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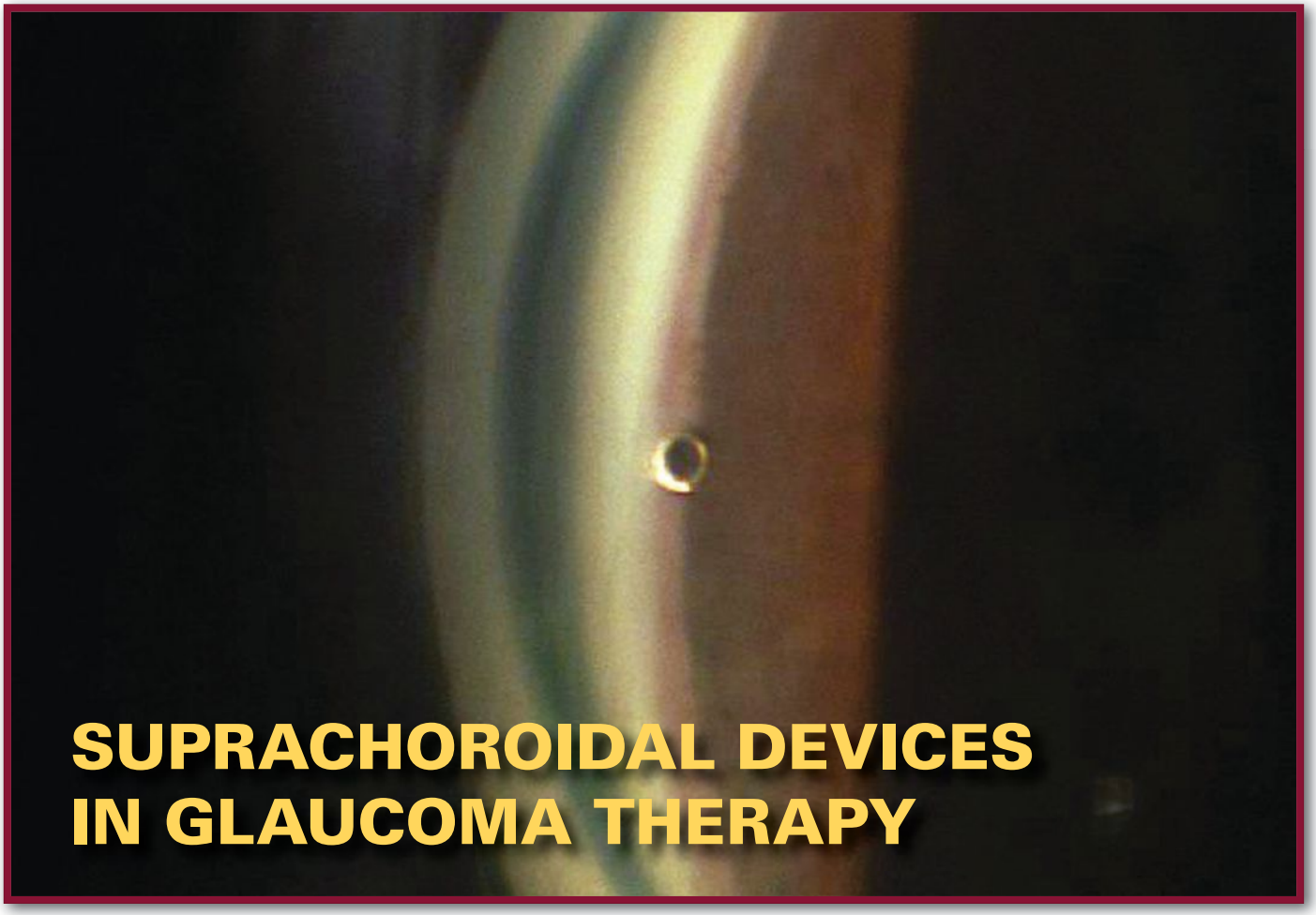

SUPRACHOROIDAL DEVICES IN GLAUCOMA THERAPY

THE NEW FRONTIER OF EPISCLERAL VENOUS PRESSURE IN GLAUCOMA TREATMENT · *Monisha M. Vora, MD; Jody Piltz-Seymour, MD*

INTRACAMERAL STEROIDS IN GLAUCOMA PATIENTS · *Michael Greenwood, MD*

OCULAR BLOOD AND AQUEOUS FLOW IN RELATION TO DEVELOPMENT OF OPEN-ANGLE GLAUCOMA · *Brian Nguyen, BS; Sahar Bedrood MD, PhD*

GLAUCOMA MANAGEMENT IN THE PREGNANT PATIENT · *Robert J. Purgert, MD, PhD; Marlene R. Moster, MD*

SUPRACHOROIDAL DEVICES IN GLAUCOMA THERAPY · *Brittany Perzia, BS; Steven D. Vold, MD*

BOLSTERING COMPLIANCE WITH PRESERVATIVE-FREE GLAUCOMA THERAPIES · *Jason Bacharach, MD*

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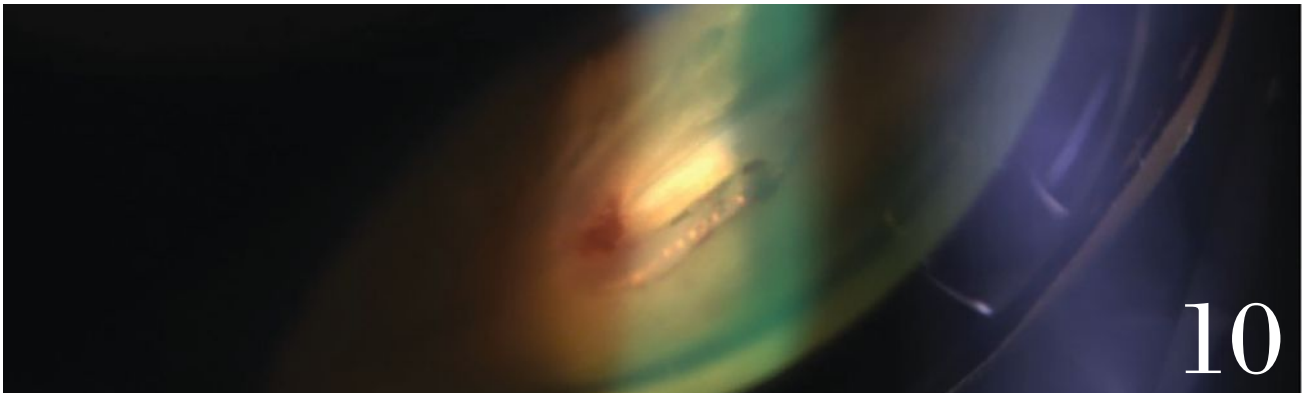
Table of Contents

DECEMBER 2020



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Features

10 Suprachoroidal Devices in Glaucoma Therapy
Brittany Perzia, BS, and Steven D. Vold, MD

20 Glaucoma Management in the Pregnant Patient
Robert J. Purgert, MD, PhD, and Marlene R. Moster, MD

24 Bolstering Compliance With Preservative-free Glaucoma Therapies
Jason Bacharach, MD

28 The New Frontier of Episcleral Venous Pressure in Glaucoma Treatment
Monisha M. Vora, MD, and Jody R. Piltz-Seymour, MD

30 Intracameral Steroids in Glaucoma Patients
By Michael Greenwood, MD

35 Ocular Blood and Aqueous Flow in Relation to Development of Open-angle Glaucoma
Brian Nguyen, BS, and Sahar Bedrood, MD, PhD

Departments

6 From the Editor
Pivot Toward Improving Your Practice

8 Glaucoma News Briefs
The latest clinical and industry news in glaucoma

57 Product Spotlight
Redesigned Probe Delivers Consistency and Simplification to IOP Reduction

59 Coding
Unbundle Modifiers

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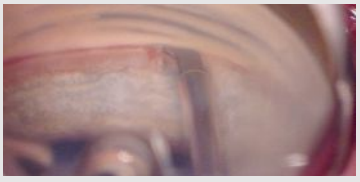
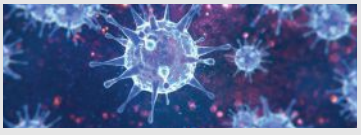


Anesthesia Considerations for Glaucoma Surgery
Omar Saeed, MPH, and Lorraine M. Provencher, MD



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Suprachoroidal Devices in Glaucoma Therapy

Is there still a role?

By **Brittany Perzia, BS,** and **Steven D. Vold, MD**

Brittany Perzia, BS, is a fourth-year medical student at Stony Brook School of Medicine in Stony Brook, New York. She reports no related disclosures.

Steven D. Vold, MD, is a glaucoma and cataract specialist and founder of Vold Vision in Fayetteville, Arkansas. He reports consultancy to and research grants from Alcon, Allergan, Glaukos, iStar Medical, Ivantis, and Sight Sciences. Reach him at svold@voldvision.com.

The efficacy and safety of topical prostaglandin medications in lowering intraocular pressure (IOP) by enhancing uveoscleral outflow are well known.[1] Consequently, significant interest and investment in developing minimally invasive stenting procedures of the suprachoroidal space have been undertaken in recent years. Despite these efforts, clinical challenges related to surgical technique, device encapsulation, device migration, chronic inflammation, and endothelial cell loss (ECL) have resulted in device failure and product recalls. With these failures, concerns regarding the ultimate effectiveness and safety of utilizing suprachoroidal-space stenting have arisen. This article will review the lessons of the past and explore possible future solutions to unlocking the potential of the suprachoroidal space in the management of glaucoma.

AB-EXTERNO APPROACH

SOLX Gold Shunt

The SOLX Gold Shunt (SOLX Inc.) is a 24-karat-gold suprachoroidal implant for the treatment of primary open-angle glaucoma (POAG) with or without cataract surgery. The shunt is implanted through scleral incision and dissection; the proximal end of the long rectangular plate is positioned in the anterior chamber to provide ingress for aqueous humor, while the distal end remains in the suprachoroidal space to promote drainage of the fluid from the anterior chamber to the suprachoroidal space.[2] The SOLX Gold Shunt received the European CE mark in 2005 and is cleared for use in Canada, although its inflammatory effects have prevented FDA approval and use of this device in the United States **(Figure 1).**

PHOTOS COURTESY OF STEVEN VOLD, MD

Figure 1. Images showing encapsulation of SOLX Gold Shunt.

Clinical Evidence

A 2009 pilot study of the SOLX Gold Shunt in 38 patients reported a success rate of 79%, which was defined as an IOP between 5 mmHg and 22 mmHg.[2] In a more recent prospective randomized clinical trial, Skaat et al compared the efficacy of 2 versions of the SOLX Gold

Shunt to the Ahmed valve over a follow-up of more than 3 years. The success rate, defined as an IOP between 5 mmHg and 22 mmHg and an IOP decrease of ≥20%, was >70% in both groups with similar efficacy to the Ahmed valve.[3] Conversely, a 2013 retrospective study reported an extremely high failure rate in the first year after Gold-Shunt surgery; 30 of 31 patients met at least 1 criterion for surgical failure, including the need for additional glaucoma surgery due to elevated IOP and device explanation in 2 patients due to inflammation and rubeosis iridis, respectively.[4]

Histologic analysis[5] and electron microscopy analysis[6] demonstrate that scar tissue formation around and obstructing the Gold Shunt's micropores may be important failure mechanisms and complications related to this device. A 2017 study in Japan showed that chronic anterior-chamber inflammation may be a late-onset complication.[7]

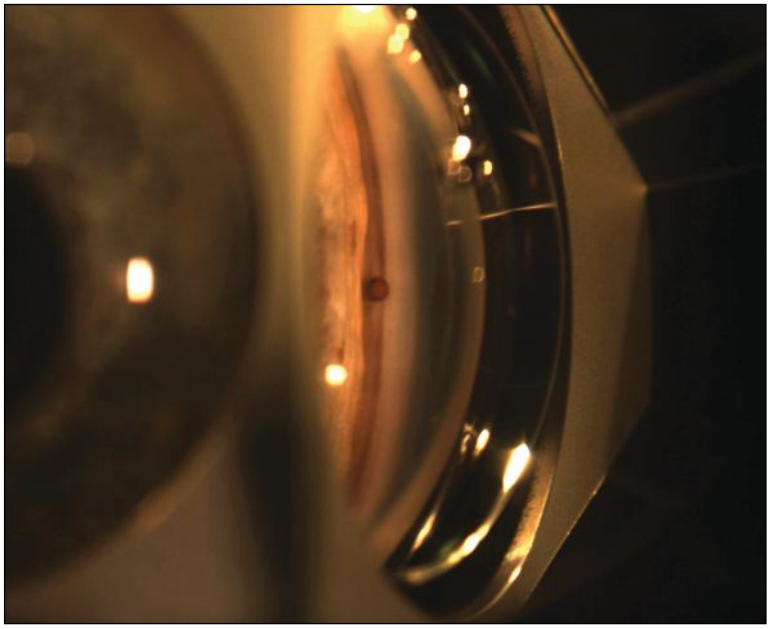

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Figure 2. Cypass Micro-Stent (Alcon).

AB-INTERNO APPROACH

Cypass Micro-Stent

The Cypass Micro-Stent (Alcon Laboratories) is a suprachoroidal device that was approved for use in the United States in 2016 **(Figure 2).** It is indicated for implantation in combination with cataract surgery for the reduction IOP in eyes with mild to moderate POAG and visually significant cataract. The Cypass implant is a fenestrated microstent made from biocompatible polyimide material, which is designed to facilitate suprachoroidal aqueous outflow once inserted into the supraciliary space. Following its insertion with a curved guidewire, the Cypass bends to follow the scleral contour along the supraciliary space. The stent's inherent stiffness and a series of retention rings at its proximal end secure the stent within the angle and the supraciliary space. As an ab-interno, minimally invasive procedure, the Cypass Micro-Stent was intended to be less traumatic than full-thickness penetration procedures and easier to implant.[8]

Table 1: Summary of the COMPASS Results[9,a]

Primary and Secondary Study Outcomes	Cypass + Cataract (n=374)	Cataract Alone (n=131)	Mean Difference	*P* Value
Patients with ≥20% mean decrease in IOP	72.50%	58.00%	14.20%	.002
Mean IOP reduction from baseline (mmHg)	-7	-5.30	1.70	<.0001
Patients who achieved IOP ≥6 mmHg and ≤18 mmHg	61.20%	43.50%	17.70%	.001

[a] Adapted from Lane S. Overview of the results from the 5 yr follow up study of the CyPass MicroStent. 2018. https://augenchirurgie.clinic/content/6-blog/20180922-alcon-nimmt-micro-stent-zur-glaukombehandlung-vom-markt/modules/2-text/cypassoverview.pdf

Clinical Evidence

The COMPASS clinical trial was a prospective, randomized, multicenter trial on the Cypass Micro-Stent for treatment of POAG in patients undergoing cataract surgery (NCT01085357 and NCT02700984; **Table 1**).[9] It is the largest interventional minimally-invasive glaucoma surgery (MIGS) study to date, which followed more than 500 subjects for 2 years. Overall, the trial showed a safe and sustained 2-year reduction in IOP and need for glaucoma medication following Cypass Micro-Stent implantation.[10] Of subjects who underwent combination Cypass insertion and cataract surgery, 72% achieved an IOP reduction ≥20% from baseline, whereas 58% of subjects who underwent cataract surgery only achieved an IOP reduction ≥20% from baseline (*P*=.002). Additionally, mean IOP reduction from baseline and mean reduction in glaucoma medication use were significantly greater in the Micro-Stent group at 2 years. There were no vision-threatening Cypass-related complications. The most commonly reported complications were transient early hypotony, transient IOP increases, and stent obstruction.[8,11]

A postapproval, 3-year extension study, COMPASS XT, was conducted to evaluate the long-term safety of the Cypass Micro-Stent in subjects who completed COMPASS. This observational, prospective study reported no sight-threatening adverse events related to the Micro-Stent. The most frequent adverse events were loss of ≥2 lines of visual acuity and visual field progression ≥2.5 dB, although there was no significant difference between the Cypass and control groups.[12] The most critical finding of the COMPASS XT study regarding safety was the statistically significant reduction in mean endothelial cell density (ECD) and statistically significant increase in the rate of ECL in the Cypass group compared to controls after 2 years. Interestingly, only device positioning was strongly correlated with increased ECL; a greater number of visualized retention rings on gonioscopic examination was associated with a higher long-term rate of ECL.[13]

PHOTO COURTESY OF STEVEN VOLD, MD

Figure 3. iStent Supra (Glaukos).

Recall and Response

On August 29, 2018, Alcon announced an immediate, voluntary global market withdrawal of the Cypass Micro-Stent, which was subsequently designated a Class I recall by the FDA.[14] The announcement followed the increased ECL observed in COMPASS XT. The FDA now recommends that eye-care providers use specular microscopy to monitor ECD in patients with Cypass implants until the rate of loss plateaus. They further advise evaluation of device positioning by counting the number of retention rings visible on the proximal end of the device; if ≥2 rings are visible, patients should be evaluated for ECL.[15]

Despite its recall, many glaucoma specialists still support the use of the Cypass Micro-Stent given its efficacy and otherwise good safety profile. It is also possible that the reported decrease in ECD following

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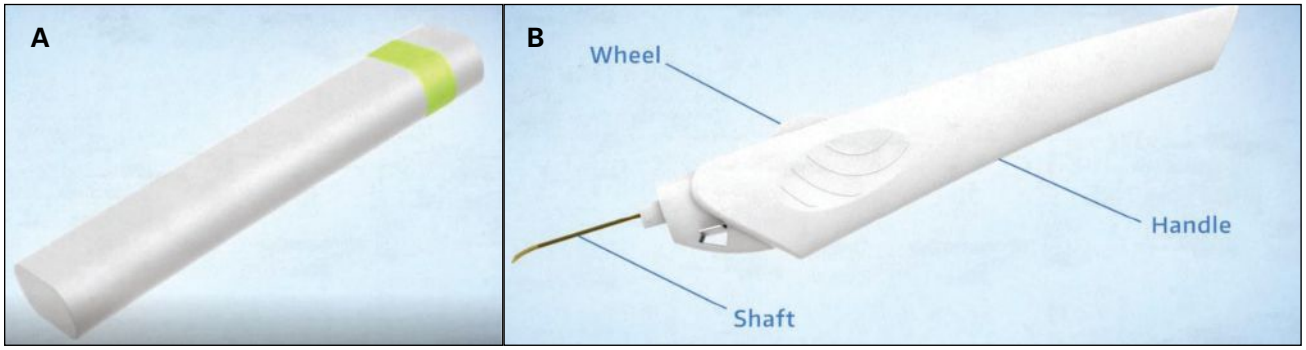


PHOTO COURTESY OF iSTAR MEDICAL

Figure 4. iSTAR MINIject device and injector.

insertion may be due to surgical technique rather than the device itself. There have been discussions surrounding the possibility of reassigning this device for stand-alone use in moderate to severe POAG as opposed to mild to moderate POAG.

iStent Supra

iStent Supra (Glaukos Corporation) is a biocompatible polyethersulfone stent with a titanium sleeve **(Figure 3).** It received the European CE mark in 2010 and is currently undergoing clinical trials in the United States. Similar to the Cypass Micro-Stent, the iStent Supra is implanted from an ab-interno approach during cataract surgery. The device is inserted into the suprachoroidal space using a pre-loaded disposable injector.

Clinical Evidence

A pilot study of the iStent was conducted by Junemann et al in 2013 on 42 eyes with advanced POAG. The reported mean preoperative IOP was 20.4 mmHg; at 12 months follow-up, after implantation and postoperative medical treatment with travoprost, mean IOP was reduced to 13.2 mmHg.[16] No major complications were reported.

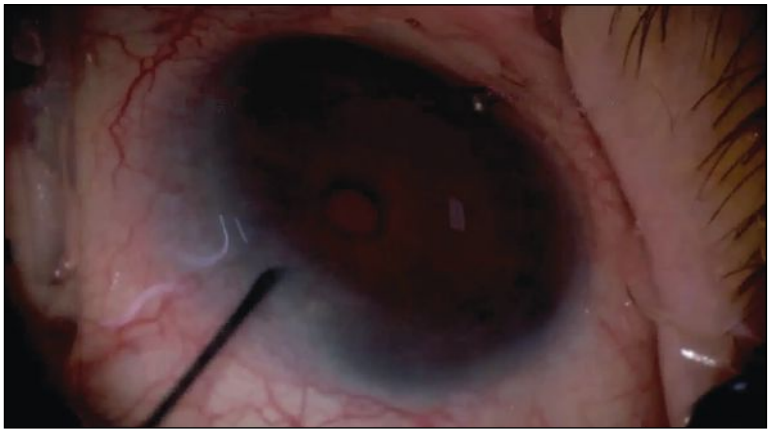
An ongoing prospective, nonrandomized, open-label study, in which patients with refractory POAG receive 2 trabecular microbypass stents, one suprachoroidal stent, and postoperative prostaglandin, has demonstrated safe IOP control at 4 years so far. A prospective, randomized, single-masked, multicenter clinical trial in the United States is currently ongoing with an estimated completion date of December 2020 (NCT01461278).

iSTAR MINIject

The iSTAR MINIject (iSTAR Medical SA) is a novel suprachoroidal device designed to overcome previous device inadequacies, with potential for reliable, powerful, and safe glaucoma treatment **(Figure 4).** Made from STAR spongy silicone structured in a microporous matrix, the MINIject is designed to conform to the eye's anatomy and promote natural flow speed without disrupting the

endothelium. The device is inserted into the supraciliary space via an ab-interno approach using a preloaded deployment wheel. It is 5 mm long with a green ring at its proximal end, which demarcates the appropriate depth of placement.[17]

This biocompatible STAR material was previously utilized in the STARflo implant, an ab-externo device that failed to hold up in clinical trials and resulted in significant ECL by the 24-month follow-up.[18] CE marking of the MINIject is expected this year. The device is still investigational in the United States **(Figure 5).**



COURTESY OF STEVEN VOLD, MD, AND ISTAR MEDICAL

Figure 5. Implantation of iStar MINIject.

Table 2: Comparison of Suprachoroidal Devices

Device (Company)	Material	Surgical Approach	Potential Uses	Efficacy	Risks	Approval Status
Cypass (Alcon)	Polyimide	ab interno	• Mild to moderate POAG • With cataract surgery	Very good. IOP-lowering effects validated in COMPASS and COMPASS-XT clinical trials.	• Significant reduction in ECD seen after 2-year follow up	• FDA approved in 2016 • Withdrawn voluntarily August 2018 • Designated Class I recall October 2018
MINIject (iSTAR Medical)	STAR silicone	ab interno	• Standalone procedure • Medically uncontrolled open angle glaucoma	Very good. Two-year outcomes of STAR I indicate powerful and safe reduction in IOP and medication usage.	• No major adverse events reported in STAR I trial • Minimal ECL loss	• CE mark expected 2020 • Investigational use in United States
iStent Supra (Glaukos)	Polyether-sulfone and titanium	ab interno	• Mild to moderate POAG • With cataract surgery • In combination with other MIGS procedures	Unclear. More published data needed.	• When used in combination with trabecular microbypass stents, ≥3-line loss of BCVA observed in 11 patients due to advacing cataract	• CE marked in 2010 • Investigational use in United States
SOLX Gold Shunt (SOLX Inc.)	24-karat gold	ab externo	• POAG, pseudoexfoliation glaucoma, refractory glaucoma • Standalone procedure or with cataract	Equivocal.	• Significant scarring and fibrosis causing stent obstruction • Difficult insertion	• CE marked in 2005 • Approved in Canada • Investigational use in United States

Clinical Evidence

There have been 2 human studies on the safety and efficacy of the MINIject to date. The STAR-I prospective, multicenter, open-label, single-arm study included 25 patients with medically refractory POAG who underwent standalone MINIject implantations. At 6 months' follow-up, mean IOP was reduced by 39%, from 23.2 mmHg on 2 IOP-lowering mediations to 14.2 mmHg on 0.3 IOP-lowering medications. No adverse events related to the device or procedure were noted.[17] Though results are not yet published, iSTAR Medical reports a mean IOP reduction of 41% at 2 years' follow-up, with 48% of patients remaining medication free at 24 months.[19]

The STAR II prospective, multicenter, single-arm trial in Europe demonstrated similar results. In 29 patients who underwent standalone MINIject implantation, 76% achieved surgical success (IOP between 5 mmHg and 21 mmHg with >20% IOP reduction from baseline) at 6 months. Mean IOP decreased by 40%, from 24.6 mmHg on 3 medications to 14.7 mmHg on 1 medication. Fifty-five percent of patients did not require any medication at 6 months. There was no significant difference in ECD at 6 months.[19]

There were 6 device-related adverse events reported in the STAR II trial: 3 cases of IOP increases and singular cases of eye pain, corneal erosion, and chorioretinal folds. In response, iSTAR Medical developed a more user-friendly, single-operator delivery tool, which will be utilized in future studies.[20]

SUMMARY

Suprachoroidal devices have evolved tremendously during the past decade **(Table 2).** Significant progress has been made in suprachoroidal device design to enhance both product efficacy and safety in glaucoma patients. Surgical techniques have continued to improve as well. Our hope is that, with continued innovation, patients will ultimately benefit from minimally invasive suprachoroidal device procedures that allow for rapid postoperative recovery, superb efficacy, and impressive safety profiles. **GP**

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