WHITEPAPER

AB-INTERNO CANALOPLASTY – THE MINIMALLY INVASIVE GLAUCOMA SURGERY THAT KEEPS ITS PROMISE

12-MONTH CASE SERIES REVIEW

ABiC™ – Canaloplasty performed with an ab-interno approach to Schlemm's canal – is a new MIGS procedure that can comprehensively restore the natural outflow pathways in glaucoma patients. Performed via a self-sealing, clear corneal incision, ABiC™ conserves the clinically-proven benefits of 360° viscodilation of Schlemm's canal provided by traditional Canaloplasty, but with the speed and ease of implementation of a MIGS procedure. Unlike other currently available MIGS procedures however, ABiC™ preserves tissue and does not require the permanent placement of an implant in the eye. It has also been shown to be effective as both a standalone procedure and when combined with cataract surgery. It is also the only MIGS indicated for use outside cataract surgery.

Traditional Canaloplasty, a restorative surgical procedure that re-establishes the natural ocular outflow system without the need for a filtering bleb, has been shown to be both safe and effective in more than 60 peer-reviewed clinical studies.[1,2] It has also been shown to be as equally effective as trabeculectomy.[1,2]

ABiC™ is a new minimally-invasive glaucoma surgery (MIGS) procedure, based on the same dilation principles of traditional Canaloplasty but via a simplified and much faster ab-interno approach. It is also the only MIGS procedure that successfully and comprehensively addresses all aspects of potential outflow resistance.

The Mechanism of ABiC

ABiC™ is based on time-tested experience with traditional Canaloplasty and is designed to access, catheterize and viscodilate all potential sites of outflow resistance, i.e., the trabecular meshwork, Schlemm's canal and the distal outflow system beginning with the collector channels. During the procedure, viscodilation of Schlemm's canal acts like angioplasty and opens up the ostia of the collector channels, re-establishing outflow.

It is important to note that ABiC™, along with its predecessor, traditional Canaloplasty, is the only currently available MIGS procedure that addresses blockages in the collector channels. Studies undertaken in human and bovine POAG eyes by Haiyan Gong, MD, PhD, from the University of Boston, have shown that when inner wall tissue of Schlemm's canal herniates into the collector channels, it blocks aqueous outflow. Specifically, in POAG eyes fixed at 0 mm Hg (n=5), 73 collector channel ostia regions were examined, with 51 showing herniations (70%). In POAG eyes fixed at 10 mm Hg (N=2), 22 collector channel ostia regions were examined, with 21 showing herniations (95%). Cannulating the whole of Schlemm's canal with ABiC™/traditional Canaloplasty, via a process of 360-degree viscodilation, may "pop" open these herniations and enable full access to collector channel ostia for the egressing aqueous.[3,4] In the case of other glaucoma treatments, where only a segment of Schlemm's canal is addressed, where the trabecular meshwork is targeted in isolation, or when a bypass shunt is inserted, any herniated tissue would most likely prevent improved outflow along the conventional pathways.

ABiC, AB-INTERNO CANALOPLASTY

The key to successful ABiC™ is the iTrack™ 250-micron microcatheter which features a fiber optic light and lumen. The device is passed through a clear corneal incision and then through a small opening in the trabecular meshwork in order to circumferentially viscodilate and intubate Schlemm's canal. Precisely controlled delivery of Healon/Healon GV during withdrawal of the catheter allows the compressed tissue planes of the trabecular meshwork to separate, and any herniated inner wall tissue to withdraw from the collector channels.

ABiC versus Traditional Canaloplasty

Traditional Canaloplasty, performed via an ab-externo approach to Schlemm's canal, is ideally suited to patients with moderate to advanced glaucoma. In contrast, ABiC™ can be introduced much earlier in the treatment paradigm for early-mild glaucoma patients. It is also worth noting that both procedures can be performed in conjunction with cataract surgery in order to optimize operating room efficiency.

In terms of technique, one key difference between ABiC™ and traditional Canaloplasty is that, in the former, no tensioning suture is required. Traditional Canaloplasty employs placement of a 9-0 or 10-0 Prolene tensioning suture to ensure added longevity in IOP reduction. A review of three-year data by Lewis et al, however, indicated that 360° viscodilation alone, i.e., Canaloplasty without a suture successfully lowered IOP.[5] Mapping the results of viscodilation to suture tension also showed that viscodilation was driving the IOP reduction more than the tension of the suture.[6] Additionally, discussions with practicing Canaloplasty surgeons indicate that patients who do not receive a suture still experience satisfactory reductions in IOP.

A Comprehensive MIGS

The most defining aspect of ABiC™ is its comprehensive approach. To-date, ABiC™ is the only MIGS procedure that successfully and comprehensively addresses all aspects of potential outflow resistance.

Other MIGS procedures lower IOP by addressing different aspects of ocular outflow system. For example, the Trabectome®, uses an electrosurgical pulse to ablate the trabecular meshwork and inner wall of Schlemm's canal, while the iStent® works as a trabecular micro-bypass by allowing aqueous humor to flow directly from the anterior chamber into Schlemm's canal, thus circumventing the trabecular meshwork.[7] Meanwhile, the Aquesys Subconjunctival Implant (an investigational MIGS device) is placed into the subconjunctival space to create a filtering bleb, thus bypassing all of the conventional outflow route.[8]

TABLE 1:
Reduction in IOP and medication use for all enrolled patients - MAHMOUD A. KHAIMI, MD

Exam	n	Mean IOP (mm Hg) ± SD	Mean Medications (n) ± SD
Baseline	106	19.5 ± 6.6	2.0 ± 1.0
3 Months	69	15.7 ± 4.4	0.0 ± 1.0
6 Months	69	15.0 ± 3.8	0.0 ± 1.0
12 Months	20	13.9 ± 1.9	0.0 ± 1.0

TABLE 2:
Reduction in IOP and medication use for all enrolled patients - MARK J. GALLARDO, MD

Exam	n	Mean IOP (mm Hg) ± SD	Mean Medications (n) ± SD
Baseline	122	18.6 ± 6.4	2.0 ± 1.0
3 Months	88	14.0 ± 3.4	1.0 ± 1.0
6 Months	65	14.1 ± 3.7	1.0 ± 1.0
12 Months	38	12.9 ± 2.0	1.0 ± 1.0

In addition to addressing all aspects of ocular outflow, ABiC™ is fast and easy to perform. On average, the procedure can be completed within five minutes and is well tolerated by patients.

Another hallmark of ABiC™ is that it preserves tissue. And because it does not require permanent placement of an implant or stent it does not preclude or compromise future surgery if it should become necessary.

Clinical Evidence

Mark J. Gallardo (El Paso Eye Surgeons, PA) and Mahmoud A. Khaimi, MD (Dean McGee Eye Institute, University of Oklahoma), each recently completed a 12-month study to evaluate the effect of ABiC in reducing IOP and dependence on anti-glaucoma medications. The preliminary results for ABiC™ are very encouraging – at this point similar to previously published Canaloplasty studies, notably the landmark multi-center prospective trial carried out at 15 clinical sites in 2005.[5]

Findings from Dr. Khaimi's study of 106 patients showed that mean IOP was reduced from 19.5 ± 6.6 mmHg preoperatively, to 15.7 ± 4.4 mm Hg (n=69), 15.0 ± 3.8 mm Hg (n=69) and 13.9 ± 1.9 mm Hg (n=20) at 3, 6 and 12 months postoperative, respectively. Medication dependency reduced from 2 ± 1 drops before ABiC™ to 0 ±1 drops at 3, 6 and 12 months postoperative, representing a total average decrease of 28.7% in IOP and 100% in glaucoma medications. (Refer to Table 1.)

Importantly, in 38 patients who underwent standalone ABiC™, mean IOP was reduced by 36.8% from 22.0 ± 8.2 mm Hg preoperatively) to 13.9 ± 1.6 mm Hg at 12 months postoperative (n=8) with a 50% reduction in medication. As early as 3 months postoperative, 43.4% of patients were recorded with an average IOP of 14.9 ± 6.6 mm Hg on 0.0 ± 0.0 medications and remained medication free through 12 months postoperative.

The results of Dr. Gallardo's study of 122 patients were very similar. Mean IOP was reduced from 18.6 ± 6.4 mm Hg preoperatively to 12.9 ± 2.0mm Hg (n=28) at 12 months postoperative, a total average reduction in IOP of 30.64%. Additionally, ABiC™ reduced the mean number of medications from 2 ± 1 drops at baseline to 1 ± 1 drops at 12 months postoperative, representing a 50% decrease in medications. (Refer to Table 2.) ABiC™ was found to be effective both combined with cataract surgery and as a standalone procedure. In patients who underwent ABiC™ alone (n=60), mean IOP reduced by 37.55% from 21.3 ±7.4 mm Hg preoperatively to 13.3 ± 2.3 mm Hg at 12 months postoperative (n=6) with a 66.66% reduction in medication

TABLE 3:
Reduction in IOP and medication use for all enrolled patients

Exam	n	Mean IOP (mm Hg) ± SD	Mean Medications (n) ± SD
Baseline	228	19.0 ± 6.5	2.0 ± 1.0
3 Months	157	14.7 ± 3.9	0.0 ± 1.0
6 Months	134	14.5 ± 3.8	1.0 ± 1.0
12 Months	48	13.3 ± 2.0	1.0 ± 1.0

TABLE 4:
Reduction in IOP and medication use for patients who underwent ABiC™ plus cataract surgery

Exam	n	Mean IOP (mm Hg) ± SD	Mean Medications (n) ± SD
Baseline	130	17.1 ± 5.0	2.0 ± 1.0
3 Months	92	13.5 ± 3.1	0.0 ± 1.0
6 Months	83	14.0 ± 3.6	0.0 ± 1.0
12 Months	34	13.1 ± 2.1	1.0 ± 1.0

use. In a subset of patients with uncontrolled glaucoma (n=85), there was a total average decrease of 39.43% in IOP and 66.66% in medications, while patients with controlled glaucoma (n=37) experienced a 50% reduction in medication use following ABiC™.

Combining the two cohorts (n= 228 eyes), the mean preoperative IOP was 19.0 ± 6.5 mm Hg and the mean number of medications was 2.0 ± 1.0. At three, six and 12 months post-treatment, mean IOP was 14.7 ± 3.9 mm Hg, 14.5 ± 3.8 mm Hg and 13.3 ± 2.0 mm Hg, respectively, while the mean number of medications was 0.0± 1.0 at three months, and 1.0 ± 1.0 at six and twelve months post-treatment (refer to Table 2). At 12 months (n = 48) the average IOP reduction was 30%, combined with a 50% reduction in the number of medications. (Refer to Table 3.)

Of the 130 patients who underwent ABiC™ in combination with phacoemulsification, the mean preoperative IOP was 17.1 ± 5.0 mm Hg. At 12 months (n = 34) mean IOP was reduced to 13.1 ± 2.1 mm Hg for an overall reduction in mean IOP of 23.39%. The number of medications was reduced by 50% from 2.0 ± 1.0 to 1.0 ± 1.0 by 12 months postoperative. (Refer to Table 4.)

Of the 98 patients who underwent ABiC™ as a stand-alone procedure, the mean pre-operative IOP was 21.5 ± 7.4 mm Hg and the mean number of medications was 3.0 ± 1.0. At

TABLE 5:
Reduction in IOP and medication use for patients who underwent standalone ABiC™

Exam	n	Mean IOP (mm Hg) ± SD	Mean Medications (n) ± SD
Baseline	98	21.5 ± 7.4	3.0 ± 1.0
3 Months	65	16.4 ± 4.3	1.0 ± 1.0
6 Months	51	15.5 ± 3.9	1.0 ± 1.0
12 Months	14	13.6 ± 1.9	1.0 ± 1.0

TABLE 6:
Reduction in IOP and medication use for patients with uncontrolled glaucoma (≥16 IOP) on maximal medical therapy (+3 gtts)

Exam	n	Mean IOP (mm Hg) ± SD	Mean Medications (n) ± SD
Baseline	73	21.5 ± 6.2	3.0 ± 1.0
3 Months	52	15.0 ± 4.0	1.0 ± 1.0
6 Months	42	14.9 ± 4.1	1.0 ± 1.0
12 Months	17	12.8 ± 1.9	1.0 ± 1.0

TABLE 7:
Reduction in IOP and medication use for patients with controlled glaucoma (≤15 IOP)

Exam	n	Mean IOP (mm Hg) ± SD	Mean Medications (n) ± SD
Baseline	67	12.9 ± 1.7	2.0 ± 1.0
3 Months	48	13.2 ± 3.0	0.0 ± 1.0
6 Months	44	13.4 ± 2.9	0.0 ± 1.0
12 Months	17	13.4 ± 2.1	0.0 ± 1.0

12 months (n=14) mean IOP was reduced by 36.74% to 13.6 ± 1.9 mm Hg while the mean number of medications was reduced by 66.66% to 1.0. ± 1.0. (Refer to Table 5.)

Of the 228 patients in the combined cohorts, 161 patients were classified as having uncontrolled glaucoma (defined as IOP ≥ 16 mm Hg), with a mean pre-operative IOP of 21.6 ± 6.1 mm Hg and an average of 2.0 ± 1.0 medications. At 12 months postoperative (n=13) mean IOP was reduced by 38.88% to 13.2 ± 2.0 mm Hg combined with a 50% reduction in the number of mean medications to 0.0 ± 1.0.

In uncontrolled glaucoma patients on maximum medical therapy (+3 gtts) ABiC™ also achieved a significant reduction in mean IOP of 40.46% from 21.5 ± 6.2 mm Hg to 12.8 ± 1.9 mm Hg at 12 months (n=17). The mean number of medications was also reduced from 3.0 ± 0.0 to 1.0 ± 1.0 (66.66%). (Refer to Table 6.)

Additionally, ABiC™ was shown to effectively lower the medication burden in controlled glaucoma patients. At 12 months medication-use was reduced by 50%, from 2.0 ± 1.0 at baseline to 1.0 ± 1.0 with IOP remaining stable in the low teens. (Refer to Table 7.)

In patients who had undergone SLT prior to ABiC™, the average reduction in IOP at 12 months was 40.29% (a reduction of 7.9 mm Hg), down to an average IOP of 12.0 ± 1.7 mm Hg. The mean number of anti-glaucoma medications was also reduced by 100% from 2.0 ± 1.0 to zero.

Case observation of ABiC™ also revealed that the safety profile of the procedure was similar to that of traditional Canaloplasty and the newer MIGS procedures. In the 12-month studies by Dr Gallardo and Dr Khaimi, overall, the frequency of surgical and postsurgical complications was low, with no serious adverse events recorded.

In Germany, Prof. Noerbert Koerber has achieved similar success with ABiC™. In an ongoing single center consecutive case series study involving 20 pseudophakic patients (20 eyes), mean IOP was reduced from 18.5 ± 3.44 mm Hg preoperatively to 14.88 ± 2.82 mm Hg (n=17), 13.80 ± 2.05 (n=12), 14.57 ± 2.59 mm Hg (n=9) and 15.47 ± 2.42 mm Hg (n=6) at 1, 3, 6 and 9 months respectively. 12-month data for two patients showed that IOP had reduced from 17 mm Hg preoperatively to 16 mm Hg in one patient and from 20 mm Hg to 13 mm Hg in the other. The mean number of medications was reduced from 2.4 preoperatively to 0.25 at the last follow-up visit. Similar to Dr. Gallardo's and Dr. Khaimi's findings, the overall frequency of surgical and postsurgical complications was low with only one reported complication of limited descemetolysis near the limbus by the viscoelastic during the dilation of Schlemm`s canal. No adverse events were reported. Although there were no cases of hyphema in Dr. Gallardo's, Dr. Khaimi's or Prof. Koerber's studies, surgeons should be aware that this may occur following ABiC™. Although some surgeons may initially be concerned about this, it should be viewed as a positive sign as it confirms that there is connection between the anterior chamber and the aqueous into the outflow system.[9,10]

Clinical Considerations

Because ABiC™ is minimally invasive and atraumatic it can be used in a broad population of patients, including both phakic and pseudophakic patients. Similar to the treatment plan for MIGS, ABiC™ is recommended early in the disease process, thus the primary indication is patients with mild-to-moderate glaucoma. However, it may also be considered as a first-line option or in patients who have undergone laser trabeculoplasty and for patients non-compliant with medications. Patients with exfoliative glaucoma and those in whom glaucoma surgery in the fellow eye has failed may also be considered for ABiC™. Early observations also suggest that ABiC may improve responsiveness to selective laser trabeculoplasty, by improving the patency of Schlemm's canal.[11,12]

ABiC™ should not be performed in patients with uveitis, neovascular glaucoma, chronic angle closure, angle recession/ peripheral anterior synechiae or narrow angle glaucoma.

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Summary

Clinical evidence indicates that ABiC™, a new MIGS procedure, is safe and effective in mild-to-moderate POAG with similar IOP-lowering effects to tried and true traditional Canaloplasty. Based on the same dilation principles as traditional Canaloplasty, ABiC™ ensures that all potential "blockages" in the ocular outflow pathway are addressed, including in distal structures such as the collector channels, which have been shown to play a key role in aqueous outflow in POAG eyes. Unlike other currently available MIGS procedures, ABiC™ preserves tissue and does not require the permanent placement of an implant in the eye. It has also been shown to be effective as both a standalone procedure and when combined with cataract surgery. Furthermore, based on preliminary data it may, potentially, offer better clinical outcomes than any other currently available MIGS procedure.

Put simply, ABiC™ is a highly effective MIGS procedure that flushes out the eye's natural outflow channels, without damaging tissue and without leaving behind a stent or shunt.

ABiC: BENEFITS AT A GLANCE

1. Comprehensive: treats trabecular meshwork, Schlemm's canal and collector channels
2. Opens outflow system behind the trabecular meshwork, thus ensuring better aqueous outflow
3. No permanent implant or stent
4. On label – patient does not have to pay additionally out of pocket
5. Patient selection criteria are similar to current MIGS procedures
6. Minimal complications/side effects

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