

# ADVANCES IN FILTERING SURGERY



Research on a gelatin stent and mitomycin C application.

BY KATEKI VINOD, MD, AND EILEEN CHOUDHURY BOWDEN, MD

## PERFORMANCE AND SAFETY OF A NEW AB INTERNO GELATIN STENT IN REFRACTORY GLAUCOMA AT 12 MONTHS

Grover DS, Flynn WJ, Bashford KP, et al<sup>1</sup>

### ABSTRACT SUMMARY

This prospective, noncomparative, multicenter study was designed to evaluate the safety and efficacy of an ab interno gelatin stent (Xen Gel Stent, Allergan). Sixty-five patients aged 45 years or older with refractory open-angle glaucoma (OAG) and a history of failed filtering or cilioablativ surgery and/or uncontrolled IOP ( $\geq 20$  and  $\leq 35$  mm Hg) on maximum tolerated medical therapy were enrolled. The study protocol required a conjunctival peritomy to allow direct sponge application of 0.2 mg/mL mitomycin C (MMC) to the scleral bed for 2 minutes. The gelatin stent was then implanted in the sub-Tenon space in an ab interno fashion via a clear corneal incision under gonioscopic guidance, after which the conjunctiva was closed.

At 12 months, 76.3% of patients had achieved a mean IOP reduction of 20% or more from baseline and were using an equal or smaller number of medications. Mean IOP reduction from baseline was  $-6.4 \pm 1.1$  mm Hg (95% CI, -8.7, -4.2) at 12 months. Among 52 patients who did not require additional surgical intervention, mean IOP decreased from a baseline of  $25.1 \pm 3.7$  mm Hg to  $15.9 \pm 5.2$  mm Hg at 12 months. The mean number of medications decreased from a baseline of  $3.5 \pm 1.0$  (N = 65) to  $1.7 \pm 1.5$  (n = 52) at 12 months.

## STUDY IN BRIEF

- A pivotal noncomparative study of the Xen Gel Stent demonstrated average IOP lowering to the midteens and a decreased need for glaucoma medication at 12 months, with mostly transient and non-vision-threatening postoperative complications.

### WHY IT MATTERS

The FDA approved the Xen for use in a patient population with more refractory disease than other available microinvasive glaucoma surgery procedures. Clinical data comparing the gelatin stent with trabeculectomy and/or tube shunt surgery are limited. A prospective randomized comparative clinical trial would provide useful data to guide patient selection for each procedure.

No intraoperative complications were observed. Postoperative adverse events included transient hypotony (IOP < 6 mm Hg; 16/65 [24.6%]), a largely self-limited loss of BCVA of 2 lines or more (18/65 [27.7%]), and bleb needling (21/65 [32.3%]). One patient (1.5%) developed device erosion requiring surgical revision, and nine patients (13.8%) needed additional glaucoma surgery.

### DISCUSSION

#### For which patients is the gelatin stent indicated?

This pivotal FDA study of the Xen evaluated a patient population with more refractory glaucoma than has been examined in other important trials of microinvasive glaucoma surgery devices. In this study, the average baseline visual field mean deviation was  $-15.0 \pm 7.7$  dB, compared with

$-3.74 \pm 3.47$  dB in the pivotal study of the iStent Trabecular Micro-Bypass Stent (Glaukos)<sup>2</sup> and  $-3.47 \pm 2.95$  dB in the pivotal study of the CyPass Micro-Stent (Alcon).<sup>3</sup> Furthermore, although previous incisional glaucoma surgery was an exclusion criterion in the iStent and CyPass studies, a majority of patients in the Xen study (41/65 [63%]) had previously undergone failed incisional glaucoma surgery. As such, the Xen received FDA approval for use in patients with refractory OAG.

#### Will the gelatin stent reduce the need for trabeculectomy and tube shunt surgery in patients with refractory glaucoma?

Trabeculectomy remains the gold standard in glaucoma surgery and the only available surgical option that allows a titratable reduction of IOP via the sequential lysis of scleral flap sutures.

Nonetheless, analyses of Medicare claims data and surveys of glaucoma surgeons suggest that the use of trabeculectomy is already in decline.<sup>4,5</sup>

Clinical data comparing the gelatin stent to trabeculectomy and/or tube shunt surgery are limited. A retrospective study comparing standalone Xen

with MMC (n = 185) to trabeculectomy with MMC (n = 169) in patients without a history of incisional surgery found a similar risk of failure and safety profiles between the two groups.<sup>6</sup> A prospective randomized clinical trial directly comparing the gelatin stent to trabeculectomy (and/or tube shunt

surgery) in patients with refractory glaucoma would provide a higher level of evidence regarding the procedures' relative safety and efficacy in this more challenging patient population, and it would help guide glaucoma surgeons in patient selection for each procedure.

## MITOMYCIN C-AUGMENTED TRABECULECTOMY: SUB-TENON INJECTION VERSUS SOAKED SPONGES: A RANDOMIZED CLINICAL TRIAL

Pakravan M, Esfandiari H, Yazdani S, et al<sup>7</sup>

### ABSTRACT SUMMARY

This multicenter randomized clinical trial compared efficacy and bleb morphology after trabeculectomy with a sub-Tenon injection of MMC versus direct sponge application of MMC to the scleral bed in 80 Iranian patients aged 25 years or older who had OAG. Blebs were imaged and graded by two masked observers per the Indiana Bleb Appearance Grading Scale. Group 1 eyes received a sub-Tenon injection of 0.1 mL of 0.01% MMC 8 to 10 mm posterior to the superior limbus prior to conjunctival peritomy. Group 2 eyes underwent application of 0.02% MMC-soaked cellulose sponges for 1 or 3 minutes after scleral flap construction.

Both groups demonstrated comparable and statistically significant decreases in IOP at 6 months ( $P < .001$  in groups 1 and 2). Complete success (IOP of 6-15 mm Hg without glaucoma medication) was achieved by 82.5% of eyes in both groups. At 6 months, blebs in group 1 (injection) eyes had lower height ( $P = .007$ ), greater extent ( $P = .045$ ), and less vascularity ( $P < .001$ ) than those in group 2. Rates of cystic bleb formation ( $P > .99$ ), bleb leakage ( $P = .462$ ), and bleb needling ( $P = .499$ ) were similar between groups. Endothelial cell counts did not change significantly in either group postoperatively.

### DISCUSSION

What are the potential advantages of intraoperative sub-Tenon MMC injection in trabeculectomy?

Since its introduction by Cairns in 1968,<sup>8</sup> trabeculectomy has undergone refinements in surgical technique to improve bleb morphology and reduce surgical complications and failure. The use of fornix-based conjunctival flaps and the diffuse application of MMC-soaked sponges have contributed to increased surgical success and reduced rates of hypotony, bleb leak, and blebitis/endophthalmitis.<sup>9</sup>

As demonstrated by Pakravan et al,<sup>7</sup> sub-Tenon injection is an effective alternative method of achieving a diffuse distribution of MMC. The investigators observed more favorable bleb morphology (ie, more diffuse, lower-lying, and less vascular blebs) after trabeculectomy using sub-Tenon MMC injection than with direct sponge application of MMC. Additional

benefits of sub-Tenon MMC injection included improved control over dose delivery, lower doses, decreased operating times, and no risk of retained sponge fragments. Retrospective studies comparing trabeculectomy with sub-Tenon MMC injection to trabeculectomy with sponge application have suggested that better IOP control with fewer glaucoma medications<sup>10</sup> and fewer postoperative visits and 5-fluorouracil injections<sup>11</sup> are achieved after trabeculectomy with the sub-Tenon injection; these outcomes, however, have not been confirmed in a prospective randomized trial.

### How might this study's results influence the surgical approach to novel subconjunctival glaucoma procedures?

New device-assisted alternatives to trabeculectomy include the FDA-approved ab interno gelatin stent (Xen) and the investigational ab externo InnFocus MicroShunt (Santen). Both of

## STUDY IN BRIEF

- ▶ A randomized clinical trial compared outcomes after trabeculectomy using an intraoperative sub-Tenon injection versus sponge-based application of mitomycin C (MMC). Investigators found more favorable bleb morphology in patients receiving MMC injections.

### WHY IT MATTERS

Sub-Tenon MMC injections offer more precise dose delivery and increased efficiency compared with MMC-soaked sponges. Although considered an off-label method of MMC administration in the United States, sub-Tenon injections may also be used with new subconjunctival procedures, including the Xen Gel Stent.

these bleb-forming procedures require adjuvant antimetabolites and carry the same potential risks as trabeculectomy, including conjunctival scarring, hypotony, and infection, in addition to the risk of device erosion. The beneficial effects of sub-Tenon MMC injection may extend to these newer microinvasive procedures. Both the ongoing InnFocus MicroShunt Versus Trabeculectomy Study<sup>12</sup> and the pivotal Xen Gel Stent study<sup>1</sup> used sponge-applied Mitosol (Möbius Therapeutics), the only preparation of MMC approved by the FDA for use in ophthalmic surgery. In real-world use of the Xen, however, surgeons likely more often employ off-label MMC injection than sponge application because injection obviates the need for a conjunctival peritomy and improves surgical efficiency. Small prospective series of Xen use with MMC injection suggest a favorable safety profile, albeit with follow-up limited to 1 year.<sup>13-15</sup> Larger studies with extended follow-up examining the effects of MMC injection on safety, efficacy, and bleb morphology

will help determine the optimal dose and delivery method for adjuvant antimetabolites with these novel subconjunctival devices. ■

1. Grover DS, Flynn WJ, Bashford KP, et al. Performance and safety of a new ab interno gelatin stent in refractory glaucoma at 12 months. *Am J Ophthalmol*. 2017;183:25-36.
2. Samuelson TW, Katz LJ, Wells JM, et al; US iStent Study Group. Randomized evaluation of the trabecular micro-bypass stent with phacoemulsification in patients with glaucoma and cataract. *Ophthalmology*. 2011;118(3):459-467.
3. Vold S, Ahmed II, Craven ER, et al; CyPass Study Group. Two-year COMPASS trial results: supraciliary microstenting with phacoemulsification in patients with open-angle glaucoma and cataracts. *Ophthalmology*. 2016;123(10):2103-2112.
4. Arora KS, Robin AL, Corcoran KJ, et al. Use of various glaucoma surgeries and procedures in Medicare beneficiaries from 1994 to 2012. *Ophthalmology*. 2015;122(8):1615-1624.
5. Vinod K, Gedde SJ, Feuer WJ, et al. Practice preferences for glaucoma surgery: a survey of the American Glaucoma Society. *J Glaucoma*. 2017;26(8):687-693.
6. Schlenker MB, Gulamhusein H, Conrad-Hengerer J, et al. Efficacy, safety, and risk factors for failure of stand-alone ab interno gelatin microstent implantation versus stand-alone trabeculectomy. *Ophthalmology*. 2017;124(11):1579-1588.
7. Pakravan M, Esfandiari H, Yazdani S, et al. Mitomycin C-augmented trabeculectomy: subtenon injection versus soaked sponges: a randomised clinical trial. *Br J Ophthalmol*. 2017;101(9):1275-1280.
8. Cairns JE. Trabeculectomy. Preliminary report of a new method. *Am J Ophthalmol*. 1968;66(4):673-679.
9. Wells A, Cordeiro M, Bunce C, Khaw PT. Cystic bleb formation and related complications in limbus- versus fornix-based conjunctival flaps in pediatric and young adult trabeculectomy with mitomycin C. *Ophthalmology*. 2003;110(11):2192-2197.
10. Lim MC, Paul T, Tong MG, et al. A comparison of trabeculectomy surgery outcomes with mitomycin-C applied by intra-Tenon injection versus sponge method. Paper presented at: American Glaucoma Society Annual Meeting; March 2, 2013; San Francisco, CA.
11. Khouiri A, Huang G, Huang L. Intraoperative injection vs sponge-applied mitomycin C during trabeculectomy: one-year study. *J Curr Glaucoma Pract*. 2017;11(3):101-106.
12. InnFocus MicroShunt Versus Trabeculectomy Study (IMS). US National Library of Medicine website. <https://clinicaltrials.gov/ct2/show/NCT01881425>. Accessed April 10, 2018.
13. De Gregorio A, Pedrotti E, Russo L, Morselli S. Minimally invasive combined glaucoma and cataract surgery: clinical results of the smallest ab interno gel stent [published online ahead of print May 29, 2017]. *Int Ophthalmol*. doi:10.1007/s10792-017-0571-x.
14. Fea AM, Spinetta R, Cannizzo PML, et al. Evaluation of bleb morphology and reduction in IOP and glaucoma medication following implantation of a novel gel stent. *J Ophthalmol*. 2017;2017:9364910.
15. Pérez-Torregrosa VT, Olate-Pérez Á, Cerdá-Ibáñez M, et al. Combined phacoemulsification and Xen45 surgery from a temporal approach and 2 incisions. *Arch Soc Esp Oftalmol*. 2016;91(9):415-421.

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