In our second installment of our MIGS Resource Center, we talk with Reay Brown, MD, of Atlanta, Georgia. Among his other accolades, Dr. Brown is this year’s recipient of the ASCRS Innovators Award. Dr. Brown’s contributions to microinvasive glaucoma surgery (MIGS) evolution have been iconic. In his talk, “Overcoming Resistance: Making Glaucoma a Surgical Disease,” he told us the title was meant as a double entendre. First, we must overcome resistance in the trabecular meshwork (which is what the MIGS procedures seek to do), but we must also overcome resistance from industry and surgeons in using surgery earlier as a means to control glaucoma.

We wanted to find out from Dr. Brown what criterion/criteria surgeons should use when determining appropriate devices for their patient populations who are no longer served well by topical medications alone.

—Thomas W. Samuelson, MD
Glaucoma is a very heterogeneous condition, ranging from those already blind to those with completely asymptomatic disease. Accordingly, it makes sense that our surgical interventions include procedures that span the spectrum of efficacy as well as safety. For many patients, a procedure that is modestly efficacious but extremely safe may be the best option, while others with more advanced disease benefit most from our most efficacious procedures, even if taking on more risk. While the holy grail of glaucoma surgery would be an extremely safe and extremely efficacious procedure, unfortunately, at least for now, efficacy and safety are inversely related. Fortunately, we now have a portfolio of procedures to offer, each with their own safety/efficacy profile. Now more than ever, surgeons must match disease risk and surgical risk as much as possible. Moreover, with a greater number of glaucoma surgical interventions performed at the time of cataract surgery, a wider array of surgeons are performing glaucoma surgery ranging from the comprehensive ophthalmologist to the highly specialized consultative glaucoma surgeon.

Glaucoma Surgery Before, During, and After Cataract

Thomas W. Samuelson, MD: Dr. Brown, years ago, while we were working together to plan the ASCRS Glaucoma Day program, you categorized interventional glaucoma as “glaucoma surgery before, during, and after cataract surgery.” That speaks to virtually all the scenarios that we encounter. There is the phakic eye that does not have a surgical cataract yet, the patient that has both cataract and glaucoma, and finally, the pseudophakic patient that perhaps developed glaucoma later in life after cataract surgery, and now they need a surgical operation. Each of these scenarios present unique challenges and likely will be managed differently now that we have many options to choose from.

Before Cataract

Dr. Samuelson: Let us start with the first scenario. If a patient who does not have a surgical cataract needs an operation, what is your thought process on how to treat that patient, given the options that you have now?

Reay Brown, MD: It is rare that my patients do not present with some degree of significant cataract, but it does happen. Patients who are not being served adequately by topical glaucoma medications and need surgery but do not have cataract are usually have more serious glaucoma than those already scheduled for cataract surgery and in whom we want to implant a MIGS device (Table). A phakic patient who has failed medical therapy and laser therapy is, in my opinion, a great candidate for the Xen45 (Allergan) as the next step, but I might also consider a goniolotomy like the gonioscopy-assisted transliminal trabeculotomy (GATT) procedure, Kahook Dual Blade (New World Medical), Trab360 (Sight Sciences), or Trabectome (NeoMedix). Personally, I have just started using the Xen45, but I have always thought it was a good idea to perform the operation from inside the eye. I think the Xen45 is a little more straightforward than GATT. What do you think?

Dr. Samuelson: I agree that phakic patients who do not have a cataract but do require glaucoma surgery are either in more advanced stages than our patients with both cataract and glaucoma, or have a more extreme elevation of IOP. Most of the time, given the terrific medical and laser options that we have today, we can manage the glaucoma until the patient is symptomatic from their lens, and the decision to go to the OR is because of the cataract, not because their glaucoma is progressing or is uncontrolled. The patient with a clear lens requiring cataract surgery typically has failed these measures and is generally in more trouble so I agree that we need something a bit more efficacious for these patients; the transscleral option, such as the Xen45 or the InnFocus MicroShunt (Santen; not available in the United States), are good choices in that situation. In my experience, the transscleral devices (Xen45 or InnFocus) may be safer than traditional transscleral surgery because they are engineered to help...
### TABLE. THE WHAT, WHEN, WHERE, WHY, WHO, AND HOW OF MIGS DEVICES

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<td>iStent Supra (Glaukos)</td>
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<td>Investigational use only, being studied as a standalone</td>
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<td>Mean IOP reduction from 16.5 ±5.7 mm Hg to 12.9 ±4.2 mm Hg at 9 months; 73% had reduction of at least 1 medication, 80% if combined with phacoemulsification</td>
<td>Device has been studied in multiple glaucomas, including but not limited to: POAG, pseudoexfoliative glaucoma, chronic angle closure glaucoma. Enrolled subjects demonstrated range of severity, from mild to severe.</td>
<td>Dual blade design makes parallel incisions to strip portions of TM and inner wall of Schlemm’s canal</td>
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<td>Trab360 (Sight Sciences)</td>
<td>Standalone or at the time of cataract surgery</td>
<td>Schlemm’s canal/TM</td>
<td>S10(K) exempt device is believed to have similar efficacy, comparable safety to on-market Trabecome. Retrospective case series of 26 consecutive eyes demonstrated mean IOP reduction from 19.8 ±6.4 mm Hg to 13.5 ±4.6 mm Hg. 83% were able to discontinue medication use.</td>
<td>Retrospective case series enrolled eyes with POAG; anecdotal reports suggest utility of device in a wide array of glaucomas</td>
<td>Polypropylene material extruded from tip is cannulated through TM for 180° and then manual force is used to unroof TM, may be repeated for up to 180° in opposite direction to achieve full 360° goniotomy</td>
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<td>Visco360 (Sight Sciences)</td>
<td>Indicated for delivery of OVD during surgical use; for use with ABIC is one example; being studied as standalone procedure</td>
<td>Schlemm’s canal</td>
<td>Ongoing clinical trial investigating device vs selective laser trabeculoplasty under FDA-granted Investigational Device Exemption; primary outcome is mean change in diurnal IOP</td>
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<td>Delivers OVD via microcatheter to Schlemm’s canal to increase patency</td>
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**Abbreviations:** ABC, ab interno canaloplasty; FDA, Food and Drug Administration; OVD, ophthalmic viscosurgical device; POAG, primary open-angle glaucoma; TM, trabecular meshwork

*second-generation iStent Inject in Phase 4 clinical trial

6. InnFocus MicroShunt outcomes: Significant reduction in medication use in cohorts of patients with baseline IOP ≥ 21 and < 21 mm Hg, reduced IOP and reduced medication use in cohorts of patients with baseline IOP ≥ 21 and < 21 mm Hg.
hypotony. There may be some residual fibrosis issues that still need work, though.

I have also had good success with GATT. For the patient with mild to moderate damage, the Kahook Dual Blade, Hydrus Microstent (when it is approved; Ivantis), or multiple iStent Trabecular Micro-Bypass Stents (multiple iStents are off label; Glaukos) may provide enough efficacy to justify a standalone procedure. As an aside, our readers may be interested to learn that your original patents involving canal drainage devices were acquired by Glaukos as part of the iStent development.

**During Cataract**

**Dr. Samuelson:** Let us move onto the patient who needs to have cataract surgery and has coincident glaucoma, or the patient who is on medication for glaucoma and is scheduled for cataract surgery. Do you combine the two surgeries, or are there times when phacoemulsification alone will suffice? How do you decide what to offer a patient? Obviously, there is individual variability, and times when your general rules may not apply, but what are some of your general principles when selecting a procedure to combine with cataract surgery?

**Dr. Brown:** I generally try to avoid trabeculectomy as a combined procedure, and have for almost my whole career. There may be times when a trabeculectomy may make sense in a combined procedure but these situations are extremely rare for me. However, I will generally do cataract surgery with an iStent and now, alternatively, with the CyPass Micro-Stent (Alcon) at whatever stage of the disease. I am still working out how to decide whether to use the CyPass or the iStent. I was part of the COMPASS study, and I operated on a number of patients with elevated pressures. I was really impressed with CyPass. We will see what happens when it gets into the hands of thousands of surgeons, and we are able to analyze more real-world data. In my group of patients in the study, none needed to revert to topical drops for at least the first year after the surgery.

**Dr. Samuelson:** That is really amazing. Has that still held true?

**Dr. Brown:** No, they have gradually gone back on medicine, but their pressures are okay with one or two medicines.

**Dr. Samuelson:** No one needed an additional surgery?

**Dr. Brown:** No. I am personally positive about CyPass. I have a lot of experience with the iStent, and now with CyPass, I may get a little bit better pressure lowering. But, in my experience, CyPass may have a little more inflammation and once in a while the chamber may just be slightly shallower for a brief period after surgery. Fortunately, these issues have always resolved relatively easily and quickly.

**Dr. Samuelson:** As surgeons, our methods evolve as we gain
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more experience with these newer modalities. How are you currently deciding what surgical procedure to employ?

**Dr. Brown:** If a patient needs cataract surgery and is on any medical therapy for glaucoma, I perform a MIGS procedure. I have only recently started using CyPass in the real world, so I was predominantly using an iStent in patients who had mild to moderate glaucoma at the time of cataract surgery. If their pressures are really high, I would consider a phaco-trabeculectomy, but I am finding myself going down that road less and less.

I have found that I have had really good results with the iStent, even in patients with elevated pressures. In fact, I did a study of patients in my own practice and found that the higher the preoperative pressure, the more the pressure came down with iStent and cataract surgery. These results have been confirmed in multiple subsequent studies so I am sure that this is a real finding.\textsuperscript{2,8} Also, patients with pseudoexfoliation seem to do particularly well.

The key for me is the visual field. As long as that is not too damaged, then I am comfortable with those choices. If the patient has a more advanced case of glaucoma, I will do a goniotomy procedure, with the Kahook Dual Blade or GATT.

**After Cataract**

**Dr. Samuelson:** You have mentioned that CyPass might be considered in place of second tube shunt for those patients who had prior drainage devices or trabeculectomies. I have had some of those cases as well. How do you decide between using a MIGS device such as CyPass, which would be off-label (in this case) or something like the Xen45, which would be covered?

**Dr. Brown:** Both are acceptable options. If I have the choice, I would prefer CyPass since it is not a transscleral procedure. That leaves us the option to use Xen45 later on.

**Dr. Samuelson:** I agree; if transscleral surgery has already failed once (or twice) it may make more sense to try the supraciliary space even after you have employed the transscleral option.

**Dr. Brown:** I have several patients who are in the “desperate” zone and the supraciliary space is a wonderful option in those cases.

**Dr. Samuelson:** We agree that you can go into the supraciliary space after you have gone into the transscleral space, and you can go into the transscleral space after you have used the supraciliary space. When would you go into the canal? Is that an earlier procedure?

**Dr. Brown:** Yes. And the other great thing about the canal is that the device itself is not going to cause problems later. I have not had any late device-related problems even after hundreds of cases.

**Dr. Samuelson:** One thing I like about canal-based procedures is that you know what to expect. You may be disappointed in the efficacy at times, and you may be genuinely surprised at how well some patients do. But from a safety and visual recovery standpoint, I am rarely surprised. That is a huge attribute that may apply more to the canal than any other glaucoma procedure we have available.

With transscleral procedures, pressures are certainly more variable and therefore the visual function more variable early on. With the supraciliary procedures, there may be transient hyphema as well as some variability in pressure. Canal surgery, on the other hand, is very predictable with visual recovery, virtually the same as with cataract surgery alone.\textsuperscript{1} However, I do think that you need to be most mindful of the steroid IOP response with canal surgery.

**Dr. Brown:** Those are critical points. When I am doing cataract surgery in these patients, my number one goal is a safe and successful cataract surgery. I avoid compromising that outcome by trying to do more with a glaucoma device than is needed. My major complaint with doing a trabeculectomy with a cataract is that the trabeculectomy brings in a very serious group of risks that too many times causes the outcome of the cataract to be forever suboptimal.\textsuperscript{9-11} The wonderful safety profile is why I like the canal. Canal-based procedures are not going to get in the way of a great visual recovery and rapid improvement of vision.

**Dr. Samuelson:** That underscores the unfortunate fact that in the current regulatory environment and FDA labeling, we are forced to decide between canal or supraciliary-based procedures as a one-and-done option. That is, we only get one chance to place either a supraciliary device or a canal device at the time of cataract surgery. It would be far better if we could place one of the devices at the time of phacoemulsification and still offer the second procedure at some later date, if needed.

In my mind, it makes far more sense to do phaco-canal, knowing we could do a supraciliary procedure down the road should the patient need more pressure reduction.

One of the strongest attributes of the supraciliary space is that it has potential for patients with significant peripheral anterior synechiae and angle closure as well as patients who may have failed transscleral surgery or canal surgery. We should not be limited to performing these procedures only at the time of cataract surgery.

**Barriers to Overcome**

**Dr. Samuelson:** What are some of the barriers we still need to overcome?
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Dr. Brown: Surgery has two components—safety and efficacy. MIGS has really delivered on safety, but the efficacy may not be enough for every patient. For the vast majority, it is a great option, but there remains that little group who needs more profound pressure lowering. Fortunately, we have great medications, and the combination of a MIGS procedure and medications is enough for most of the patients with more serious glaucoma. But there still is a need for external filtration procedures and hopefully the Xen45 will help these patients avoid the riskier trabeculectomy or tube.

We are doing cataract surgery earlier and earlier due to the low risk profile and great benefits of improved vision. This has opened the door to earlier surgical intervention in glaucoma with MIGS. My expectation is that early intervention with MIGS will reduce the need for medical therapy and limit the terrible impact of poor compliance. Also, earlier surgical intervention with MIGS should “bend the curve” of glaucoma progression away from more advanced damage and help patients avoid future blindness.

Combined MIGS Approaches

Dr. Samuelson: Do you perform any combined MIGS approaches? For example, do you perform a cilioablative procedure concomitantly with your canal procedures or supraciliary procedures? What are your thoughts on that topic?

Dr. Brown: I am a minimalist. I applaud people who try and do new things, but combining different ways of lowering the pressure just does not make sense to me. But despite my reservations, we can only learn when someone does something unconventional that may not seem intuitive.

Dr. Samuelson: There is less of a need now. When all we had was the iStent, if someone wanted to avoid a trab tube, it made sense to combine iStents with endocyclophotocoagulation. But now we have procedures we can offer patients at every stage. If we want something that is more efficacious, maybe that is what changes our decision tree from a canal-based procedure to supraciliary or to Xen45. Rather than manipulating the eye with several procedures, we have an option to go to the next, more aggressive option that will (hopefully) be enough for the patient.

Dr. Brown: Yes, that makes sense. At one point, there was some discussion about combining canal and supraciliary procedures. But we would need a study to determine if there was any additional efficacy. If you are in a zone where you need some profound pressure lowering, then something like the Xen45 is a good option. I am optimistic about CyPass in patients with higher pressures.

If we start talking about longer duration medical therapy, where you could inject something into the anterior chamber periodically, one alternative idea might be to implant a CyPass every couple of years. To me, that makes a lot of sense. I think there are still options that need to be explored.

Dr. Samuelson: No doubt. We are at the beginning of the beginning of the age of MIGS. I think we will have a lot more answers within a few years as we get more experience with these new devices.

Best Patient for a New Cataract Surgeon Trying MIGS

Dr. Samuelson: What type of patient should cataract surgeons select when performing their first MIGS angle cases?

Dr. Brown: There are several key tips for cataract surgeons selecting the best patient for performing their first MIGS angle cases. There are many other fine points, but these are the basics.

• Pick a patient with mild glaucoma who already has fairly good pressures so you are not depending too heavily on the implant for pressure control.
• The angle should be widely open. It also helps to have the meshwork deeply pigmented. Alternatively, the surgeon can stain the meshwork with vision blue much the same way that we stain the anterior capsule. The blue dye highlights the meshwork (see Watch It Now video).
• It is helpful to warn the patient preoperatively that you may not implant the device if there is not enough room in the angle. This gives you an “out” if for some reason you do not feel comfortable implanting the device and you want to abort.
• Practice delivering the implant outside the eye. You can usually get a nonsterile device from your representative and practice delivering it into a Weck-Cel sponge (Beaver-Visitec International) at the slit lamp. You need to be familiar with how to press the release button so that you are not doing it only with the device inside the eye.
• Make sure that you have a clear view through your gonio lens before you start. It is important to have practiced intraoperative gonioscopy on routine cataracts before your first implants. You need the right lens, the right viscoelastic, and to position the patient in the optimal orientation. You must have good visibility to be successful.

Dr. Samuelson: Dr. Brown, those are terrific pearls and I agree with you on each point. I would also suggest picking the eye that favors your dominant hand for your first eyes. If you favor right eyes for phaco pick a right eye for your first MIGS procedure, if you favor left eyes for phaco, select a left eye. Another tip is to lump several cases together during the first weeks of adoption because performing several cases within a short period is very helpful. Finally, while the MIGS procedure are relatively short once the surgeon is facile with the technique, for the first few cases, allow adequate time. If it takes “x” minutes for a phaco, I would allow 2x for the first several phaco-MIGS cases. Avoiding the added stress of maintaining the OR schedule is helpful early on.


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