulsification the rate is similar to a cataract alone procedure (Pfeiffer et al. 2015).

Intraoperative Complications

To avoid intraoperative complications it is very important to visualize the tip of the inserter, be careful when crossing the pupil with the inserter in phakic eyes and avoid any movement during the "injection" of the Hydrus into the Schlemm's canal. The inserter has to be held steady and kept in contact with the angular tissue with

the bevel slightly up. Also, note that the rotation knob of the inserter can be adjusted so the position of the bevel is comfortable for the surgeon.

Bleeding When the procedure is performed correctly some bleeding is very common and also indicates the reflux of blood from the venous system. This bleeding will not affect the patient's recovery or the final outcome. The presence of blood in the Schlemm's canal can also help to detect the best areas for implantation. If when touching the trabecular meshwork the blood prevents the correct visualization of the tip or the progression of the device it may be necessary to retrieve the implant, wash out the blood and viscoelastic, wait for the bleeding to stop, and then proceed again with the implantation. If the device touches/ruptures the iris or is implanted in the ciliary body, the bleeding could be more severe and may take some time to stop. If visualization is not good and the surgeon is unsure of a possible damage to the iris or ciliary body, cancelling the procedure should be considered and then wait for the eye to recover.

Incomplete/incorrect insertion The implant should be inserted so that only the inlet is outside the canal. The insertion angle is extremely important and after opening the meshwork the bevel should be angled up so that the device finds its way into the Schlemm's canal. If the bevel is positioned to facilitate a "direct" insertion into the Schlemm's canal (parallel to iris root) this may result in the implant going downwards damaging the angular structures or even the ciliary body and the iris.

Occasionally if resistance is found and the implant does not progress smoothly during implantation, the device should not be released. Sometimes if the device is stuck, movement is transferred to the inserter, moving it in the opposite direction to the injection movement thus exposing the implant that should remain in the same position, as it is not being introduced further in the Schlemm's canal. It is very important to recognize this situation and retract the device into the inserter again. The first step is to check the insertion angle and if after a second attempt, the device is stuck in the same place a good option is to move to another area even if a new incision is needed. In any case, the implant should not be released until the surgeon is sure that it is correctly and completely implanted in the canal. Although the device can be pushed into the Schlemm's or pulled out with a manipulator or a blunt instrument, these maneuvers are only effective when correcting a minor positioning problem. If any of the windows of the implant are even partially seen in the anterior chamber, removal of the device should be considered. If trabecular damage is not significant, the surgeon can consider implanting a second one. Depending on the damaged area it may be necessary to target or find another implantation site (Fig. 2.2).

Adequate position of the implant should be checked after implantation. As some bleeding is very common sometimes it might be necessary to remove the viscoelastic and the blood. Although not always possible, it is recommended to check the whole implant from the distal end to inlet.

Tearing of the trabecular meshwork If the grip is not firm enough or there are movements during the insertion, the device may rupture the trabecular meshwork

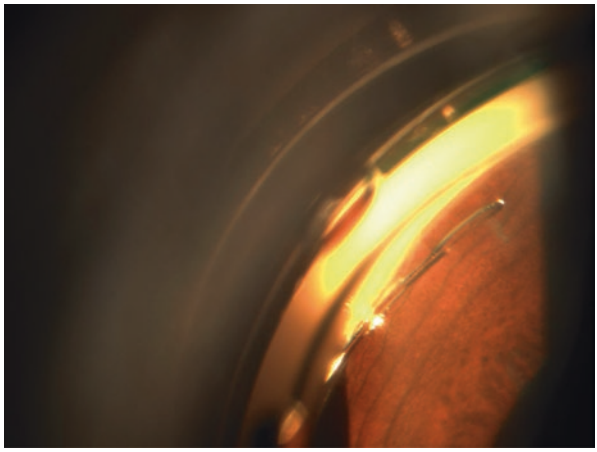

Fig. 2.2 Incomplete/incorrect placement of Hydrus implant, with most of the implant in the anterior chamber

exposing the external wall of the Schlemm's canal. If there is not much bleeding a second implantation attempt can be performed.

Supraciliary/suprachoroidal implantation As in the case of the iStent, if the angle structures are not correctly identified there is an increased risk of damaging the ocular structures. The implantation of a device like this in the ciliary body is painful and involves a high risk of severe bleeding. It is important to recognize this situation as soon as the implant starts to dissect the ciliary body tissue and retract the device into the inserter. If the implant was completely released it should be removed using retina forceps. Depending on the ocular situation and the possible damage to the ciliary body and iris a new device could be implanted.

Iris or lens damage Rupture of the iris During the surgical procedure the surgeon should visualize the tip of the inserter and be careful to avoid touching the lens (in phakic eyes), cornea or the iris. Extra movements or surgical maneuvers increase the risk of damaging the ocular structures. If these maneuvers are needed for any reason, correct visualization is key to prevent further damage. If the device has to be removed, it is important to proceed slowly and control both ends of the device, also forceps should be used with care to avoid capturing the iris. If visualization of the device and/or angular structures is not good enough (blood or mixture of viscoelastic and blood), it can be improved by waiting for the bleeding to stop and then washing out the blood and viscoelastic.

Early Postoperative Complications

Hyphema Some bleeding is common and is not usually a problem. Pfeiffer et al. did not report any severe complications related to bleeding.

Malposition If for any reason, the position of the device could not be checked intraoperatively it should be as soon as possible. If the device is dislocated, or par-

tially out of the Schlemm's canal it is probably better to remove it. Depending on the ocular conditions and IOP a new device can be implanted in the same surgery.

Late Postoperative Complications

There is little published evidence on the long-term complications; however, this device seems to be very safe.

Corneal Endothelial Cell damage If the surgery is uneventful and the device position correct, the possibility of significant endothelial damage is very low.

Peripheral Anterior Synechiae (PAS) and Inlet Obstruction Pfeiffer et al. reported that 18.8 % of patients may develop anterior synechiae after 2 years. These PAS were located at or near the inlet segment of the implant and consisted in focal iris tissue adhesion to the device or chamber angle usually of less than 1 clock hour. However, PAS did not have a negative impact on the success rate. In this series, no cases of complete blockage of the inlet by the iris were found.

2.2.3 Trabectome

The Trabectome (NeoMedix, Tustin, USA) is designed to electrosurgically ablate the trabecular meshwork and inner wall of Schlemm's canal. This enables aqueous to bypass the juxtacanalicular trabecular meshwork and inner wall of Schlemm's canal, which is thought to be the main site of resistance in open-angle glaucoma (Overby et al. 2009).

2.2.3.1 Safety and Efficacy

Results from the use of the Trabectome were first reported by Minckler et al. (2005). Company data for 4659 treatments show that it safely reduces the need for drops for several years and reduces IOP by 26 % (Mosaed 2014). A retrospective study suggested that Trabectome is less effective than trabeculectomy (Jea et al. 2012a). To date, there are no published randomized controlled trial data.

Rates of successful IOP control decline with time, particularly in the first year postoperatively (Ahuja et al. 2013; Minckler et al. 2008; Mosaed 2014). Success rates reported in case series vary from 64 % to over 80 % at 12 months postoperatively, and from 62 % to more than 75 % at 24 months. Interpretation of results is hampered by the absence of clear criteria for the use of IOP-lowering medications in the postoperative period and by loss to follow-up of a significant proportion of patients.

Trabectome treatment may be more effective when combined with cataract surgery (Ahuja et al. 2013; Francis 2010; Jordan et al. 2013). Phacoemulsification itself has been shown to lower IOP (Chen et al. 2015; Mansberger et al. 2012), and the relative contributions of Trabectome and phacoemulsification are not yet defined by randomized trials.

Recently, it has been reported that Trabectome treatment may be effective in relatively narrow angles (Bussel et al. 2015a) and also in patients after failed trabeculectomy (Bussel et al. 2015b). Trabectome does not violate the integrity of the conjunctiva, and one cohort study suggests that the success of subsequent trabeculectomy is not compromised (Jea et al. 2012b).

In a single-center case series (Ahuja et al. 2013), the commonest complications were hyphema (46 %), microhyphema (27 %), and IOP spike (22 %). Other complications that have been reported include reduction in visual acuity >2 lines (0–5 %) (Ahuja et al. 2013; Minckler et al. 2008), delayed onset hyphema (5 %) (Ahuja et al. 2012), and aqueous misdirection (0.4 %) (Ahuja et al. 2013). In the manufacturer's case series (Mosaed 2014), hypotony (IOP < 5 mmHg) at day 1 occurred in 1 % but sustained hypotony at 1 month was rare (0.2 %). Secondary surgery was required in 7 % of cases.

2.2.3.2 Patient Selection and Procedure

Trabectome surgery may be performed under local anesthesia. The Trabectome probe consists of an irrigating-aspirating handpiece which is introduced into the anterior chamber through a 1.6 mm temporal incision in clear cornea. Under gonioscopic guidance, the end of the probe is advanced across the anterior chamber towards the nasal trabecular meshwork. The footplate of the probe is inserted through the trabecular meshwork into the lumen of the nasal part of Schlemm's canal. The footplate is then advanced along the lumen of Schlemm's canal while electrosurgical power is applied to ablate the inner wall of Schlemm's canal and the overlying trabecular meshwork.

Phacoemulsification can be performed after the Trabectome surgery through the same corneal incision, following enlargement, or via a separately placed incision. Some surgeons argue that phacoemulsification should be performed prior to Trabectome surgery, not afterwards. This way, the surgical view is less likely to be compromised by blood reflux following Trabectome surgery and the drainage angle may be more open and accessible. On the other hand, any reduction in corneal clarity at the end of phacoemulsification is likely to produce a poor gonioscopic view for Trabectome surgery.

Patients need to have surgically visible and accessible nasal drainage angles. To permit a gonioscopic view of the drainage angle, the patient must be able to rotate his or her head away from the surgeon. Inability to do this is a contraindication for surgery. Similarly, corneal opacities are a relative contraindication to surgery. Angles that appear to be relatively narrow on gonioscopy in the clinic may nonetheless be accessible surgically because the pressure of irrigation from the handpiece causes the lens-iris diaphragm to move posteriorly. However, angles that have peripheral anterior synechiae are unlikely to be amenable to treatment, because the iris tissue may not ablate easily and is liable to bleed heavily. The pupil is usually dilated if combined Trabectome-phacoemulsification is planned. Otherwise, preoperative application of pilocarpine eye drops may assist with opening the drainage angle. Through miosis, folds of iris are moved away from the ablation site and the crystalline lens is

relatively protected from trauma. If, despite these precautions, iris is being aspirated into the handpiece, the surgeon should reduce the aspiration flow rate.

It is advisable to deflate the anterior chamber prior to introduction of the Trabectome probe. This allows blood to reflux into Schlemm's canal from the collector channels, thereby permitting easier identification of the canal, particularly in unpigmented angles. Although the blood may drain back into the collector channels following pressurization of the eye by the irrigating Trabectome probe, the operator will have had an opportunity to identify the location of the Schlemm's canal.

In order to minimize the risk of trauma to the crystalline lens, cornea or iris, the surgeon should hold the handpiece in such a way that the tip can be comfortably manipulated in the fingers of one hand. Electrosurgical power should never be activated when the tip of the probe is dry as this may cause damage to the handpiece.

Rotating the goniolens with one hand and the eye using the handpiece will enable a greater length of the nasal trabecular meshwork to be visualized. Thus, the potentially treatable area can be maximized.

Reflux of blood from the collector channels into the anterior chamber following removal of the irrigating handpiece from the eye is to be expected. Indeed, such reflux is regarded as a sign of correct ablation, and helps to identify the extent of ablation. The surgeon should quickly repressurize the eye to tamponade the reflux. Viscoelastic may be used as the tamponading agent if the next step is phacoemulsification. The viscoelastic is injected so as to displace blood, maintaining the red reflex for the capsulorhexis to be performed.

Following surgery, IOP-lowering drops should be continued. They may be cautiously withdrawn some weeks or months postoperatively if surgery has been performed as a drop-sparing procedure for patients who are allergic to or intolerant of one or more eye drops. Patients should be prescribed a course of topical steroids, antibiotics, and pilocarpine. The pilocarpine drops are intended to prevent the formation of peripheral anterior synechiae, which may occlude the opening in Schlemm's canal.

Blood is commonly noted in the angle or on the iris at day 1 postoperatively. However, it has usually cleared by week 1 (Minckler et al. 2005). Patients should be counseled preoperatively that their vision may be blurred in the first week owing to the reflux of blood into the anterior chamber.

2.2.3.3 Complications

Intraoperative Complications

Poor Visibility

Excellent visibility of the area to be treated is key to the success of the procedure. The surgeon must use adequately high microscope magnification when introducing the footplate into Schlemm's canal and when ablating tissue. Bubbles of air between the goniolens and the cornea are to be avoided through the use of sufficient coupling

medium. However, care should be taken to avoid contaminating the top surface of the goniolens with the coupling medium, as this will reduce visibility. Equally, the manufacturer's instructions for setting up the equipment need to be followed meticulously to avoid introducing air into the anterior chamber via the handpiece during the procedure. Air bubbles in the anterior chamber will block the surgeon's view. As the handpiece's own aspiration function is insufficient to remove intracameral air, the handpiece needs to be removed in order for the air to be exchanged first with viscoelastic and then with balanced salt solution. Surgeons are advised to avoid using the Trabectome probe with viscoelastic in the anterior chamber as this may adversely affect heat dissipation.

Insertion of Footplate

To minimize any difficulty introducing the footplate into the lumen of Schlemm's canal, the surgeon should insert the footplate through the trabecular meshwork at a point that is not directly opposite the corneal incision. In this way, the tip of the footplate is directed obliquely (and not parallel to) the plane of the trabecular meshwork. It is also important to ensure that the tip of the footplate is not inadvertently bent or blunted by contact with hard surfaces. Particular care should be taken to avoid damaging the footplate during the removal of the plastic cap from the end of the handpiece.

Incomplete Ablation

Incomplete ablation occurs if the footplate of the probe is not introduced properly into the lumen of Schlemm's canal. Clean ablation of tissue is thought to be important to prevent resealing and closure of Schlemm's canal. Before starting ablation, the surgeon should verify correct placement of the footplate by gently tenting up the tissue with the probe. During ablation, the surgeon must ensure that sufficient electrosurgical power is applied. Application of insufficient power may result in tearing of the tissues and clogging of the tip with tissue. On the other hand, application of excessive power risks thermal damage to Schlemm's canal and the orifices of the collector channels. Visible charring of tissues is an indication for treatment power to be reduced. Following ablation, the deroofed Schlemm's canal should be visible as a shiny white gutter. It can be helpful to use the blunt heel of the footplate as a manipulator to verify that the canal has been successfully deroofed. Parts of the canal that have not been deroofed successfully may be retreated, with care to avoid thermal damage.

False Passage

False passage with damage to Schlemm's canal can be avoided by verifying correct placement of the footplate before starting ablation. Because the tissue to be ablated is quite thin, it should be easily tented up with the probe. Also, there should be minimal resistance to the advancement of the probe. Resistance may signify that the tip of the probe is misdirected and has engaged the outer wall of Schlemm's canal. The surgeon should reorientate the probe.

Bleeding

During ablation, the pressure of irrigation prevents blood reflux from the collector channels. Therefore, overt bleeding suggests that a vessel containing blood at arterial pressure has been damaged. This may be due to an unintentionally posterior ablation at the iris root, or due to unrecognized vascular tissue overlying the trabecular meshwork. Regardless of the cause of the bleeding, the surgeon needs to assess quickly whether blood is going to prevent proper visualization of the drainage angle. If so, the Trabectome procedure cannot be completed. The Trabectome probe should be withdrawn and the bleeding tamponaded immediately with viscoelastic injected into the anterior chamber. Once done, the surgeon may cautiously evaluate whether clotting has occurred by exchanging the viscoelastic for balanced salt solution. If so, there is the option to proceed with phacoemulsification (if this was planned). Otherwise, the eye should be closed and managed for hyphema.

Cyclodialysis Cleft

A cyclodialysis cleft may be created if ablation is performed too posteriorly, at the root of the iris. This may be heralded by bleeding, or by the appearance of the iris falling posteriorly. Unless there is bleeding, this complication may be managed conservatively, at least initially. A low intraocular pressure is to be expected at day 1 and in the first few weeks postoperatively. Indeed, an unexpectedly low intraocular pressure found postoperatively is reason to suspect that a cyclodialysis cleft has been created. Some surgeons withhold pilocarpine postoperatively to encourage the cleft to heal. Small clefts heal spontaneously. Large ones may require formal repair. Anterior segment imaging techniques such as optical coherence tomography may allow the size of clefts to be quantified.

Descemet's Membrane Detachment

Detachment of Descemet's membrane may occur if the ablation is performed too anteriorly or if the trabecular meshwork tissues are being torn rather than ablated. The measures to ensure correct placement of the ablation and to avoid tearing tissue have been outlined previously. If the detachment is small and confined to the peripheral cornea, it is unlikely that visually significant corneal edema will develop.

Trauma to Lens, Iris or Cornea

In order to minimize the risk of trauma to the crystalline lens, iris or cornea, the surgeon should hold the handpiece in such a way that the tip can be comfortably manipulated in the fingers of one hand. The probe needs to be passed across the anterior chamber with due care, ensuring that the handpiece irrigation is switched on continuously. The surgeon needs to be prepared to perform lens extraction should the capsule of the crystalline lens be inadvertently punctured during Trabectome surgery.

Early Postoperative Complications

Bleeding

The presence of a microhyphema or clotted blood in the angle or on the iris is to be expected immediately after surgery. Early postoperative hyphema is reported in 46 % of cases (Ahuja et al. 2013), but unless it is large should probably not be considered a complication of surgery.

IOP Spike

A spike in intraocular pressure of greater than 10 mmHg has been reported in 6–22 % of cases with a median onset of 34 days (Ahuja et al. 2013; Minckler et al. 2008). To avoid this, patients' usual IOP-lowering eye drops should not be withdrawn in the early postoperative period.

Hypotony

Early postoperative hypotony should cause the surgeon to suspect that a cyclodialysis cleft has been created. This may be verified gonioscopically or by use of anterior segment imaging such as optical coherence tomography. Some surgeons withhold pilocarpine postoperatively to encourage the cleft to heal. Small clefts heal spontaneously, whereas large ones may require formal repair.

Late Postoperative Complications

Bleeding

Spontaneous late bleeding, occurring more than 2 months postoperatively and sometimes recurrent, has been reported by different authors (Ahuja et al. 2012; Kassam et al. 2014). In one case series (Ahuja et al. 2012), bleeding occurred in 5 % (12 of 262 cases). All patients had noted a transient decrease in vision, mostly on waking. Only one case required secondary surgical intervention in the form of trabeculectomy for refractory high IOP. The remainder were managed conservatively with steroid eye drops, with resolution of the hyphema within 2 weeks. Laser coagulation of collector channel orifices has also been employed (Kassam et al. 2014). Some authors have advocated discontinuation of anticoagulants prior to surgery (Minckler et al. 2005). Bleeding during and after subsequent trabeculectomy has also been reported (Kassam et al. 2014; Knape and Smith 2010).

Failure of IOP Control

Secondary surgery is reported to be required in 7 % of cases (Mosaed 2014), with the commonest secondary procedures being trabeculectomy (4 %) and aqueous shunt insertion (2 %). Trabectome treatment does not violate the integrity of the conjunctiva, and one cohort study suggested that failed Trabectome surgery does not compromise the likelihood of success of subsequent trabeculectomy (Jea et al. 2012b).

Practical Tip: Trans-trabecular Meshwork Surgeries

- Anterior vitrectomy should be performed if there is any chance of vitreous loss into the AC from previous surgery. Positioning of head of patient and tilting the microscope are essential for good visualization.
- Blood reflux into the anterior chamber is NOT a complication, it simply signals a direct communication between the anterior chamber and collectors had been established.
- Membrane formation covering the inlets of iStent & Hydrus as well as exposed collector channels after Trabectome surgery may benefit from YAG laser disruption.

2.3 Suprachoroidal Implants

2.3.1 CyPass

2.3.1.1 Safety and Efficacy

The CyPass Micro-Stent (Alcon Inc., Fort Worth, Texas, USA) is implanted into the supraciliary space to provide a permanent drainage conduit for aqueous along the suprachoroidal pathway (Saheb et al. 2014) (Fig. 2.3).

In a multicenter single-arm interventional study, patients with open-angle glaucoma and uncontrolled medicated intraocular pressure >21 mmHg at baseline were enrolled to receive CyPass Micro-Stent implantation alone (Garcia-Feijoo et al. 2015). Of 65 eyes treated, results for 55 were available at 12 months owing to loss to follow-up and early termination. Mean IOP decreased by 35 % from 24.5 mmHg at baseline to 16.4 mmHg at 12 months. Mean number of medications also reduced from 2.2 at baseline to 1.4 at 12 months. Of 64 eyes that were originally indicated for conventional glaucoma surgery, 83 % did not require secondary surgery at 1 year. The commonest adverse events were cataract progression (12 %), IOP increases > 30 mmHg beyond 1 month (11 %), and transient hyphema (6 %).

In a separate study examining the implantation of CyPass combined with phacoemulsification (Hoeh et al. 2016), patients who had open-angle glaucoma with IOP of 21 mmHg or higher despite topical medication or prior surgical glaucoma treatment (cohort 1) were analyzed separately from those who had IOP <21 mmHg with medical treatment (cohort 2). For cohort 1, there was a reduction in mean IOP from 25.9 mmHg at baseline to 16.2 mmHg at 3 months. The IOP-lowering effect was sustained at 12 months. The mean number of glaucoma medications was also reduced from 2.1 at baseline to 1.1 at 12 months. Although no IOP-lowering effect was found for cohort 2, there was a 75 % reduction in mean number of medications prescribed at 12 months, with 65 % of the patients still in the study at 12 months being medication-free. Interpretation of these results is hampered by the lack of

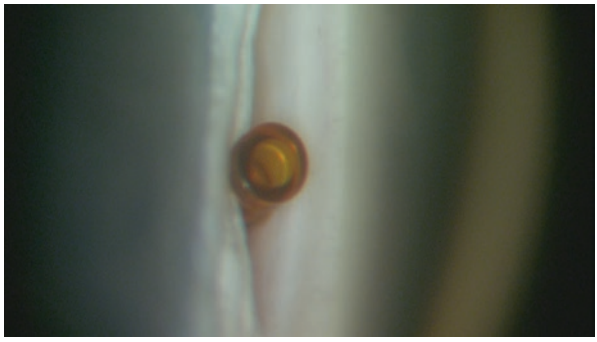

Fig. 2.3 A CyPass in its correct position in the anterior chamber

prespecified criteria for the management of IOP-lowering medications, the absence of a control group receiving phacoemulsification alone and by loss to follow-up. 25 of 65 patients in cohort 1 and 31 of 102 patients in cohort 2 were not followed up at 12 months. In terms of adverse events, 14 % of treated eyes had transient hypotony (IOP < 6 mmHg) which resolved by 1 month without visual sequelae. Elevated IOP > 30 mmHg and more than 9 mmHg above baseline occurred in 3 % of patients overall. Other complications included partial or complete obstruction of the implant (5 %) and endothelial touch (1 %). Secondary surgery, including stent repositioning, explantation or penetrating glaucoma surgery was required in 6 %.

2.3.1.2 Patient Selection and Procedure

The CyPass is a 6.35 mm long fenestrated stent made of polyimide. The device has three retention rings in its proximal end. These in combination with the fenestrations ensure the stability of the implant in the supraciliary space. It is threaded on a curved guide wire to facilitate its implantation into the suprachoroidal space following the scleral curvature. The guide wire tip is blunt to minimize the risk of tissue damage. The first step in the surgical procedure is to thread the CyPass on the retractable guide wire of the inserter.

The procedure can be performed under topical anesthesia and the setup (positioning of the patient's head and microscope and use of goniolens) is the same as in the angular surgeries described above. The implantation is usually performed using a 1.5 mm clear corneal incision opposite to the place where implantation is planned. Smaller incisions can be considered, as no lateral movements are required. When performed in combination with phacoemulsification the same incision can be used. The injection of acetylcholine is recommended then filling the anterior chamber with a viscoelastic agent to open the angle and improve access to the iris insertion. The CyPass inserter is then introduced in the anterior chamber and directed to the iris root aiming at the iris insertion just below the ciliary band. The suprachoidal space is virtual and the small rupture of the iris root and the creation of the dissection plane between the ciliary body and the sclera is easily done with the blunt tip of the guide wire. If resistance is found it is most likely that the angle of insertion is too flat (too parallel to the iris plane) so the tip hits the sclera. If this occurs the insertion angle should be increased to facilitate the access to the

suprachoroidal space. If the insertion angle is correct, very little resistance to the inserter advance is to be expected. The CyPass should be introduced until only two retention rings are seen, then the guide wire is retracted leaving the device in place and the inserter can be withdrawn. Some bleeding is common and usually does not interfere with the surgical procedure. Surgery is completed with the removal of the viscoelastic agent and the blood. At the end of surgery it is recommended to check the position of the CyPass: Ideally just two of the retention rings should be visualized in the anterior chamber.

The advantage of a procedure that uses the suprachoroidal drainage is that the efficacy is not limited by the condition of the posttrabecular outflow system. But an accessible and sufficiently open-angle is required to prevent the CyPass touching the cornea or come too close to the corneal endothelium. The indications of this procedure are potentially wider than trabecular/Schlemm's Canal surgeries and include secondary open-angle glaucoma. Garcia-Feijoo et al. reported that after 1 year 25 % of the patients achieved an IOP < 13 mm Hg. If this data is confirmed, and given the safety profile of the procedure, CyPass implantation could be considered in more advanced glaucoma cases or after filtration surgery failures. However, the success rate of these possible indications is still to be established.

2.3.1.3 Complications

Intraoperative Complications

In the majority of cases, intraoperative complications arise owing to an inappropriate surgical procedure. So it is most important that an adequate visualization of the angle is obtained and the implant is inserted at the correct angle.

Inadequate position of the CyPass If the CyPass is too deep or too superficial, it may cause problems. The recommendation is to check the position of the implant once surgery is complete. If it is too deep the anterior opening could be blocked by the iris/ciliary body tissue, the created opening may close leading to a surgical failure. On the other hand if the implant is too anterior it may come into contact with the cornea damaging the corneal endothelium. If malposition is evidenced during surgery the device can be repositioned using retinal forceps.

Bleeding This is one of the most frequent complications arising during surgery. Some slight bleeding can be expected given that a small perforation has to be made in the iris. In order to prevent excessive bleeding the implant should be inserted while avoiding lateral movements. Also if patent iris vessels are seen close to the angle or running parallel to the iris root, this area should be avoided.

Cyclodialysis. Disinsertion of the Iris For the CyPass insertion no lateral movements are required and should be avoided. Lateral movements during insertion not only increase the chances of significant bleeding but also could cause sectorial disinsertion of the iris. In this case a wide area of direct communication between the

anterior chamber and the suprachoroid space will be created thus increasing the chances of hypotony or choroidal detachment.

Ciliary Body Damage Although this is theoretically possible, the inserter curvature has been designed to follow the scleral curvature and also the point of the guide wire is blunt making it very difficult to penetrate the ciliary body tissue. In the published papers no relevant damage to the ciliary body has been reported.

Early Postoperative Complications

Early complications are mostly related to the surgical procedure. After uneventful surgery complications are infrequent but can include hyphema, iris damage or disinsertion, and endothelial damage. Choroid effusion or detachment is a potential risk in any anti-glaucoma surgical technique and more so in surgery that involves the suprachoroid space as an evacuation route for the aqueous humor.

Hyphema As mentioned above in a multicenter single-arm interventional study, around 7 % of the patients had a transient hyphema that resolved in the first month. Excessive manipulation of the iris root/supraciliary space and specifically lateral movements could increase the risk of severe bleeding.

Suprachoidal Hemorrahage This is a risk in any anti-glaucoma surgery and it could be speculated that might be more likely in suprachoridal surgeries. However, in the published series this complication has not reported. So it seems that the risk of having this complication is very low.

IOP spikes In the mentioned follow-up study by Garcia-Feijoo et al., the authors defined as transient IOP elevation after surgery an IOP >30 mm Hg during a study visit but that resolved either on its own or with reintroduction of glaucoma medications on a subsequent visit. These transient spikes were observed in 10.8 % of the cases. It can be hypothesized that the spikes could be related to the scar tissue covering the device. Most of the cases resolved with glaucoma medication.

Hypotony This is a possible complication of any suprachoidal surgery, although no cases of hypotony have been reported.

Late Postoperative Complications

We lack published evidence on long-term complications, as the follow-up of the published series is short.

CyPass Displacement The combination of the fenestrations, the retention rings and the scarring response around the device result in the stabilization of the device in position. However, migration of the device is theoretically possible. An anterior migration could result in a device touching the cornea or coming too close to the endothelium. On the other hand, posterior migration could introduce the CyPass deep in the suprachoroidal space facilitating the obstruction of the CyPass by the

iris. Anterior migration could be more likely and intrasurgical incorrect positioning and/or excessive scarring/scarring response around the device might play a role in the displacement of the CyPass.

Corneal Endothelial Damage An anterior position of the anterior tip of the CyPass can result in endothelial damage. There are no data on the long-term repercussion on the corneal endothelium of well positioned devices.

IOP Spikes As mentioned before the failure of the surgery can be associated with an IOP spike. Garcia-Feijoo et al. reported that 16.9 % of the patients needed additional surgery to control the IOP (second CyPass or trabeculectomy).

Obstruction of the CyPass/Synechia The iris can partially or totally obstruct the anterior opening of the device. In these cases Nd-YAG laser can be used to clear the synechia. This complication is more likely if the device was inserted too deep. If this is the case surgical repositioning of the CyPass could be necessary.

Practical Tip: Suprachoroidal Implants
Positioning of head of patient and tilting the microscope are essential for good visualization.

Membrane formation covering the inlets of Suprachoroidal implant may occur.

2.4 Subconjunctival Implants

2.4.1 XEN Gel Implant

2.4.1.1 Safety and Efficacy

The Xen Gel Implant (Allergan, Dublin, Ireland) is a 6 mm long porcine collagen implant cross-linked to prevent degradation. It is designed to be injected *ab interno* from the anterior chamber to drain into the subconjunctival or subtenon's space. No safety or efficacy data have yet been published in peer-reviewed journals. Two industry-sponsored studies are ongoing (Clinicaltrials.gov NCT02036541 and NCT02006693), but neither is a randomized controlled trial.

A recent conference poster (Rekas et al. 2014) reported outcomes from 107 subjects. The mean preoperative, best medicated IOP was 21.8 mmHg. Mean postoperative IOPs were 15.9 at 12 months, 15.1 at 18 months, and 14.2 at 24 months. Anti-glaucomatous medications were reduced from the preoperative median of 2.8 (patients not washed out presurgery) by 64 % at 12 and 18 months, and by 57 % at 24 months. 6 % had secondary glaucoma surgery by 24 months, but no major adverse events were reported.

In another conference report (Reitsamer 2014), 74 patients had preoperative Mitomycin C (MMC) injection followed by XEN implantation, with or without concomitant cataract surgery. The mean preoperative, best medicated IOP was 22.3 mmHg (patients not washed out presurgery). Mean postoperative IOPs were 15.5 mmHg at 3 months, 14.9 mmHg at 6 months, and 14.7 mmHg at 9 months, though not all patients had reached 9 months of follow-up. Mean number of preoperative anti-glaucoma medications was 3.2, and was reduced to 0.5 at 3 months, 1.0 at 6 months, and 0.8 at 9 months. No secondary glaucoma surgery or major adverse events were reported by 9 months.

2.4.1.2 Patient Selection and Procedure

The Xen Gel Implant, because of its apparently greater pressure-lowering efficacy, is an alternative to trabeculectomy as a standalone procedure in a proportion of patients. As it is seems less likely to achieve low long-term IOP levels than trabeculectomy, but does have greater IOP-lowering efficacy than TM procedures, the Xen seems most appropriate for those with significant IOP elevation who do not have very advanced glaucoma and hence do not need very low target IOPs.

On the other hand, when used in combination with phaco, the converse argument might be that the Xen, because of its greater potential pressure-lowering efficacy, might be more appropriate than TM procedures.

Xen implantation differs from the trabecular meshwork procedures in that, by consensus view, Mitomycin C (MMC) injection is required just before implantation to reduce the subconjunctival healing response. A common contemporary technique is to inject 0.1 ml of 0.2 mg/ml MMC to the superior subconjunctival space away from the limbus, just before implantation. The MMC bleb can then be massaged gently to the superonasal subconjunctival space. Injecting away from the limbus and superiorly, rather than superonasally is intended to avoid creating a very avascular bleb close to the limbus in the inter-palpebral conjunctiva.

The superonasal conjunctiva is then dried with a sponge and ink marks made 3 mm from the limbus to indicate the target zone for the implantation.

A corneal paracentesis is made inferotemporally 1 mm into clear cornea from the limbus. A second paracentesis is made superotemporally for a second instrument such as a Vera Hook or iris repositor. If an iris repositor is to be used as the second instrument, a helpful technique is to make a further paracentesis diagonally opposite to allow the iris repositor to transfix the globe. There are a few advantages to this as follows:

- While the Vera hook can be used to plug the side port tightly, this is not the case with the iris repositor or other types of second instrument that are loose and can move around. In general, while the surgeon is concentrating on the superior conjunctival area when injecting the Xen, a second instrument such as an iris repositor that is mobile will not provide stable fixation, and worse still maybe touch and traumatize intraocular structures such as lens and iris.

- Use of the iris repositor to transfix the globe facilitates rotation of the globe and implantation closer to the superior limbus and less nasal, reducing the likelihood of dysesthesia from a bleb below the upper lid.
- Use of the iris repositor in the above manner, protects the lens in phakic eyes from trauma from the injector if the patient moves suddenly during implantation.

After making the initial incisions, the anterior chamber is inflated using a viscoelastic such as Healon GV.

The injector is then briefly checked by advancing the Xen slightly to ensure the device is correctly loaded and then wet with a small amount of balanced salt solution. The Xen is then gently repositioned back to its original position and the injector introduced into the anterior chamber. A 20 gauge MVR blade incision just fits the Xen injector snugly so it may be necessary to wiggle from side to side to get the shoulder of the injector past the internal opening into the anterior chamber.

The injector is directed into the angle in a line aiming to traverse the angle and sclera in a line that would result in it exiting sclera just at the 3 mm mark from the limbus.

If a goniolens is to be used, it should be placed on the cornea at this juncture. It is impossible to perform gonioscopy and inject at the same time because of the need for counter-traction with a second instrument. The goniolens can be used to position the injector at the correct position in the angle if the position can be maintained while the lens is removed and the second instrument inserted. An indirect goniolens such as the Ahmed 1.5× Surgical Goniolens (Ocular Instruments, Bellevue, Washington, USA) is most suitable for this.

After checking the position of the injector tip in the angle on gonioscopy, the goniolens is removed and the second instrument positioned via the side port. Gentle pressure is then applied to advance the injector through sclera, taking care not to advance the slider or inject. As the injector advances, it is important to attempt to direct it so that it emerges from sclera at the level of the 3 mm marks. If it emerges anterior to the marks, the result will be a more corneal injection. Behind the marks will result in an implantation closer to iris, potentially traversing suprachoroidal space before traversing sclera. If the implant is too close to iris, there is a greater chance of iris occlusion. If the injector appears to be exiting sclera too far forward or back, then it is a simple matter to withdraw into the anterior chamber, reposition and re-advance.

Once the injector tip has exited sclera in the correct plane and is visible subconjunctivally, it is worth advancing slightly further to ensure that the injected implant does not get stuck in episclera. The injector is then rotated through 90 degrees either clockwise or anticlockwise. At this point the slider on the injector is slowly advanced to inject the implant. It is important to maintain forward pressure with the injector at this point to prevent the injector sliding back into the anterior chamber prematurely. Once the slider has moved the full length of its travel, the needle tip will have retracted and the implant should be visible in the subconjunctival or subtenon's space.

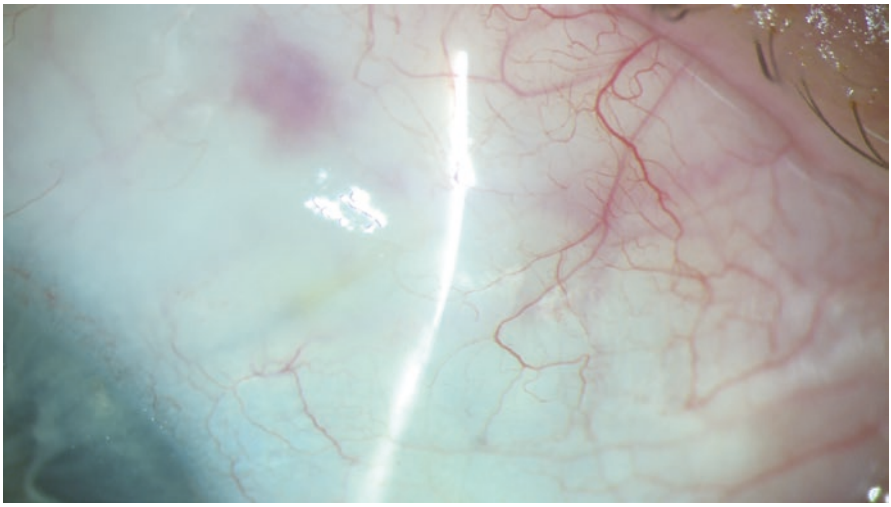

Fig. 2.4 A diffuse subconjunctival bleb surrounding a Xen implant

At this point the viscoelastic should be removed from the anterior chamber using either a manual or automatic irrigation system. One should then be able to see a bleb developing over the device in the subconjunctival space.

If no bleb is visible, one should firstly look at the device. If the device is curled up in a *pigtail* appearance, it may be embedded in Tenon's capsule and the external aperture obstructed by Tenon's. This can be remedied by taking a pair of tying forceps and gently stroking the implant to straighten it. Often a bleb will start to appear at that point. If the tube is deemed to be too long, it can be fed back towards the anterior chamber using the forceps and vice versa if it is too short (Fig. 2.4).

If no bleb is still visible it is worth performing gonioscopy again to ensure that the anterior chamber positioning is correct and the tube is patent at its internal ostium.

2.4.1.3 Complications

Intraoperative Complications

Intraoperative complications with Xen relate either to difficulty with implant positioning or hyphema. In phakic eyes, the potential for lens touch exists, e.g., if the patient moves during surgery. Management of hyphema and avoidance of lens touch are as for the procedures previously described.

Early Postoperative Complications

Apart from hyphema and rarely infection, the risks in the early postoperative period are low pressure and high pressure. Low IOP is not uncommon, especially in younger patients. Significant anterior chamber shallowing is relatively uncommon but occasionally requires topical atropine or serial injections of viscoelastic in out-patients. In the author's experience (KB), hypotony does not last more than 2 weeks in the most extreme case.

High IOP during the first few days might be indicative of retained viscoelastic, but more likely occurs from obstruction of the Xen, either externally by Tenon's, or occasionally internally, by iris.

Late Postoperative Complications

As the Xen has only been available for just over 2 years, long-term experience is almost non-existent. Dysesthesia, blebitis, and endophthalmitis are a possibility though they seem to be rare. One of the authors (KB) has experienced two cases of implant exposure in around 120 cases, both necessitating implant removal. Other than that, the longer term risk is failure of IOP control, but much greater experience will be required to quantify this accurately.

2.4.2 MicroShunt

The MicroShunt (Innfocus, Miami, Florida, USA) is an 8.5 mm flexible tube of 70 μm lumen diameter made from a polyolefin triblock polymer (poly(Styrene-block-IsoButylene-block-Styrene)) that is designed to drain from the anterior chamber to the subtenons space behind the limbus. In that respect, the mode of action is similar to the Xen. However, the MicroShunt differs from the Xen and any other MIGS-type procedure in that it is implanted via an *ab externo* approach. Although some would regard this as a disadvantage, the mode of implantation does benefit from minimal anterior chamber intervention, making it an attractive proposition in stand-alone cases that are not undergoing concomitant cataract surgery.

2.4.2.1 Safety and Efficacy

At the time of writing, there are no published high-quality trials of MicroShunt safety and efficacy in peer-reviewed journals but a US and European randomized surgical trial is underway with the stated objective to obtain FDA approval as an alternative to trabeculectomy.

2.4.2.2 Patient Selection and Procedure

Implantation of the MicroShunt is believed to be indicated in patients who would otherwise be suitable for trabeculectomy. The absence of published high-quality evidence at present makes this difficult to verify.

The implantation procedure involves making a superior limbal conjunctival incision at the 12 o'clock position, similar to that for trabeculectomy. A subtenon's dissection is made in order to open up the subtenon's space for MMC application. Light cautery is applied to the episclera to achieve hemostasis in order to ensure that contact with blood does not blunt the effect of the MMC. MMC is applied in a similar fashion to a trabeculectomy procedure on a number of sponges over a wide area. The MMC is then irrigated away using 20 ml of BSS.

A point 3 mm behind the limbus is then marked with ink. A scleral tunnel is then created with a 1 mm diameter slit knife that is advanced 2 mm to a predefined mark. The slit knife is then withdrawn and a 25 gauge (orange) hypodermic needle gently

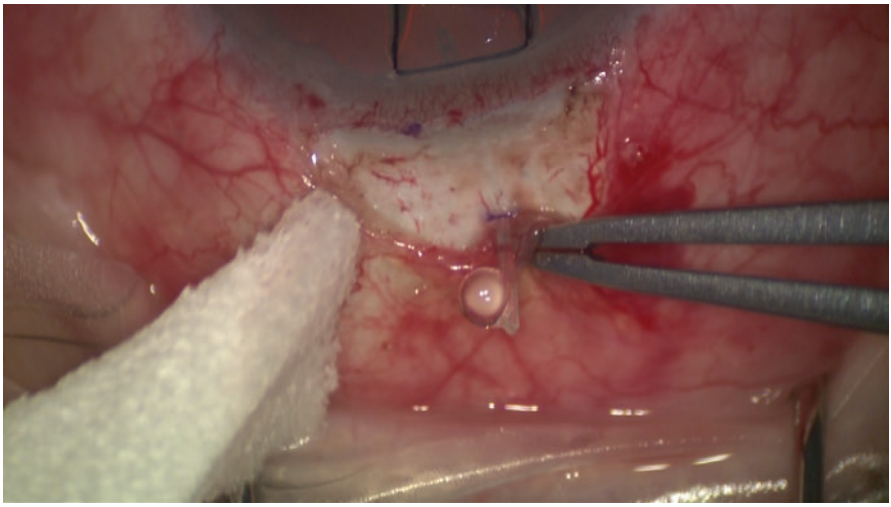

Fig. 2.5 Demonstration of aqueous flow through a Microshunt implant before conjunctival closure

inserted into the tunnel and advanced to its apex. The needle is then angled in order to advance it into the anterior chamber parallel to the plane of the iris and subsequently withdrawn.

The implant is washed with BSS in order to eliminate static electricity, gently grasped with tying forceps just in front of the fin and advanced into the anterior chamber via the tunnel. The Tunnel is designed in a manner to allow the fin to sit snugly intrasclerally. At this point, the tube portion should be visible in the anterior chamber, away from iris and cornea and the implant should be immobile in the tunnel without sutures.

It is important to ensure that the tube is draining aqueous before closure. This can be achieved by observing aqueous egress at the external aperture of the tube using a small sponge or fluorescein. If no flow is observed initially, it can usually be initiated by pressing on the eye gently at the limbus. If repeated firm pressure is insufficient to initiate flow, a wide bore, thin-walled 23 gauge cannula has been sourced by the manufacturer of the implant that can be placed over the length of the tube and used to flush it (Fig. 2.5).

After confirming that the implant is draining, the Tenon's and conjunctiva are closed. It is important before reapposing the conjunctiva at the limbus to ensure that Tenon's is lifted up over the implant and also brought towards the limbus. This is to ensure that the implant does not become caught in Tenon's or bent forward when conjunctiva and Tenon's are reapposed.

It is often helpful, where feasible, to suture conjunctiva and Tenon's separately. Firstly, one can ensure that Tenon's does not slip back around the implant. Secondly, this avoids drawing Tenon's right up to the limbus, which occasionally, if tight, can predispose to ptosis.

2.4.2.3 Complications

Intraoperative Complications
There are relatively few challenges with MicroShunt insertion. These include bleeding on needle insertion that might result in a postoperative hyphema, malpositioning of the shunt either in iris or cornea, which is simply remedied by removal and creation of a separate tunnel, and failure to observe flow the through the tube.

Early Postoperative Complications
Possibly early postoperative complications include hyphema, hypotony, or obstruction of the tube. To date these are all relatively uncommon. Hypotony is likely to be an issue in some patients as the internal diameter of the device at 70 μm does not provide sufficient resistance in a device 8.5 mm long to maintain intraocular pressure without some additional resistance from conjunctiva and Tenon's. The reported hypotony rate from company information is <10 % and all have been stated to resolve spontaneously within 1 week. The choroidal effusion rate has been reported to be 5 %.

Late Postoperative Complications
At the time of writing, there are no long-term reports upon which to assess safety or efficacy.

Practical Tip
- Start 2 mm from the limbus with a smooth single entry initially in the plane of the sclera then angling forward parallel with the iris plane once half of the bevel is in the sclera.
- Ensure a single movement without retraction and advancement (as this can create a false pocket).
- Enlarge the track slightly on exit to aid with initiating the tube entry.
- Check for watertight fit with 2 % fluorescein, suture adjacent to the tube if leaking.
- Persistent leaks may be stopped by plugging with Tenon's tissue.
- Ensure flow through the tube at the end of the surgeries. In the case of Xen, bleb formation is critical at the end of surgery.
- Bleb encapsulation can occur, and needling with 5-fluorouracil should be considered postoperatively.

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