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TAILORING THE APPROACH TO IOP LOWERING WITH MIGS DEVICES

Interim results from a 24-month study indicate ABiC is effective as a combined or standalone procedure.

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While most glaucoma treatment guidelines stress the need to individualize the management plan, specialists have historically been somewhat limited by the available treatment options in their ability to follow that guidance. Topical therapy, the most frequent starting point for lowering IOP, is certainly a reasonable approach. Yet, in the past, when medical therapy failed, patients were typically steered toward filtering procedures. The risks associated with surgical techniques were more acceptable among individuals with severe or recalcitrant glaucoma, but there were few options for those with mild to moderate glaucoma and for whom medical therapy was insufficient to control IOP.

The emergence of microinvasive glaucoma surgery (MIGS) techniques and devices has allowed us to rethink this paradigm. Procedure-based management of glaucoma—which, in general, is predicated on the idea of restoring a mechanism of aqueous outflow—offers a way to durably lower IOP independent of patients' compliance.

Furthermore, in my experience, the MIGS class is associated with a much more favorable safety profile than traditional filtration procedures and IOP-lowering efficacy sufficient to benefit eyes with mild to moderate glaucoma. MIGS also provides the additional benefit of reducing the need for medications. Filtering procedures, including trabeculectomy and use of glaucoma drainage devices, are still very much part of the armamentarium for advanced and/or recalcitrant cases where the urgent need to lower IOP outweighs risks of complications. Meanwhile, MIGS procedures offer a more favorable safety profile with IOP-lowering efficacy for less severe cases.

However, not all MIGS procedures are equal, which is actually to the great benefit of patients, as the extent of procedural options suggests a facility to truly individualize the approach based on the patients' circumstances. Understanding the modes of action of the various devices is helpful for determining a plan of action.

RESTORING PHYSIOLOGIC OUTFLOW

With MIGS procedures, failure on medical therapy is not necessarily a predetermining factor, and although many of the procedures are used in conjunction with cataract surgery, newer options are proving to be viable standalone options. Still, many of the MIGS devices have only been studied as combined procedures, and so discerning their effectiveness and whether they provide a true benefit over topical therapy in terms of IOP lowering is somewhat complicated.

One way MIGS procedures can be assessed is by what mechanism of outflow they address. While many aspects of a patient's glaucoma can be characterized, the exact point of outflow obstruction cannot always be readily appreciated. Several components of the outflow system are vital to maintaining physiologic outflow, including the trabecular meshwork, Schlemm canal, collector channels, and the scleral venous plexus.

Thus, when determining how best to restore physiologic outflow, options that function at all relevant outflow components would seem to provide the greatest benefit.

This last point is a key reason why ab interno canaloplasty (ABiC, Ellex) has become a favored approach to treating mild to moderate glaucoma in my clinic. During ABiC, the iTrack illuminated microcatheter (Ellex) is advanced circumferentially through the canal of Schlemm, which has several functions: (1) mechanical lysis of herniations of the inner wall of Schlemm canal and the trabecular meshwork plexus that obstruct collector channels; (2) viscodilation of the canal and distal system; and (3) creation of microperforations in the inner wall of Schlemm canal to counter the reduction of micropores within and between the endothelial cells lining the inner wall of the canal (see *What is iTrack?*).

The microcatheter is then withdrawn as viscodilation is performed, which dilates the canal and widens collector channels and the distal system. The complete 360° viscodilation of the aqueous tract provides the surgeon with confidence that the entire system is being treated as opposed to hoping that the distal system in the nasal quadrant is patent and functioning. Because ABiC modifies the conventional outflow system, there is no hypothetical risk for hypotony. Furthermore, because ABiC does not ablate or remove the trabecular meshwork, a very important blood-aqueous barrier, there is no risk of recurrent hyphema development. In previous clinical studies, whether performed as a standalone procedure or at the time of cataract surgery, ABiC yielded an average reduction in mean IOP of 30% and a 50% reduction in medication use.[1]

INTERIM DATA FROM A 2-YEAR STUDY

I have been performing ABiC for over 2 years and am retrospectively evaluating the efficacy and safety of ABiC, performed either as a standalone procedure or in conjunction with cataract surgery, in reducing IOP and glaucoma medication dependence in patients with mild to moderate primary open-angle glaucoma. This pilot data was collected from a single-center, nonrandomized, noncomparative study that reviewed the outcomes of ABiC in 75 consecutive eyes.[1]

The final 2-year follow up has not yet been completed in all patients; however, an interim analysis suggests substantial treatment benefits associated with ABiC. Overall, among 73 eyes of patients who completed 12 months of follow-up, mean IOP dropped from 20.39 ±4.68 mm Hg at baseline to 13.52 ±1.90 mm Hg (a 34% reduction), with a drop in medication use from a mean 2.83 ±0.10 to 1.11 ±0.13 (a 61% reduction). Although only 33 eyes were available with 24 months of follow-up, there was a trend toward continued decline of mean IOP to 12.42 ±1.98, and these patients were only using a mean 0.84 ±0.21 medications at that time point.

The Table summarizes data on a subgroup analysis of eyes treated with ABiC as a standalone procedure compared with eyes treated with ABiC in conjunction with phacoemulsification.[1] Although the analysis is incomplete, there are important trends to note. First, the data at the 12-month follow up are comparable between the two groups. Of note, there was a slightly lower IOP in the standalone group at 24 months, although there was a greater drop in medication use in the combined procedure group at that time. As more data is curated, it will be interesting to see if these trends persist; nevertheless, there were significant numerical reductions in IOP and medication use at 12 and 24 months compared to baseline in each group that could be considered clinically meaningful. For instance, pressure in the teens after about a 35% reduction and the elimination of an average of 2 medications from the daily

TABLE. IOP AND MEDICATION USE IN SUBGROUPS OF PATIENTS UNDERGOING ABIC AS A STANDALONE PROCEDURE OR IN CONJUNCTION WITH PHACOEMULSIFICATION

	ABiC + Phaco		ABiC Standalone	
	Mean	% reduction from baseline (*P*)	Mean	% reduction from baseline (*P*)
IOP (mm Hg)				
Baseline (n)	19.41 ±3.68 (34)	-	21.20 ±0.83 (41)	-
12 month (n)	12.97 ± 1.82 (34)	34% (*P* <.001)	14.00 ±0.3 (39)	34% (*P* = .001)
24 month (n)	12.72 ±1.68 (18)	34% (*P* <.001)	12.07 ±0.61 (15)	43% (*P* = .001)
Medication use				
Baseline (n)	2.59 ±0.24 (34)	-	3.02 ±0.11 (41)	-
12 month (n)	0.85 ±0.24 (34)	67% (*P* <.001)	1.33 ±0.24 (39)	56% (*P* <.001)
24 month (n)	0.56 ±0.25 (18)	79% (*P* <.001)	1.21 ±0.35 (14)	60% (*P* <.001)

routine 1 to 2 years after having surgery would likely be a positive outcome for most patients.

That the data in the two subgroups do not deviate considerably from the results in the overall population also provides some assurance as to the robustness of the efficacy findings. A more complete analysis will be performed when the study is complete. In the meantime, the interim data provide suggestion of expected outcomes 1 and 2 years after ABiC.

COMPREHENSIVE AND COMPLEMENTARY MIGS APPROACHES

The outcomes evident in the interim analysis of this ongoing study, especially with respect to the suggestion of a durable response, are likely attributable to the comprehensive restoration of the outflow mechanism with ABiC. This feature makes ABiC unique among MIGS approaches. It is reasonable to assume that repair and restoration of the various components of the outflow system would augment physiologic outflow, such that the final result should be significant and long lasting; however, long-term data is necessary.

The most common MIGS-based strategy for reducing aqueous resistance involves modification of the trabecular meshwork, either via implant (iStent Trabecular Micro-Bypass Stent; Glaukos) or via ablation, which can be either focal or complete. Options for focal trabecular ablation include electrocautery (Trabectome; NeoMedix) and the Kahook Dual Blade (New World Medical), which is used to excise a strip of the trabecular meshwork overlying Schlemm canal. The entire proximal outflow system may be incised using the Trab360 device (Sight Sciences) or by performing gonioscopy-assisted transluminal trabeculotomy (also known as the GATT procedure), which shears through the trabecular meshwork and the inner wall of Schlemm canal for 360°.

While each of these approaches is valuable, stent implantation requires enhanced knowledge of the aqueous drainage system to effectively target the placement of the stent for maximum efficacy. Ablative techniques, on the other hand, eliminate an important blood-aqueous barrier and, in my experience, can allow blood from the episcleral venous system to enter the clear aqueous in the anterior chamber, temporarily clouding vision. I have seen cases of recurrent hyphema development following trabecular ablative procedures from conditions that raise the episcleral venous pressure, which can include something as simple as sleeping on the side of the operative eye.

More recent additions to the MIGS class include options to bypass the conventional outflow system and target drainage to the supraciliary (CyPass Micro-Stent; Alcon) or subconjunctival space (Xen45; Allergan). Unlike the conventional outflow system, the supraciliary and subconjunctival

WHAT IS iTRACK?

As a procedure, ab interno canaloplasty (ABiC; Ellex) is a logical and elegant approach to treating an important mechanism that drives glaucoma pathogenesis. If the canal is closed, even partially, adequate outflow will not occur, and pressure will rise inside the eye; thus, reopening the canal will facilitate physiologic outflow so that pressure does not rise inside the eye.

In reality, however, the seemingly simplistic mechanism of ABiC belies the fact that every step of the procedure has been carefully and meticulously designed, and that includes the technology used in the surgery. The iTrack system (Ellex), which includes the iTrack microcatheter, the ViscoInjector viscoelastic injector, and the iLumin illumination source, is a crucial element in the success of ABiC.

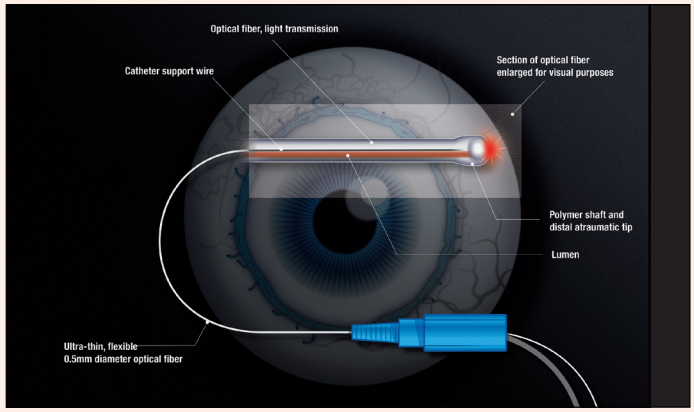

Figure. The iTrack microcatheter features an illuminated tip, allowing the operator to monitor its position inside the canal to avoid broaching the collector channel ostia.

The iTrack microcatheter features an illuminated tip, allowing the operator to monitor its position inside the canal to avoid broaching the collector channel ostia (Figure). Based on surgeon preference, the diode can be toggled to be continuously on or intermittently blinking. Due to its rounded tip, the iTrack is atraumatic to the local tissue.[1] Yet, the surgeon is able to maintain excellent control of the tip and maneuver through tight areas or structures of the canal. The small gauge support wire provides excellent tactile feedback as the tip is advanced, letting the surgeon know if the canal is tight, grainy, or completely open.

An equally important component of the surgical system is the ViscoInjector, which attaches to the iTrack microcatheter. Manually operated using a tactile and audible knob with clicks every 1/8 turn, the 200–µm-diameter shaft precisely and accurately delivers ophthalmic viscoelastic device as the iTrack is withdrawn. The delivery of ophthalmic viscoelastic device to the canal accomplishes a crucial complementary function to the mechanical opening achieved with the iTrack, as viscodilation maintains patency after the surgery is complete.

1. Ellex iScience. Inc. Data on File.

spaces do not have a safety net to prevent hypotony, and, therefore, such procedures must be performed with caution. In my algorithm of treatment, I try to enhance the functionality of the conventional outflow system first, as it is the safest system to manipulate. Although we do not currently have definitive science to evaluate the health and patency of the different systems, gonioscopic cues can provide insight into the health of the conventional outflow system. Homogenous banding of the various angle landmarks suggests homogenous filtration through the trabecular meshwork into the canal, whereas highly segmental variegated pigmentation of meshwork likely suggests segmental outflow through the proximal system. In the latter circumstance, manipulating nonconventional outflow outweighs the potential risk of hypotony.

Because it lowers IOP without any alteration to the trabecular meshwork, ABiC appears to have a much safer profile than other MIGS procedures,[1] which, as a class, are already associated with relatively few complications. Yet, there may be additional potential applications for ABiC in combination with the above referenced procedures. For example, the iTrack can be a valuable diagnostic tool to evaluate the patency of the distal system, useful for determining the ideal location for iStent implantation or trabecular ablation with the Kahook Dual Blade or Trabectome. This is possible because of our ability to visualize blanching of the episcleral venous system upon viscodilation of the canal and distal system. Furthermore, should the surgeon prefer, fluorescein or trypan blue can be used in the catheter to highlight areas of the distal system that have maximum patency. Because ABiC does not ablate any tissue, it also does not hinder a patient's suitability for additional ocular surgery in the future, if it is needed, including iStent implantation and/or supraciliary/suprachoroidal shunt implantation.

CONCLUSION

Patient selection is an important part of success with MIGS procedures. The breadth of options at the surgeon's disposal means he or she is no longer confined to a one-size-fits-all approach; instead, the various types of surgeries can be applied as needed, perhaps even combined to achieve greater benefit.

In addition to disease severity and fitness for surgery, additional factors may warrant consideration when choosing a MIGS procedure. For instance, activities of life, current medication use, and comorbidities might help guide the selection process. Younger, active patients may desire a procedure with a lower risk of hypotony and/or recurrent hyphema development. In some cases, such patients may want a procedure that neither leaves an implant inside the eye nor involves ablation of an important blood-aqueous barrier. As for medication use, although it is not a primary reason for performing MIGS, patients on multiple drops may be more accepting of options that will help simplify their daily routines. Another important factor for medication reduction is the knowledge that the long-term application of drops containing the preservative benzalkonium chloride induces apoptosis of the endothelial cells lining the trabecular columns, which leads to fusion of the trabecular lamellae and reduction of the effective filtration area.[2] As evidenced in the interim analysis presented above, ABiC is likely to reduce medication use 1 and 2 years after the procedure.[1]

Comorbidities, in particular the lens status of the patient, are also important. Most MIGS procedures are only approved for use at the time of cataract surgery, with limited data as to their efficacy as a standalone option. The data from the interim analysis presented here should provide confidence that ABiC is viable either used with phacoemulsification and lens extraction or as a single surgery. Each of the subgroups in the study achieved a 34% reduction in IOP at 1 year, and a 50% or greater reduction in medication use.[1]

I look forward to more data on ABiC, both as a combined procedure and as a standalone option. Already, the results from the interim analysis confirm my belief that MIGS will become the standard of care for mild to moderate glaucoma. In particular, there is great benefit to removing medication requirements from the treatment schema, as they can be associated with cost and compliance issues that limit their effectiveness in treating glaucoma, as well as continued damage to the trabecular meshwork. I am confident that, as we learn more about the various components of the aqueous outflow pathway, we will also learn more about the benefit of comprehensive restorative approaches, such as ABiC, that function within the canal of Schlemm, at the trabecular meshwork, and in the distal collector channels. ■

1. Ellex iScience. Inc. Data on File.
2. Ammar DA, Kahook MY. Effects of benzalkonium chloride- or polyquad-preserved fixed combination glaucoma medications on human trabecular meshwork cells. *Mol Vis*. 2011;17:1806-1813.

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