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Combined Circumferential Canaloplasty and Trabeculotomy Ab Interno with the OMNI Surgical System

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Abstract

In the normal eye the conventional outflow pathway is responsible for the majority of aqueous humor egress and plays a key role in the maintenance of healthy intraocular pressure. However, in the glaucomatous eye pathologic changes to the pathway in the trabecular meshwork, Schlemm's canal, and collector channel ostia can introduce abnormal resistance to outflow with consequent increase in intraocular pressure. The OMNI Surgical System (Sight Sciences, Menlo Park, CA USA) is a relatively new surgical device and the only one that combines two ab interno minimally invasive treatments in a single procedure, canaloplasty and trabeculotomy. This new technology allows surgeons to address outflow resistance wherever it may be, both proximally (juxtacanalicular trabecular meshwork and inner wall of Schlemm's canal), and distally (Schlemm's canal and the collector channels). This review covers several recent clinical studies of the OMNI device with the aim of collating what is known and what remains to be learned.

Keywords: *canaloplasty, trabeculotomy, MIGS, minimally invasive glaucoma surgery, glaucoma, OMNI, viscodilation, ab interno*

Introduction

Management of glaucoma is directed at lowering intraocular pressure (IOP) as elevated IOP is the cardinal risk factor and the only treatable one for both development and progression of the disease [1-3]. Prior to the advent of minimally (or micro) invasive glaucoma surgery (MIGS), first-line treatment was generally medical (one or more topical ocular hypotensive drugs) or in some cases laser trabeculoplasty [4] with surgery reserved for eyes with IOP control inadequate to prevent progression despite maximum tolerated medical therapy. However, treatment norms have been evolving over the past 10-15 years. The introduction of MIGS devices and procedures has lowered the threshold for surgical intervention such that it is now an accepted early disease treatment option [4,5].

MIGS share several features in common: an ab interno approach, small clear corneal incision with minimal tissue trauma; rapid patient recovery; good safety profile with generally mild adverse events; demonstrable IOP-lowering efficacy [6]. Despite these commonalities, MIGS approaches to IOP lowering are a diverse group including technologies aimed at aqueous suppression (e.g., cyclodestructive laser procedures), at enhancing outflow through conventional or uveoscleral pathways, or through creation of a filtration bleb. Most currently available MIGS target the conventional (or canalicular) outflow pathway.

The OMNI Surgical System (Sight Sciences, Inc., Menlo Park, CA, USA) is a relatively new addition to the MIGS armamentarium used to perform circumferential viscodilation and trabeculotomy. Although OMNI itself was introduced in early 2018, from a procedural standpoint, there is a rich and deep evidence base for both canaloplasty and trabeculotomy [7]. OMNI, like the trabecular implants, treats the conventional outflow pathway but is differentiated in that it addresses outflow resistance at multiple points in the pathway including trabecular meshwork (TM), Schlemm's canal (SC), collector channels (CC) and not simply proximally (TM) (Figure 1). This paper reviews recently published clinical study data for the OMNI surgical system and discusses future research directions that would further clarify the therapeutic utility of OMNI. A comprehensive review of the foundational procedures (i.e. canaloplasty and trabeculotomy) is beyond the scope of this mini-review. The interested reader is encouraged to access recent reviews that cover this material [7,8].

The OMNI Surgical System has been 510k cleared (original clearance Dec 21, 2017; updated August 11, 2020 and March 1, 2021) by the US Food and Drug Administration (FDA).

The OMNI device is used by surgeons to viscodilate SC and cut trabecular meshwork tissue with the long flexible microcatheter. While the microcatheterization of SC for viscodilation or trabeculotomy has been performed using other types of devices, the OMNI allows the procedures to be performed sequentially in the same surgical session using a single corneal incision, a single device, operated by a single operator (i.e. the surgeon) using either hand in either eye in conjunction with cataract extraction or as a standalone intervention in phakic or pseudophakic eyes. In addition, the OMNI device delivers a precise and controlled amount of viscoelastic reducing inter-surgeon and inter-procedure variation.

The OMNI device is designed to allow repeated advancement/retraction of the microcatheter, to allow the surgeon to complete the intended procedure(s) either for 360 degrees or partial treatment as per surgeon's discretion and patient's medical needs. The microcatheter can be fully cycled (i.e. advanced/retracted) up to 5 times (i.e. 5 full cycles of 20 mm each).

OMNI dispenses fluid on the principle of exchanging volumes much like a syringe. The handheld instrument includes a cannula, a microcatheter that can be used for viscodilation or tissue cutting, an internal reservoir, a plunger tube and finger wheel(s). The

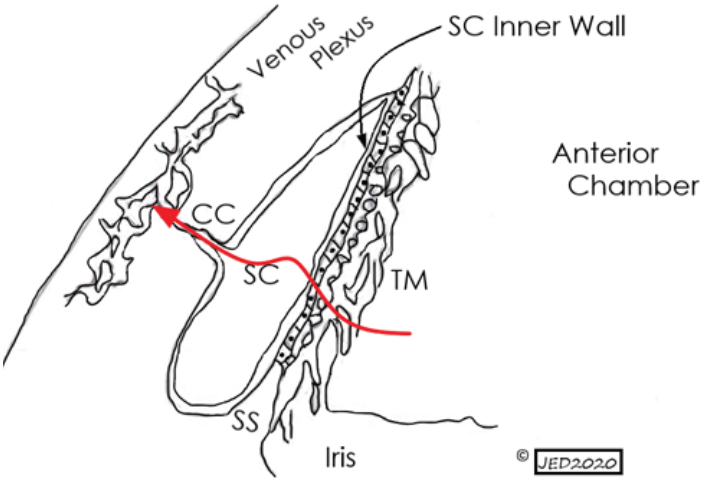

Figure 1: *Artist's diagrammatic rendering of the conventional (canalicular) outflow pathway (not to scale). SC, Schlemm's canal. TM, trabecular meshwork. CC, collector channel. SS, scleral spur. Red arrow indicates flow of aqueous humor. (Figure by the authors)*

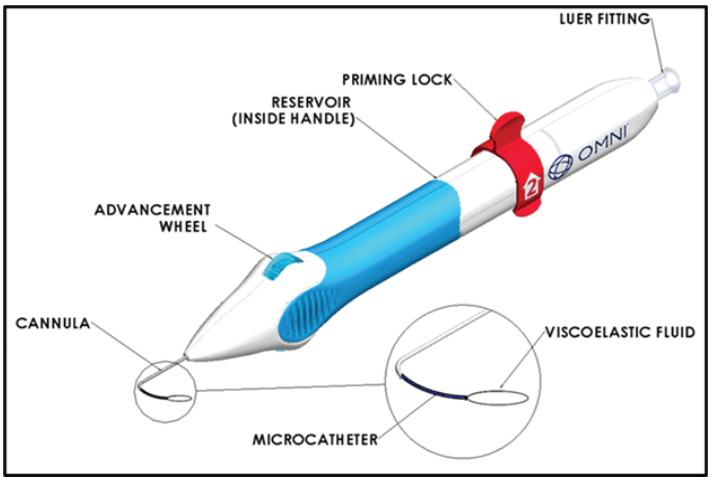

Figure 2: *The OMNI Surgical System (Figure used with permission from Sight Sciences, Inc)*

finger wheel(s) on the handle of the device are used to advance the plunger tube into the viscoelastic fluid reservoir thereby dispensing viscoelastic fluid. The finger wheel(s) are placed on both sides of the handle facilitating viscoelastic delivery in either the left or right eye using either hand. (Figure 2) displays the OMNI product and its components.

The OMNI device is placed within the eye and advanced across the anterior chamber to the iridocorneal angle under gonioscopic visualization to viscodilate SC and/or to cut trabecular meshwork. The cannula tip is used to pierce the trabecular meshwork and the finger wheel is rotated to advance the microcatheter into SC. To perform canal viscodilation once the canal has been micro catheterized, the microcatheter is retracted back into the cannula using the finger wheel to automatically dispense viscoelastic into the canal. To perform trabeculotomy the microcatheter is again inserted into the canal and the cannula is then withdrawn from the corneal incision causing the microcatheter to cut through the TM and unroof SC upon cannula withdrawal.

The underlying logic for the OMNI is based on the compartmentalization of outflow resistance in the conventional outflow pathway. A large component of the resistance resides proximally, i.e., in the juxtacanalicular TM and the inner wall of SC. Proximal resistance has been measured to account for between 50% and 71% of total resistance to outflow [9-11] leaving a substantial portion of resistance in distal structures (i.e. SC,the CC, and deep scleral plexus). Bench studies of enucleated normal and primary open angle glaucoma (POAG) human eyes showed that the cross-sectional area of SC averages 54% lower and mean outflow facility 55% lower in POAG eyes compared to normal eyes, implicating canal collapse and/or narrowing as a source of resistance [12]. The CC ostia may also contribute to resistance. In a bovine eye model, increasing IOP resulted in herniation of the inner wall and juxtacanalicular tissue into the ostia of the CC [13]. Addressing resistance, both proximal and distal, by combining viscodilation with trabeculotomy is appealing theoretically and practically. A single surgery with a minimally invasive approach provides maximum safety and minimum tissue disruption. While OMNI is a relatively recent development that uniquely permits both canaloplasty and trabeculotomy to be performed with the same instrument in the same surgical session, the component procedures have been performed for many years and are the subject of a substantial body of literature. The following sections are not intended to provide a comprehensive review of the published literature for canaloplasty and trabeculotomy. Rather they highlight publications generally recognized as important studies for both of these procedures.

Canaloplasty

Canaloplasty is a procedure that can trace its origins to non-penetrating ab externo techniques such as deep sclerectomy [14] and viscocanalostomy [15]. However, with viscocanalostomy it was believed that enhanced outflow was achieved through creation of a "Descemet's window" and a "scleral lake" from which aqueous would flow into the cut ends of SC which had been dilated 4-6 mm in either direction with viscoelastic. In contrast, canaloplasty involves the dilation of the full circumference of SC using a microcatheter and was originally an ab externo procedure surgically similar to viscocanalostomy [16]. In this early iteration of canaloplasty a tensioning suture was placed in SC which applied inward tension on the TM with the idea that this might increase TM permeability [16].

The idea that a tensioning suture might maintain the distension and stretch of the TM thereby increasing the facility of outflow proximally through the TM seems logical. However, Smit and Johnstone demonstrated in ex vivo primate and human cadaver eyes that viscodilation alone without the use of a tensioning suture created significant and measurable disruptions of the inner wall of SC that would relieve proximal (i.e., juxtacanalicular TM and inner wall of SC) resistance to outflow [17]. In Lewis' seminal paper describing the ab externo approach to canaloplasty, 74 of 94 patients treated with ab externo canaloplasty had a tensioning suture placed while 20 did not. There appeared to be little if any difference in the IOP reductions between all patients (with or without suture) and for those with the suture at any of the reported time points (-9.4 mmHg and -8.6 mmHg, respectively at 12 months) [16]. Consistent results were reported for 24 months where the group of all patients (excluding combined with cataract surgery) with or without a suture went from a baseline of 23.7 mmHg to 16.6 (-7.1 mmHg) and 23.2 mmHg to 16.3 mmHg (-6.9 mmHg) for cases with successful suture placement. While

there was no apparent additional IOP-lowering benefit due to a tensioning suture, it did appear that when a suture was present the amount of TM distension that could be visualized was related to IOP-lowering efficacy [18]. However, in a study specifically designed to assess the relationship between distension of the TM (measured with both OCT and UBM) and IOP reduction, no conclusive relationship was documented [19].

Canaloplasty ab externo requires a conjunctival dissection, the creation of a partial thickness scleral flap, and a second deeper flap nearly to the ciliary body/choroid to expose and unroof SC. The current ab interno approach is considerably less disruptive to ocular tissues as the anterior chamber angle is accessed through a clear corneal incision (~2 mm) and then SC via a small goniotomy created with the tip of a microcatheter/cannula. Mechanistically there is no difference in the procedures. Canaloplasty ab externo and canaloplasty ab interno both decrease resistance to aqueous humor outflow in the distal outflow system (i.e., SC, CC ostia and CC) through circumferential viscodilation using viscoelastic fluid. Direct head-to-head comparison of the two approaches was made in a paired eye study (each patient served as his/her own control)

Table 1: *Published Canaloplasty Studies; Ab Externo and Ab Interno*

Reference	Procedure	Diagnosis	N	Baseline IOP	IOP at Last Follow-up (length of follow-up)	Percent Change	Medication Change
AB EXTERNO (N= 777; % IOP reduction averaged across studies: -29%)							
Cameron et al. 2006 [23]	180° to 360°	POAG	56	25.1±8.7	16.7±4.4 (6 month)	-33.5	-1.9
Voykov et al. 2015 [24]	Ab externo 360° w/suture	OAG	18	25.7±6.6	14.2±3.4 (60 month)	-44.7	-1.7
Lewis et al. 2009 [18]	Ab externo 360° w/suture	OAG	127*	23.6±4.8	16.0±4.2 (24 month)	-32.2	-1.4
Gallardo et al. 2018 [20]	Ab externo 360° w/suture	POAG	12	18.1±3.7	13.5±2.2 (12 month)	-25.4	-1.5
Vastardis et al. 2019 [25]	Ab externo 360° w/suture	POAG	Standalone Advanced 172 Moderate 51 Early 39 With Phaco Advanced 212 Moderate 51 Early 39	 19.2±6.4 20.7±5.0 21.3±5.7 19.4±7.5 19.5±5.9 19.4±7.3	(12 month) 13.3±4.5 15.2±4.0 18.1±3.8 14.5±4.7 ~14.5†† ~14.5††	 -30.7 -26.5 -17.7 -25.3 -25.6 -25.2	 -2.4 -2.1†† -2.0†† -2.4 -1.9†† -2.0††
AB INTERNO (N= 443; % IOP reduction averaged across studies**: -28%)							
Gallardo et al. 2018 [20]	Ab interno 360°	POAG	12	18.5±3.4	13.8±2.2 (12 month)	-25.4	-1.6
Körber 2018 [26]	Ab interno 360°	POAG	20†	18.5±3.4	15.5± 2.4 (9 month)	-16.2	-2.1
Davids et al. 2019 [27]	Ab interno 360°	POAG	 36 Standalone 20 With Phaco 16	 19.8±4.1 19.7±4.1 20.2±4	(12 month) 13.8±3 14.3±2.5 13.6±3.6	 -30.3 -27.4 -32.7	 -0.5
Ondrejka and Körber 2019 [22]	Ab interno 360°	POAG	IOP ≥18 mmHg 72 IOP <18 mmHg 34	 24.6±7.1 14.9±1.8	(12 month) 14.6±2.8 13.6±2.3	 -40.7 -8.7	 -1.9 -1.6
Tracer et al. 2019 [28]	Ab interno 360°	OAG	IOP ≥18 mmHg 111 IOP <18 mmHg 69	 22.0±5.5 14.3±2.3	(12 month) 17.2±5.1 15.4±4.1	 -21.8 7.7	 no change -0.5
Hughes and Traynor 2020 [29]	Ab interno 360° or 180°	OAG	89	24.5±8.3	15.8 ± 2.5 (18 month)	-35.5	-0.8

*Includes 19 patients where no suture was used and 37 eyes where procedure was combined with phacoemulsification cataract surgery; †n=6 at 9 months; ††data not published, medication change estimated from published figure; ** excludes patients from studies where treatment goal was NOT IOP reduction (i.e. where baseline IOP <18 mmHg).

conducted by Gallardo et al [20]. One eye of each patient was treated with ab externo canaloplasty and a tensioning suture while the other eye received ab interno canaloplasty. Preoperative IOP and medication usage were essentially identical between the ab externo and ab interno groups (18.1 mmHg on 2.4 medications, 18.5 mmHg on 2.4 medications). 12 month results for the two groups remained identical (13.5 mmHg on 0.9 medicatons; 13.8 mmHg on 0.8 medications) suggesting that the IOP-lowering efficacy of SC viscodilation is not dependent on the surgical approach in accessing the canal and also underscoring the irrelevance of the tensioning suture [20].

Comparison of safety between ab externo and ab interno canaloplasty is somewhat difficult because of limited head-to-head study data, and differences in the reporting of adverse events (AE) between the generally case series studies that do exist. The Gallardo et al. paired eye study reported the following adverse events for the ab externo group: IOP spikes thought to be related to peripheral iris obstruction of the Descemet's window (16.7%), and a trace filtration bleb at the site of the scleral dissection (8.3%). No AE were recorded for the ab interno eyes aside from microhyphemas which were seen in both groups and all resolved within the first postoperative week [20]. In a three-year study of 157 eyes treated with the ab externo procedure, Lewis et al reported a 12% incidence of microhyphema, 0.6% incidence of hypotony, and a 2.5% incidence of bleb formation [21]. With canaloplasty ab interno, Ondrejka and Körber reported a similar incidence of hyphema (13%) but aside from one eye with fibrin in the pupillary plane, no other AE [22]. Taken together it seems reasonable to conclude that the safety of the ab interno procedure is better owing to the absence of scleral dissection.

Data supporting the efficacy of canaloplasty for reduction of IOP is listed in (Table 1).

Trabeculotomy

360° trabeculotomy originated as a pediatric procedure and like canaloplasty, was originally performed ab externo [30]. Circumferential ab externo trabeculotomy came with several advantages over other trabeculotomy procedures. Fully opening SC to the anterior chamber resulted in a higher proportion of surgical successes [31], which aligns with results from study of the extent of trabeculotomy and outflow resistance in perfused human eyes [10]. Ab-interno approaches such as gonioscopy-assisted transluminal trabeculotomy (GATT), or TRAB360 and OMNI have largely supplanted ab externo trabeculotomy except in cases where corneal opacity does not allow direct visualization. The ab-interno approach avoids the tissue trauma of the ab externo procedure while maintaining the effectiveness. (Table 2) summarizes circumferential trabeculotomy data from recent published studies.

Canaloplasty Combined with Trabeculotomy: OMNI

Voykov et al. demonstrated additional IOP reduction by using the tensioning suture placed during canaloplasty to perform an ab interno 360° trabeculotomy in patients previously treated (1-54 months) with ab externo canaloplasty but who were inadequately controlled [36]. Similarly, Seuthe et al. showed a 41.2% reduction in IOP and reduction in medications from 2.7 to 1.6 [37]. In these studies, trabeculotomy was performed after canaloplasty, but only after many months, and only when there was insufficient IOP reduction. Combining the two different modalities and simultaneously addressing multiple points of outflow resistance could therefore prove more effective than either alone.

The OMNI device can perform both 360° canaloplasty and trabeculotomy in a single surgical session using a single implant-free device and through a single small (< 2 mm) clear corneal incision. Brown et al. reported short-term results (mean follow-up of 4.1 months) for 41 eyes where the OMNI procedure was combined with phacoemulsification cataract surgery [38]. IOP reduction was 5.6 ± 4.5 mmHg when all eyes were considered however the cohort included eyes with baseline medicated IOP as low as 8 mmHg. When results were stratified by baseline IOP, the eyes that were not well controlled at baseline (IOP ≥ 22 mmHg) achieved a nearly 10 mmHg reduction (9.6 ± 4.5 mmHg); 100% of eyes with baseline IOP > 16 mmHg had an IOP reduction following OMNI. Interestingly, the authors had previously carried out a nearly identical analysis of eyes implanted with the iStent Inject [39]. In this study the mean IOP reduction for all eyes (N = 47) was 3.2 mmHg and for the high IOP cohort was 7.5 mmHg.

Klabe et al. [40] treated 38 eyes of 27 patients with the OMNI device as a standalone procedure. All patients had mild to moderate OAG which was medically uncontrolled. Of interest, most of these standalone procedures (74%) were in phakic eyes. IOP was reduced by 10.1 mmHg at 12 months, from a preoperative baseline of 24.6 mmHg on 1.9 medications. Nearly all eyes (97%) had at least a 20% reduction in IOP and 63.3% were medication free.

Hirsch et al. [41] conducted a retrospective multicenter study including 12 surgeons across eight states in the United States. The study included 81 patients treated with OMNI in combination with cataract surgery and having 12 months of follow-up. Primary success was met by over 80% of patients. Further analysis was stratified by baseline IOP; >18 mmHg (Group 1), ≤ 18 mmHg (Group 2). Mean IOP was reduced in Group 1 (21.9 to 15.1 mmHg, $p < 0.0001$), and remained controlled in Group 2 (14.1 to 13.4 mmHg, $p = 0.3177$). Medications went from 2.0 ± 1.3 to 1.1 ± 1.1 (Group 1) and from 1.6 ± 1.3 to 0.9 ± 1.2 (Group 2). Adverse events were typical for cataract or angle surgery. Mild inflammation (11%), IOP spikes (5%), hyphema (4%). Subgroup analysis of patients with baseline IOP > 22 mmHg showed a mean reduction of 8.9 mmHg.

A similar study was conducted by Vold et al. but with the goal of evaluating OMNI effectiveness when used as a standalone procedure in pseudophakic eyes [42]. In this study primary success was met by 73%. Analysis was similarly stratified by baseline IOP (≤ 18 mmHg and > 18 mmHg). Mean IOP was reduced in Group 1 (21.8 to 15.6 mmHg, $p < 0.0001$), and remained controlled in Group 2 (15.4 to 13.9 mmHg, $p = 0.24$). Medications went from 1.7 ± 1.3 to 1.2 ± 1.3, $P = .024$ (Group 1) and from 2.0 ± 1.3 to 1.3 ± 1.3, $p = .003$ (Group 2). Subgroup analysis of patients with baseline IOP > 22 mmHg showed a mean reduction of 8.6 mmHg. Adverse events were typical for the patient population undergoing angle surgery. Those reasonably related to the procedure were mild inflammation (13%), IOP spikes, (6%), hyphema, corneal edema, and BCVA loss, all (4%).

Grabska-Liberek et al. [43] reported 12-month outcomes for a case series of 17 eyes of 15 patients that continue to be prospectively followed through two years postoperatively. Mean IOP was reduced from 20.4 mmHg to 12.7-13.7 mmHg through 12 months of follow-up ($p<0.001$ at every time point) and mean ocular hypotensive medication use was reduced from 2.5 to 0.1-0.6 ($p<0.001$ at every time point). IOP reductions in eyes undergoing standalone surgery were approximately 2-4 mmHg greater at each time point compared to eyes undergoing surgery combined with phacoemulsification however the authors note that this may be

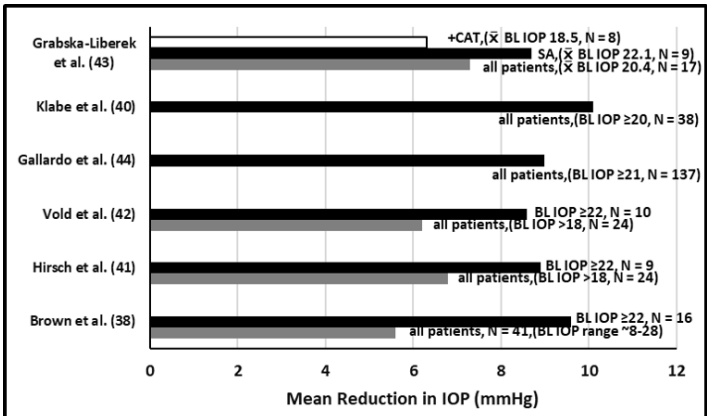

Figure 3: *Mean IOP reduction from clinical studies of the OMNI Surgical System. +CAT = OMNI procedure combined with cataract surgery; BL = baseline (preoperative); SA = standalone OMNI procedure. Grabska-Liberek et al. is a single center prospective case-series without medication washout. Klabe et al., and Brown et al. were single center retrospective case-series without medication washout. Klabe et al. included only standalone cases, Brown et al. included only combined with cataract surgery cases. Hirsch et al. was a multicenter retrospective single arm study without washout and including only combined with cataract surgery cases. Vold et al. was a multicenter retrospective single arm study without washout and including only standalone cases. Gallardo et al. was a prospective, multicenter, historical controlled study including medication washout and only in combination with cataract surgery.*

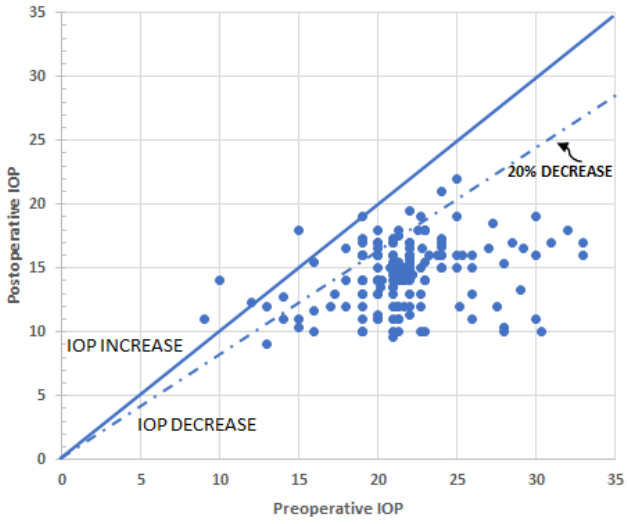

Figure 4: *Scatterplot of preoperative IOP versus postoperative IOP (last follow-up) for eyes from five studies where patient level data was available. N = 159. Data from references 38, 41-44. Diagonal represents line of no change; dashed line represents a 20% decrease in IOP.*

related to a higher baseline IOP in the standalone procedure eyes (22.1 versus 18.5 mmHg).

A prospective, historical-controlled study employing a pre-operative medication washout was conducted by Gallardo et al. [44]. The study was designed to closely follow the eligibility criteria used for the pivotal randomized controlled trials for MIGS implants (e.g. [45]). The study enrolled and treated 137 patients. Mean diurnal IOP after washout was 23.8 ± 3.1 mmHg at baseline. At month 6, 78% (104/134) were medication free with IOP of 14.2 mmHg, a mean reduction of 9.0 mmHg (38%). 100% (104/104) had a ≥ 20% reduction in IOP and 86% (89/104) had IOP ≥ 6 and ≤ 18 mmHg. The mean number of medications at screening was 1.8 ± 0.9 and 0.6 ± 1.0 at month 6. Similar to the other OMNI studies, adverse events included transient hyphema (4.6%) and IOP elevation ≥10 mmHg (2%).

While cross-study comparisons should be made with abundant caution due to the different patient populations, the eligibility criteria for the Gallardo et al. study [44] was, as noted above, intentionally the same as for the MIGS implant registration trials for Hydrus and iStent inject. The IOP reduction at 6-months for OMNI in patients on zero medications of 9.0 mmHg compares favorably with the 7.0 mmHg reduction observed at 24 months for iStent inject [46] and the 8.5 mmHg reduction for Hydrus at 12 months [45].

In a recent report at the American Glaucoma Society annual meeting (March 2021), Kalarn et al. reported results of a retrospective chart review of patients (majority with severe POAG) treated with either the Kahook Dual Blade or with OMNI. Six-month outcomes favored OMNI (-3.0 mmHg vs. -1.33 mmHg from baselines of 17.9 and 17.3; decrease of about 0.5 medications in both groups from 2.8 and 2.7, respectively) although the study was not adequately powered to demonstrate statistical significance.

The consistency of the results observed across these OMNI studies is striking (Figure 3). While there is some diversity in study designs (retrospective, prospective case series, prospective controlled with washout) and in the included cases (standalone, combined with cataract surgery) the IOP reductions achieved are remarkably consistent when similar baseline IOP subgroups are considered. In the subgroups with a baseline IOP of at least 20 mmHg, mean reduction in IOP was between about 8.5 – 10 mmHg for all six studies including a combined 219 eyes. It is noteworthy that the Hirsch and Vold study patient populations were nearly identical in demographics and glaucoma severity differing only in lens status (phakic with cataract and pseudophakic, respectively) [41,42]. Baseline IOP and medication usage was also similar as was the IOP and medication reduction at 12 months suggesting that in these patients (mild-moderate glaucoma with open-angles) cataract surgery contributes little to the observed IOP-lowing effect observed after treatment with the OMNI. Adverse events observed in all of these studies were mild, transient and self-limiting, and consistent with other MIGS studies.

It is often true that a therapeutic treatment (pharmaceutical or surgical) is not universally efficacious. This is why various responder analyses are often employed. Perhaps the best measure of response to treatment for a presumptive IOP-lowering therapy is change in IOP. A scattergram plot can be employed to demonstrate visually the overall response to treatment. When all available patient data are plotted (pre-op IOP abscissa, post-op IOP ordinate) and a 45-degree diagonal is drawn, points above the diagonal would represent a post-op increase in IOP, no change if on the diagonal, and a decrease in IOP if below the diagonal. For the 5 studies where patient level data could be obtained, 155 of 159 (97.5%) eyes had a decrease in IOP at last follow-up and the majority (120, 75%) were decreased at least 20% (Figure 4).

Except for Gallardo et al. [44] all of the other OMNI studies measured medicated IOP at both baseline and the last follow-up. In general, medication usage was significantly decreased between baseline and last postoperative follow-up for all of the studies (Table 3). There is some variability in the extent of medication

Table 2: *Published Trabeculotomy Studies; Ab Externo and Ab Interno*

Reference	Procedure	Diagnosis	N	Baseline IOP	IOP at Last Follow-up (length of follow-up)	Percent Change	Medication Change
AB EXTERNO							
Chin et al. 2012 [32]	Ab externo 360 °	OAG	43	27.8±12.2	12.9±2.5 (18 month)	-53.6	-2.3
AB INTERNO							
Grover et al. 2018 [33]	Ab interno 360 °	POAG			(24 month)		
		Phakic	46	26.0±6.9	15.6±5.7	-40	-1.4
		w/Phaco	36	22.5±5.4	14.1±3.2	-37.3	-1.9
		Pseudo	37	24.7±6.2	15.8±7.4	-36	-1
		Other*					
		Phakic	30	30.9±10.0	13.8±4.5	-55.3	-2
		w/Phaco	25	25.7±6.3	14.5±4.4	-43.6	-1.8
		Pseudo	24	26.8±7.9	13.4±4.7	-50	-2.1
Sarkisian et al. 2019 [34]	Ab interno 360 °	POAG (83%)	81	23.7±6.3† (12 month)	15.7±5.5†	-33.8	-0.6
Areaux et al. 2020 [35]	Ab interno 360 °	Pediatric	N	30.9	20.3	-34	-1
			Success Rate††				
		PCG	21				
			81%				
		JOAG	6				
		GANASDS	83%				
			8				
		GANOA	50%				
			20%				
		GAAC	4				
			50%				
		GFCS	5				
			60%				

OAG: Open-Angle Glaucoma; POAG: primary OAG; PCG: Primary Congenital Glaucoma; JOAG: Juvenile OAG; GANASDS: Glaucoma Associated with a Nonacquired Systemic Disease or Syndrome; GANOA: Glaucoma Associated with a Nonacquired Ocular Anomaly; GAAC: Glaucoma Associated with an Acquired Condition; GFCS: Glaucoma Following Cataract Surgery.

*Other included chronic angle closure, pseudoexfoliation, pigment dispersion, uveitic, mixed mechanism. Other OAG, trauma, steroid

†Standard deviation estimated from error bars in published figure

††Success defined as postoperative IOP ≤ 24 mmHg with or without medications and no additional surgery

reduction, and this is most probably related to individual surgeon preferences and/or lack of standardized protocols for medication re-introduction. Some surgeons prefer to discontinue all ocular hypotensive medications at the time of surgery adding medication, as needed, depending on post-operative IOP. See for example Grabska-Liberek et al. where baseline medications were 2.6 but 0.06 (zero for all but one eye) at week 1 [43]. In contrast, some surgeons take a more conservative approach continuing all preoperative medications post-surgically and discontinuing incrementally as warranted by IOP at follow-up visits [38].

Secondary Open-Angle Glaucoma: Pseudoexfoliation and Pigmentary

Pseudoexfoliation glaucoma (PXG) and pigmentary glaucoma (PG) are forms of open angle glaucoma where pseudoexfoliative material, in part derived from the anterior lens capsule, or pigment derived from the iris pigmented epithelium, are implicated or at least contribute to the development of glaucoma [47]. In general, IOP in these glaucomas is more challenging to control, especially for PXG [47]. For example, Grover et al. included PXG and PG patients (pooled as secondary open angle glaucoma [SOAG]) in a 24-month study of GATT [33]. They found that while these patients tended to have higher pre-operative baseline IOP and under treatment with more medications then the POAG patients in the study, they also had greater postsurgical IOP reductions [33].

There is limited data available on the performance of OMNI in PXG and PG. The Hirsch et al. [41] and Vold et al. [42] studies included only six patients diagnosed with PXG and one with PG. Demographics for the PXG patients were generally unremarkable when compared to the overall pooled study populations; 73 years of age versus 75 for all patients, 67% versus 54% female, 100% white versus 79%. Glaucoma may have been slightly more advanced as the mean visual field mean deviation was -6.6 dB compared to -5.4 overall. Mean baseline IOP in this subgroup was slightly lower (16.2 mmHg compared to 18.6 mmHg) but required more medication (2.7 medications on average versus 1.9). Interestingly, while the 12-month percentage reduction in IOP for these SOAG patients was similar to the overall group, medication reduction was notably higher (-69% versus -39%) with 5 of 7 medication-

Table 3: *Change in Ocular Hypotensive Medications Following OMNI*

Reference	Procedure	Diagnosis	N	Baseline Medications (mean, SD)	Medications at Last Follow-up (mean, SD) (length of follow-up)	Percent Change	Medication Change
Hirsch et al. 2020 [41]	OMNI +catract surgery Cohort 1 (BL IOP>18) Cohort 2 (BL IOP</=18)	OAG	 24 57	 2.0 ± 1.3 1.6 ± 1.3	 1.1 ± 1.1 0.9 ± 1.2 (12 month)	 -45% -43%	 -0.9 -0.7
Vold et al. 2020 [42]	OMNI standalone (pseudophakic) Cohort 1 (BL IOP>18) Cohort 2 (BL IOP</=18)	OAG	 24 24	 1.7 ± 1.3 2.0 ± 1.3	 1.2 ± 1.3 1.3 ± 1.3 (12 month)	 -29% -35%	 -0.5 -0.7
Grabska-Liberek et al. 2021 [43]	OMNI, +cataract surgery and standalone	OAG	17	2.6 ± 0.7	0.6 ± 0.7 (12 month)	-77%	-2
Klabe et al. 2021 [40]	OMNI standalone (74% phakic)	OAG	38	1.9 ± 0.7	0.6 ± 0.6 (12 month)	-68%	-1.3
Gallardo et al. 2021 [44]	OMNI +cataract surgery	OAG	137	1.8 ± 0.9	0.6 ± 1.0 (6 month)	-67%	-1.2

OAG: Open-Angle Glaucoma, BL: Baseline

free at 12 months. Gallardo et al. [44] included 10 patients with SOAG (9 pseudoexfoliation, 1 pigmentary). Mean medicated IOP pre-operatively was similar to the overall study population (17.6 versus 17.3 mmHg) as was unmedicated washed out IOP (24.4 versus 23.7 mmHg) and preoperative medication usage (2.1 versus 1.8). The SOAG patients also resembled the overall group for visual field MD (-2.8 versus -3.7 dB) and demographically (66.2 and 68.5 years, majority female [80% and 61%]). Mean IOP at six months was 18.3 mmHg, -6.1 mmHg compared to -9.0 mmHg for the overall group, while 9 of 10 eyes (90%) remained off of medication compared to 78% for the study as a whole. The number of patients in these two studies is too small to draw definitive conclusions as to the relative effectiveness of OMNI in SOAG compared to POAG. However, what is clear is that OMNI can be effective in SOAG as well as in POAG.

Pediatric Glaucoma

While OMNI is primarily used in adult open-angle glaucoma, its combination of trabeculotomy and canaloplasty suggest utility in childhood glaucomas. Trabeculotomy ab interno (i.e. goniotomy as it was termed by Barkan) has been the treatment of choice for primary congenital and other pediatric glaucomas since it was developed in the 1930's by Otto Barkan [48]. Circumferential trabeculotomy was developed over 20 years ago for congenital glaucoma [30]. Treating the entire circumference rather than the maximum ~120 degrees possible with traditional techniques has been reported to result in better outcomes including decreasing the need for reoperation [31,49]. Areaux et al. [35] retrospectively evaluated outcomes for a group of 46 eyes with a diversity of pediatric glaucomas (Table 2) that had been treated with the TRAB360, a precursor of the OMNI lacking the canaloplasty functionality. Median age when treated was 12 months and median follow-up was 14.5 months. Overall, success was achieved in 67% of all eyes, and in 81% of those with primary congenital glaucoma. There is a single case report published of OMNI used to perform canaloplasty and trabeculotomy in an infant with glaucoma associated with Sturge-Weber. Preoperative IOP was > 30 mmHg and surgery with the OMNI was performed when the infant was 4 months of age. Through 10 months of follow-up, intraocular pressure was adequately controlled without the need for adjunctive medical therapy [50].

Conclusion

The OMNI Surgical System provides a practical approach to treating outflow resistance, wherever it may occur, in the conventional outflow pathway. Proximal (juxtacanalicular TM and inner wall of SC) as well as distal (SC and the CC) resistance are both addressed through sequential canaloplasty and trabeculotomy. True to the MIGS paradigm, the procedure is accomplished with minimal tissue trauma sparing sclera and conjunctiva; recovery is rapid, there is demonstrable efficacy, and a very good safety profile. In contrast to microstent procedures, there is no implant that could have unintended long-term consequences [51].

The OMNI has only been marketed for a few years and there is a need for additional studies. Laboratory study of the mechanism of action including the individual contributions of canaloplasty and trabeculotomy to efficacy, and angiography work confirming reestablishment of outflow could further validate the speculated mode of action (addressing three points of outflow resistance). Likewise, study of OMNI effectiveness in glaucomas of diverse etiology will better define the device therapeutically and mechanistically. Studies that will provide longer term data confirming the duration of effectiveness as well as long-term safety are currently underway. Head-to-head comparative effectiveness studies versus other MIGS technologies and ocular hypotensive drops will also help shape the evolution of glaucoma treatment in years to come. Some such studies are currently in early stages (e.g. clinicaltrials.gov IDs NCT04658095, NCT04769453) and when complete will provide valuable data allowing informed treatment decisions.

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