Xen and Preserflo: Their Places in the Glaucoma Toolkit

Used for lowering eye pressure when medication, laser, or other surgery has failed or has a high risk of failure, glaucoma tube shunts have enjoyed a decades-long spot in the traditional glaucoma toolkit. Then along came microinvasive glaucoma surgeries (MIGS). "These interventional glaucoma procedures are minimally disruptive to the structures of the eye, causing few intra- or postoperative complications," said Sahar Bedrood, MD, PhD, a glaucoma and cataract specialist in Pasadena, California.

Of the many MIGS devices, the Xen Gel Stent and the Preserflo MicroShunt (not yet FDA approved) come closest to approximating glaucoma drainage devices. Although the definition of MIGS keeps evolving, these two devices are slightly more invasive than classic MIGS approaches, said Michele C. Lim, MD, at the University of California Davis Eye Center in Sacramento. "They are like a hybrid technology—able to treat glaucoma along the spectrum of moderate to severe disease." Lauren S. Blieden, MD, at the Cullen Eye Institute, Baylor College of Medicine in Houston, agreed. "I think of Xen and Preserflo as relatively microinvasive, conjunctival-based surgeries that create new drains for the eye—a bit of a different animal than the angle-based MIGS such as iStent inject and Hydrus Microstent, which improve outflow."

As bleb-forming MIGS devices, it's clear that Xen and Preserflo occupy a unique position along the continuum of glaucoma care, but how do they stack up against the traditional glaucoma drainage device?

Surgical Niches

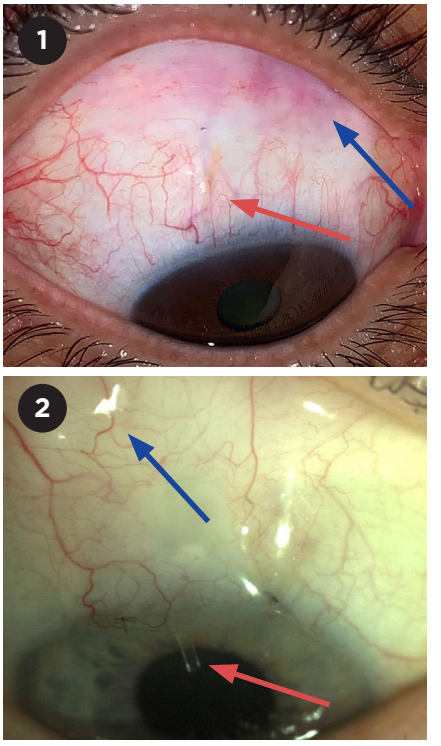
From their physical aspects to their applications, glaucoma drainage devices, Xen, and Preserflo each have distinctions.

Physical aspects. Tube shunts are composed of silicone, and the physics of their relatively large lumen size often allows for a good reduction in intraocular pressure (IOP), said Dr. Bedrood.

By contrast, the Xen is a hydrophilic tube composed of porcine dermis, with a lumen of 45 µm.[1] Approved by the FDA in 2016, the Xen is 6 mm long and just the thickness of an eyelash, Dr. Bedrood said.

Approved in Canada and Europe, the Preserflo MicroShunt is 8.5 mm long with a 70-µm lumen, and it is made of poly(styrene-block-isobutylene-block-styrene), known as SIBS, said Dr. Bedrood. Its biocompatible, thermoplastic elastomer was first used successfully in cardiac stents.[2] This led to its proposed use in glaucoma filtering surgery, said Dr. Lim, who describes the device as a tiny flute with fins. Time will tell if it's inert enough to not produce a fibrotic reaction in the eye, added Dr. Bedrood.

Candidates for glaucoma drainage devices. "Historically, tube shunts have been reserved for advanced glaucoma," said Dr. Bedrood. "The larger lumen size, more extensive surgical time, and possibility of postoperative complications are not ideal in early glaucoma." Additionally, Dr. Bedrood will use tubes in patients at risk for inflammation, such as those with uveitis or neovascular glaucoma. "These eyes will have a tendency to be more inflamed and scar down smaller tubes," like the Xen or Preserflo, she said.



THE DEVICES AT POST-OP MONTH 1. *(1) Xen implant, red arrow, with a well-formed bleb, blue arrow, and a (2) Preserflo implant, red arrow, and its bleb, blue arrow.*

(1) Courtesy of Lauren S. Blieden, MD. (2) Courtesy of Laura Baker.

BY ANNIE STUART, CONTRIBUTING WRITER, INTERVIEWING **SAHAR BEDROOD, MD, PHD, LAUREN S. BLIEDEN, MD,** AND **MICHELE C. LIM, MD.**

Challenges of tube shunts. Because a tube shunt is larger than Xen or Preserflo and its plate must be inserted 8 to 9 mm behind the limbus, said Dr. Bedrood, it requires more dissection of tissue and more manipulation of the conjunctiva, turning it into a longer procedure.

Candidates for Xen and Preserflo. Although adults of any age may be good candidates for either a glaucoma drainage device or a MIGS device such as Xen or Preserflo, patients with significant disease who are in their 40s, 50s, or 60s and in the workforce may benefit greatly from the MIGS devices because of the potential for a quicker recovery, which could get them back to work faster, said Dr. Lim. She said that suitable candidates "may have more advanced disease than a less-invasive MIGS (such as iStent or Hydrus) could help them with, but you don't want to subject them to a long recovery or the potential for serious adverse events that they might experience with a glaucoma drainage device."

Patients with early-stage glaucoma tend to have good central vision, said Dr. Bedrood, so performing a less-invasive surgery that helps maintain their good refractive status is easier for these patient to tolerate. The Xen and Preserflo devices may also help reduce glaucoma drops in patients who have developed an allergy or intolerance to their topical medications.

In addition, Dr. Blieden defines a good Xen patient as one who in earlier days would have undergone a trabeculectomy with minimal or no mitomycin-C (MMC). "I would choose Xen for people whose goal is minimal surgery, sedation, and time in the OR," she said.

Challenges of Xen and Preserflo. Despite being microinvasive, both Xen and Preserflo may pose a risk for conjunctival scarring and should be used with antifibrotic agents like MMC, said Dr. Blieden. She cautions against using Xen or Preserflo in patients who scar easily, have active lifestyles like swimmers or other athletes, or have to wear contact lenses. "These are cases where you may not want a conjunctival bleb," she said.

On the upside, both devices are made of material that limits postsurgical inflammation, and they have a valveless, flow-limiting design that decreases the risk of hypotony.[3] "I tell all of my patients that the most common "risk" of these (or any) glaucoma surgeries is that they may need another intervention later to control their disease—whether drops, laser, or more surgery," said Dr. Blieden.

The Xen Procedure

"I find Xen to be a really robust step before doing a trabeculectomy, and it doesn't preclude me from doing either a trab or a tube shunt later on," said Dr. Blieden.

Ab interno versus ab externo. For Xen, the on-label approach is ab interno. Surgeons may perform the procedure alone or at the same time as a cataract surgery.[4] "You go through the anterior chamber using the same type of incision as you would for cataract surgery, and then insert the device through the angle and out underneath the conjunctiva," said Dr. Bedrood. Many ophthalmologists are now adopting off-label ab externo technique, she said. (See "More Online" for video of each technique.)

"I had a hate-love relationship with Xen when it first came out," said Dr. Blieden. "I disliked the ergonomics of the injector with the ab interno approach. But when Won Kim, MD, popularized the ab externo approach, I decided to try it and now do all Xens this way." This type of placement can be performed with or without conjunctival dissection.[1]

The procedure. Surgeons perform the ab externo procedure under local anesthesia.[4]

Using a superior peripheral corneal traction suture to infraduct the eye, Dr. Blieden marks off 2 mm and then 4 mm from the limbus using calipers to gauge the entry and length of the implant after deployment.

"I make absolutely certain the Xen is lying flat against the sclera, away from Tenon's," said Dr. Blieden. "With the eye rotated down and marked, I take a tissue forceps way back at the fornix, pick up Tenon's and conjunctiva, so I know the needle is skimming along sclera as I move forward. Then I use a Weck-Cel sponge to gently move the tissue across the needle as it advances toward the limbus to avoid causing any microperforations. Once at the marked entry point, I enter the sclera with the injector needle, confirm position of the needle tip in the anterior chamber, and deploy the device." After deployment of the device and confirming the position by bleb formation, Dr. Blieden occludes the distal tip with gentle pressure from a Weck-Cel sponge prior to injecting MMC into the sub-Tenon space of the superior quadrant.

Postsurgical results. Studies with Xen generally show a decrease in IOP to the low- or mid-teens and a decreased need for medications afterward,[5] said Dr. Bedrood. "It may not get the patient off all medications, but even eliminating one or two is a success."

If needed, a postoperative revision of the implant can free it from scar tissue and get fluid flowing again. In a variety of Xen studies, needling has been required in 22% to 49% of patients.[1] Because it's a small implant, it is prone to clogging, said Dr. Blieden. "I recently had a couple of cases where this occurred. One was a uveitic patient who flared after surgery, which caused the Xen to fail." Another patient had excellent results initially. "She'd previously had a corneal transplant, her inflammation was controlled, and we didn't want to put in a huge tube shunt. But after a cataract surgery, the Xen clogged." One patient required a tube and the other a trabeculectomy to control their disease.

Dr. Bedrood said that postoperative management of the bleb includes "examination for bleb failure, cystic changes, erosions, or leaks." These postoperative issues are not common and often can be managed by either the comprehensive ophthalmologist or the glaucoma physician, she said.

The Preserflo Procedure

Dr. Blieden was an investigator in Preserflo clinical trials, and she sees the device as having a role similar to Xen. However, she said that the Preserflo may be a little more broadly applicable because it is a bigger implant—the

length is longer and the lumen is bigger. In her experience, she said, "It's easier to needle because the material is more robust in my hands." As with the Xen, this may be a standalone procedure or combined with cataract surgery.[6]

Use of MMC. The phase 2 Preserflo study used sponges with a fairly high concentration of MMC: 4 µg per mL for 4 minutes, said Dr. Blieden. "In the phase 3 study, we used a half-dose for 2 minutes, also on sponges." However, a Canadian study showed that a higher dose of MMC gave better pressure-lowering results, said Dr. Lim, who was also an investigator in the Preserflo trials. Assuming that the FDA approves Preserflo, she said, surgeons will learn what works best for certain patients and will titrate the dosing of MMC. "In addition, injecting mitomycin-C may allow surgeons to perform surgery with smaller incisions in the conjunctiva, which can help with the healing process," she said. In the future, Dr. Blieden anticipates injecting MMC as she does for all her conjunctival procedures.

The procedure. The Preserflo involves a quick, straightforward open ab externo procedure, said Dr. Blieden. "A specialized blade comes with the device to help create an anterior wound. The surgeon can easily slide the device directly into the scleral pocket, and then ensure that the device is clear of Tenon's when closing the peritomy." (See "More Online" for a Preserflo video recommendation.)

A unique bleb. "The Preserflo bleb is different in morphology than anything else I've seen," said Dr. Blieden. "It tends to be flat and form more posteriorly and out of the way, whereas the Xen is more anterior. A low and posterior bleb makes it possible to resume contact lens wear in some patients." Dr. Lim added that the Preserflo bleb's low profile and more posterior position may reduce the risk of bleb breakdown and bleb leak over time.

Postsurgical results. The Preserflo has achieved results comparable to Xen in terms of surgical success, IOP lowering, and safety profile.[7] In the Preserflo patients whom Dr. Lim has followed, she's noticed a faster recovery and return to comfort than with a trabeculectomy or glaucoma drainage device. And Dr. Blieden added, "Many patients end up on just one drop, which is very reasonable." Study results presented at AAO 2020 showed that compared with 71% of trabeculectomy patients about half the Preserflo patients achieved a 20% reduction in mean diurnal pressure from baseline without increasing glaucoma medications.[8] However, said Dr. Lim, trabeculectomy resulted in a higher percent of patients with hypotony, early bleb leaks, and post-op interventions. "The value of Preserflo, therefore, may be its superior safety profile over trabeculectomy," she said.

The need for needling. Another poster presented at AAO 2020[9] showed that about 19% of patients required needling within the first two or three months and then do very well, said Dr. Blieden, adding that this parallels her own experience. "I've also found needling of the Preserflo to be easier than with the Xen, which is a bit more fragile."

Special cases. Although patients with neovascular glaucoma or uveitic glaucoma have done well with glaucoma drainage devices, it remains to be seen how well they will do with Preserflo, said Dr. Blieden.

Physician Adoption?

Dr. Blieden noted that Xen and Preserflo could be a natural fit for many glaucoma surgeons, as the surgeries may translate relatively easily into their algorithms and management styles. She added that Xen and Preserflo may also serve as a great procedure for comprehensive physicians when a glaucoma surgeon is not available.

"It's a big decision to take someone from medications to a tube or trab," said Dr. Blieden. The traditional devices easily take three or four times longer in the OR than a Xen or Preserflo, and clinicians lose more real estate in the process, she said. "It's really exciting to have new options available."

1 Fea AM et al. *Clin Ophthalmol.* 2020;14:1805-1832.

2 Pinchuk L et al. *Biomaterials.* 2008;29(4):448-460.

3 Do AT et al. *Curr Opin Ophthalmol.* 2020;32(2):132-183.

4 Buffault J et al. *J Fr Ophtalmol.* 2019;42(2):e37-e46.

5 Poelman H et al. *J Clin Med.* 2021;10:1118.

6 Sadruddin O et al. *Eye Vis* (Lond). 2019;6:36.

7 Scheres LMJ et al. *Acta Ophthalmol.* Published online Sep. 10, 2020.

8 Panarelli et al. Poster #189, One-year safety and effectiveness of microshunt vs. trabeculectomy in sites in the USA and Europe in a randomized study. Presented at: AAO 2020 Virtual; Friday, Nov. 13, 2020.

9 Moster M et al. Poster #193, Safety outcomes of microshunt implantation vs. trabeculectomy in patients with POAG. Presented at: AAO 2020 Virtual; Friday, Nov. 13, 2020.

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SUBSPECIALTY DAY

Subspecialty Day is Friday, Nov. 12, and Saturday, Nov. 13.

Friday: Retina (day 1), Glaucoma, Neuro-Ophthalmology, Ocular Oncology and Pathology, Pediatric Ophthalmology, and Refractive Surgery. **Saturday:** Retina (day 2), Cornea, Oculofacial Plastic Surgery.

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