Clinical and Experimental Vision and Eye Research (2019), 2, 30–37

REVIEW ARTICLE

XEN gel stent: A review

Sonal Dangda[1], Maria V. Castanos[1], Anna Do[1], Joseph F. Panarelli[2]

[1]New York Eye and Ear Infirmary of Mount Sinai, Icahn School of Medicine at Mount Sinai, New York, United States, [2]Department of Ophthalmology, NYU Langone Health, New York, United States

Key words:

Glaucoma surgery, micro-invasive glaucoma surgery, XEN gel stent

Address for correspondence:
Dr. Sonal Dangda, New York Eye and Ear Infirmary of Mount Sinai, Icahn School of Medicine at Mount Sinai, New York, United States. E-mail: sonaldangda@gmail.com

Accepted: 07-05-2019
Received: 27-05-2019
doi: 10.15713/ins.clever.25

Abstract

Over the last decade, several new surgical devices and treatment options have been developed for the management of glaucoma. Together, known as micro-invasive glaucoma surgery, they aim to provide a safer approach to glaucoma surgery. Although the early devices were used to either stent or ablate a segment of the trabecular meshwork, newer devices such as the XEN gel stent (Allergan Inc., Dublin, Ireland), offer the possibility of creating a safer, more predictable filtering bleb. Since its FDA approval in 2016, several retrospective case series and prospective studies have highlighted the efficacy of the XEN gel stent with regards IOP lowering and reduction in the need for glaucoma medications. The XEN gel stent has also been shown to have a favorable safety profile in terms of intraoperative and post-operative complications. The major concern is the need for bleb intervention in the form of needling and injection of anti-fibrotic agents. This review focuses to summarize the current knowledge on the XEN gel stent for treatment of various subtypes of glaucoma.

Introduction

A variety of newer surgical techniques have emerged for the treatment of glaucoma. They are minimally invasive and are useful as adjunct procedures combined with phacoemulsification. Together, known as micro-invasive glaucoma surgery (MIGS), they allow for glaucoma surgeons to tailor surgical treatment options based on the severity of disease.[1] MIGS has greatly widened the management options available to the current day glaucoma surgeon. However, a limitation with these devices is that they use the traditional outflow pathway for drainage, which is the trabecular meshwork and Schlemm's canal system. This limits the amount of IOP lowering, which can be achieved since aqueous humor outflow critically depends on the venous outflow. Thus, most devices are unable to reduce IOP below the pressure of the distal outflow system, when performed as a stand-alone procedure. Devices which drain into the subconjunctival space, allow aqueous humor to pool subconjunctivally, from where it can diffuse through the conjunctiva, into the venous system, as well as into the lymphatic pathways.[2] Subconjunctival outflow has proven to deliver the greatest IOP reduction and is utilized in traditional glaucoma filtering surgery, i.e. trabeculectomy, which is still the gold standard procedure. Glaucoma drainage implants (GDI) have also gained popularity in the past two decades, especially as a primary procedure in low-risk eyes.[3] However, both trabeculectomy and GDI have a potential for long-term complications, as seen in the tube versus trabeculectomy study.[4] Thus, there has been a slow but steady shift in finding safe and effective alternatives.

The only FDA approved "MIGS" device which utilizes subconjunctival filtration is the XEN gel stent (Allergan Inc., Dublin, Ireland). It is a hydrophilic tube composed of porcine gelatin, a non-silicone biocompatible material derived from collagen, and cross-linked with glutaraldehyde.[5,6] It is thought to reduce the post-operative inflammatory and fibrotic reaction, which usually leads to failure of glaucoma surgical procedures. Animal studies noted that 2–4 mm of scleral tunnel was optimally required for the formation of a bleb. The length of the XEN gel stent was optimized at 6 mm, and it was initially available in three models, each of which had a different internal luminal diameter: 140 microns, 63 microns, and 45 microns.[6] The stent has an intrinsic flow-limiting design which is based on the Hagen–Poiseuille equation (for laws governing Newtonian fluids). Amongst the stent sizes, the XEN45 was noted to achieve a steady-state pressure of 7.56 mm Hg at 2.5 μL/min as compared to 0.09 and 0.01 mm Hg by the express device and

Baerveldt tube, respectively, thus theoretically minimizing the risk of hypotony.[7]

Although there are no strict criteria as to what defines a MIGS procedure, Drs. Saheb and Ahmed have provided five common characteristics which these procedures share, and the XEN appears to satisfy all of them:

1. Procedure performed through a microinvasive approach: When an *ab interno* approach is taken, the XEN is inserted through a clear corneal incision. When an *ab externo* approach is taken, a small conjunctival peritomy is required, but the surrounding dissection is extremely limited compared to traditional glaucoma surgeries.
2. Minimally traumatic to the targeted tissue: Very little tissue is manipulated during this procedure regardless of the surgical approach taken.
3. Efficacious: The effectiveness of this procedure has been demonstrated in numerous studies, which will be discussed later. However, additional randomized, prospective, multicenter trials comparing this device to traditional glaucoma procedures will be essential to understanding the full potential of this procedure.
4. Rapid visual recovery: This has been reported anecdotally. Additional studies are underway to evaluate this benefit of the procedure.[11]
5. Favorable safety profile: The number of vision-threatening complications is extremely low with this procedure, and a complete analysis of the complication profile will be discussed later. In general, hypotony-related complications are seen far less frequently with this device as compared to trabeculectomy and tube shunt surgery.

Surgical Technique

The stent, which is preloaded into an injector system [Figure 1a and b], is deployed most commonly through an *ab interno* approach. The inserter is designed to protect the XEN gel stent and aides inaccurate placement of the implant into the correct anatomical location.

An overview of the main suggested surgical steps are as follows:[5]

1. After sterile draping of the eye, the intended landing zone (3 mm from the limbus) in the superior/superonasal quadrant of the conjunctiva is visualized and marked. It is advised to attempt to position this device as close to the 12 O'clock position if the anatomy allows.
2. Anti-fibrotics, such as mitomycin C (MMC), are being routinely used when placing a XEN gel stent. A dose of 20–40 mcg can be injected into the subconjunctival/sub Tenon's space just posterior to the implant site either before or after stent implantation.[8]
3. The main corneal incision and paracentesis are created in the appropriate quadrant, depending on the eye and dexterity of the surgeon.
4. A preloaded single-use injector, as previously described, is inspected to ensure that the stent is correctly seated in the device.
5. Through the main corneal incision, the injector needle is passed across the anterior chamber to the superonasal/superior angle.
6. An indirect gonioscopy lens can be used to visualize the angle. The needle should be seated either at the level of the trabecular meshwork or slightly anterior. If the device is deployed too posterior in the angle, the proximal tip will become obstructed by the peripheral iris. Surgeons should be careful not to overinflate the anterior chamber with viscoelastic if they are not using a gonioscopy lens as they may artificially deepen the angle and misjudge placement of their pass.
7. The needle is pushed through the sclera (while holding counter-traction with their second hand) and into the subconjunctival space. Ideally, the intrascleral tunnel should be 2–3 mm in length. If the pass is too long or short, slight modifications can be made by retracting the needle slightly and either pushing down or angling upward to re-advance.
8. With this approach, the needle bevel angle at the exit site is almost parallel to the conjunctiva. This leads to the Tenon and conjunctival layers above the needle bevel to be rather pushed up versus being engaged in a penetrating fashion. As a result of this, perforating the conjunctiva with the needle bevel when coming out of the sclera can be avoided.
9. The goal at this point is to ensure that the needle is completely through the Tenon's layer and seated in the subconjunctival space before delivering the stent. The XEN gel stent can then be deployed by slowly advancing the slide located on the inserter. As the stent is slowly deployed forward, the needle fully withdraws itself into the sleeve of the injector. Care must be taken to maintain gentle forward pressure so that the device does not "flick" back into the eye.
10. The surgeon then withdraws the injector out of the eye, evacuates the viscoelastic from the anterior chamber, and hydrates/sutures the corneal incisions. The stent immediately begins to shunt fluid from the anterior chamber to the subconjunctival space, and a low diffuse bleb can be seen to be formed.

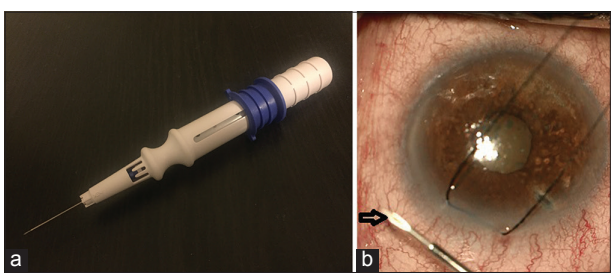

Figure 1: (a) XEN gel stent injector, (b) injector tip with the preloaded XEN gel stent

During the implantation procedure itself, the Xen gel stent hydrates and swells in place to become a soft non-migrating drainage channel that is tissue conforming. The cross-linked gelatin material makes a fixed inner diameter wall that does

not change after swelling. This regulated flow helps mitigate hypotony-related issues.[5]

Various modifications have been suggested to enhance outcomes with the XEN gel stent. Recently, surgeons have begun to implant the device into the subconjunctival space through an *ab externo* approach, while others are implanting beneath the Tenon's layer (after making a small conjunctival peritomy) also through an external approach.

Clinical Results

The early clinical studies on the XEN gel stent evaluated the XEN140 and XEN63 implant as a stand-alone procedure and in combination with phacoemulsification. Sheybani *et al.* noted an initial complete success rate of 40–47% (85–89% qualified success), with a 32–47% bleb needling rate and a 9–35% incidence of hypotony on day 1.[9,10] As the XEN 45 is the primary version currently utilized worldwide, this review article will further focus only on the results of the XEN 45 implant. The current clinical practice also advocates the use of MMC, which was not utilized in the initial studies.

Intraocular pressure control

The pivotal US trial was a prospective, multicenter, single-arm, open-label study, and conducted for FDA approval. It included patients above 45 years of age who had refractory open-angle glaucoma, which was defined as either a prior failure of filtering/cilioablative procedure or uncontrolled IOP (>20 and <35 mm Hg) on maximally tolerated medical therapy, i.e. >4 topical glaucoma medications. Requisite was the presence of an area of healthy, free, and mobile conjunctiva in the target quadrant. The authors noted a 36% IOP reduction and a decrease in mean glaucoma medications from 3.5 ± 1.0 to 1.7 ± 1.5 at 12 months postoperatively.[11]

Studies done subsequent to the FDA approval were mostly retrospective (multi-center as well as single-center) and evaluated XEN gel stent implantation either combined with phacoemulsification (phaco-XEN) or as a stand-alone procedure. The XEN implant has been reported to achieve significant IOP reduction, along with a decline in post-operative medication use, across all the studies. The mean baseline IOP in prospective studies has been in the range of 16-25 mm Hg, with an IOP drop of 23–42% on 0.3–1.7 glaucoma medications at 1 year postoperatively.[12-17] Table 1 shows the comparative results of both the prospective and retrospective studies.

Karimi *et al.* retrospectively reviewed 259 eyes across four centers and noted a success rate of 62%; this study included patients with previously failed filtration surgery as well as combined phaco-XEN cases.[18] No difference in IOP reduction or medication use between phaco-XEN and stand-alone XEN surgery was found. However, Mansouri *et al.*, in a prospective study on 149 eyes, noted that patients who underwent stand-alone XEN procedure had a higher success rate as compared to phaco-XEN cases (40% vs. 22.9%, respectively).[12] Widder *et al.* reported a higher success rate in pseudophakic eyes (73%) as compared to phakic eyes (53%) or combined surgery (55%).[19]

The IOP reduction after XEN surgery has been noted to be maintained long-term, up to 36 months with currently available literature. Reitsamer *et al.* noted success rates of 68% and 66% at 12 and 24 months, respectively, with 45% eyes remaining medication free at 24 months.[20] In a study by Fea *et al.*, the success rate was 40% at 36 months, with a 72% reduction in medications, across stand-alone XEN, and phaco-XEN.[17]

Most of the above studies evaluated eyes with primary open angle glaucoma (POAG). Eyes with secondary open-angle glaucoma may have as good or potentially better success with the XEN gel stent. Mansouri *et al.* compared 57 eyes with POAG and 53 eyes with PXG and demonstrated equal efficacy and safety for both treatment groups.[21] The PXG eyes were noted to have a 31% IOP drop at 12 months and a 63% success rate as compared to 30% and 42%, respectively, for POAG eyes. In a study on 24 uveitic eyes, Sng *et al.* noted a 60% IOP decline at post-operative month 12 with 83% eyes requiring no further glaucoma surgery.[23]

To summarize, the XEN gel stent has shown early favorable data. However, as with other filtering procedures, the true question remains whether or not these blebs will stand the test of time. As with many procedures, early success is common, but failure results down the road as the wound healing process continues. To date, there is limited long term data on this procedure. In addition, there is a paucity of data with regard to newer surgical techniques utilizing the device. Many studies are currently underway, and we look forward to the published data when it becomes available.

Bleb revision/needling

The filtering bleb created post-XEN gel surgery requires care similar to that of a trabeculectomy bleb, and surgeons should be comfortable with various approaches for revising a bleb.[16,19]

A post-operative needling rate of 2–50% and 22–51% has been reported in prospective studies and retrospective studies, respectively.[11-19,25-27] The time to initial needling/revision ranged from 6–582 days (median – 59.5 days) and the median number of interventions was 2.[16,26] Smith *et al.*, in their study on 68 eyes, noted a 70% qualified success rate in eyes which underwent bleb needling or revision.[27]

Widder *et al.*, in their study on 233 eyes, performed an "open" revision for those who initially failed and achieved a success rate of 84–92% in all subgroups of patients. A conjunctival peritomy was made, and the area adjacent to and posterior to the distal end of the stent was dissected.[19] This procedure leads to the development of a more broad, diffuse, and posteriorly directed bleb post-revision.

In eyes with failed filtering surgery, the bleb intervention rates have been noted to be slightly higher at 53% with a mean of 2.4 post-operative bleb interventions needed per case.[24] The higher intervention rate may be attributable to separate inclusion of both physical and pharmacological interventions (needling and/

Table 1: Clinical Outcomes of the various Xen45 studies

???	Study design	No. of eyes at Baseline	No. of eyes at 12 months	Baseline IOP Mean±SD	IOP at 12 months Mean±SD (mm Hg) Percentage drop (−%)	Baseline medication Mean±SD	Medication at 12 months Mean±SD	Complete success (qualified success) IOP reduction > 20% and IOP < 18mm Hg
Grover *et al.*[11]	Prospective multi-center	65	52	25.1±3.7	15.9±5.2 (−35.6)	3.5±1.0	1.7±1.5	(75.4%)
Mansouri *et al.*[12]	Prospective single-center	149	87	20.0±7.1	13.9±4.3 (−31)	1.9±1.3	0.5±0.8	62% (78%)
De Gregorio *et al.*[13]	Prospective single-center	41	40	22.5±3.7	13.1±2.4 (−41.8)	2.5±0.9	0.4±0.8	80.4% (97.5%)
Galal *et al.*[14]	Prospective single-center	13	13	16±4	1.2±3 (−23)	1.9±1	0.3±0.5	42% (66%)
Pérez-Torregrosa *et al.*[15]	Prospective single-center	30	30	21.2±3.4	15.0±2.8 (−29.34)	3.1±0.7	0.2±0.7	27% (90%)
Tan *et al.*[16]	Prospective single-center	39	39	24.9±7.8	14.5±3.4	3.0	0.7	87% (92%)
Fea *et al.*[17]	Prospective single-center	12	10	21.8±2.8	14.9±2.1 (−31.62)	2.9±1.2	0.5±0.5	50% (50%)
Karimi *et al.*[18]	Retrospective multi-center	259	89	19.3±6.0	14.2±4.4	2.6±1.1	0.8±1.0	37.4% (61.6%)
Heidinger *et al.*[26]	Retrospective single-center	199	89	22.8±6.9	17.1±5.9 (−22.7)	2.9±1.0	1.8±1.4	15.4% (25%)
Hengerer *et al.*[25]	Retrospective single-center	246	148	32.2±9.1	14.2±4.0	3.1±1.0	0.3±0.7	55.4%
Smith *et al.*[27]	Retrospective single-center	68	68	22.1±6.4	14.8±5.1 (−33)	2.9±0.8	1.1±1.1	33.8% (67.6%)
Widder *et al.**[19]	Retrospective single-center	233	82	24.3±6.6	13.5±3.3*	2.6±1.1	0.2±0.7	66% (90%*)

*Study allowed one bleb revision and post-operative glaucoma medications were not added as protocol

or injections) as bleb interventions as well as a lower threshold to intervene. They note that the quadrant of XEN gel stent implantation was different (superonasal) from the quadrant of the previously operated trabeculectomy (superior).

In a retrospective study of 19 eyes with failing XEN gel stent surgery, Arnljots *et al.* found that the mean time from XEN implantation to needling was 121.9 ± 120.9 days (range, 19–449 days) and the rate of success was 90% the authors reported that 13 (68%), 3 (16%), and 3 (16%) eyes underwent 1, 2, and 3 needling revisions, respectively. Among these, 57% of the revisions were performed on the slit lamp, 43% in the operating room while 4% were open revisions.[28]

In uveitic eyes, Sng *et al.* noted a bleb needling rate of 42% (performed at the slit-lamp) within the first 12 months of surgery, while 21% eyes underwent bleb revision in the operating room with dissection of the Tenon's layer within the first 4 months after XEN gel stent implantation.[23]

In a study to assess the predictors of needling post-XEN gel stent implantation, Midha *et al.* reported that eyes with lower IOP on day 1 were less likely to require a needling procedure and that a significant association was seen between lower day 1 IOP and lesser number of post-operative needling procedures.[29] The probability of needling was up to 80% in patients having a post-operative day 1 IOP >20 mm Hg while this number decreased to 35% if the day 1 IOP was <10 mm Hg. However, no significant association was observed between day 1 IOP and needling interventions in phaco-XEN eyes. The authors also noted that the mean IOP on day 1 in XEN alone group was significantly lower as compared to a phaco-XEN group, and this translated to significantly better outcomes at 1 year in the XEN alone group as compared to phaco-XEN group (complete success rate – 81% vs. 56%). They postulate that due to the minimal manipulation of subconjunctival and episcleral tissues with the current technique of XEN gel stent implantation, there is a high chance of blockage of the stent lumen by the Tenon's, blood, or exudates, which translates into a higher day 1 IOP and thus increased rates of a needling procedure.

Adverse events

The XEN-45 implant has demonstrated a 6–8 mm Hg resistance to outflow, theoretically minimizing the risk of hypotony.[7]

Although various studies report an incidence of 1–37% for early hypotony, it has been noted to be self-limiting and seen to resolve by post-operative week 1 in a majority of the eyes.[11-14,16,18,19,25-27] Table 2 provides the details of the main adverse events seen post-XEN gel stent surgery.

Other complications reported as unique by Rooney *et al.* include suprachoroidal hemorrhage and retinal detachment due to hypotony, retraction of the XEN gel stent into the subconjunctival space due to Tenon's fibrosis, and occlusion of the internal ostium of the XEN gel stent by Descemet's membrane.[30]

In general, the XEN gel stent has an extremely favorable safety profile. Vision-threatening complications have been reported in literature but are mostly case reports, as they are very uncommon. The biggest issue with the device is the rather high rate of early failure, necessitating needle revision. The percentage of patients requiring revision varies in literature but is significantly higher than what many would prefer it to be. At present, surgeons are varying their implantation approach as well as the use of anti-metabolites to enhance the surgical success rates. Hypotony, as defined by a low intraocular pressure alone, can be seen in the early post-operative course in a few cases, but complications such as hypotony maculopathy are rare. Even when the IOP is low, the anterior chamber depth is *usually* maintained, and if choroidal effusion develops, it is transient and responds to medical therapy/observation. Overall, the procedure appears to be safer than our traditional glaucoma surgeries, as evidenced by literature previously cited.

Comparison with trabeculectomy

In comparison to trabeculectomy (with MMC), Schlenker *et al.* noted no detectable difference in the risk of failure and safety profile with XEN gel stent implantation (with MMC), in a study comprising 354 eyes (185 eyes with XEN gel stent and 169 eyes with trabeculectomy).[31] The primary outcome measure was hazard ratio of failure, where failure was defined as two consecutive IOP measurements (after post-operative month 1) of <6 mm Hg (with vision loss) or >17 mm Hg (without glaucoma medications). At 1 year follow-up, 25% of XEN gel stent eyes and 36% of trabeculectomy eyes were noted to be receiving post-operative glaucoma medications. Bleb interventions like needling were performed in 43% and 31% of XEN gel stent eyes and trabeculectomy eyes, respectively. Anterior chamber reformations were noted to be more in XEN gel stent eyes while bleb repair and conjunctival suturing were seen more with trabeculectomy eyes. A higher number of XEN gel stent eyes were noted to undergo additional glaucoma surgery in comparison to trabeculectomy (10% vs. 5%), although not statistically significant. The baseline characteristics which were noted to affect the surgical success, in terms of number of post-operative interventions such as needling, anterior chamber reformations, bleb repair, and laser procedures (117 in XEN gel stent eyes and 165 in trabeculectomy eyes) were: pre-operative IOP, ethnicity and pre-operative best corrected visual acuity (BCVA). Eyes with pre-operative IOP >21 mm Hg trended better with XEN gel stent while eyes with IOP <21 mm Hg trended better with trabeculectomy. Although ethnicity was less correlated with overall surgical success for XEN gel stent, nonwhite eyes who underwent XEN gel stent trended better than nonwhite eyes who underwent trabeculectomy. In terms of pre-operative vision, eyes with BCVA better than 0.4 log MAR fared better with XEN gel stent while eyes with BCVA worse than 0.4 log MAR trended better with trabeculectomy.

Evaluation of the XEN Blebs

Blebs obtained post-XEN gel stent surgery [Figure 2] are diffuse, broad, and usually have low elevation.[5] Studies utilizing the anterior segment optical coherence tomography (AS-OCT) have provided useful insights into the morphology of post-XEN gel stent blebs and have been helpful in the assessment of predictors for functionality.[17,32,33]

De Gregorio *et al.* noted the presence of subconjunctival microcysts near the implant at 12 months post-operative.[13] Olate-Pérez *et al.*, in a study on 30 eyes with phaco-XEN, noted that blebs with cystic pattern and low reflectivity have better postoperative outcomes in terms of IOP at 12 months.[32] Similarly, Fea *et al.* reported that the bleb wall reflectivity was significantly lower in functioning versus nonfunctioning blebs at 6 months postoperatively.[17] In their study, both maximal heights of the bleb and total area of the cystic hypo-echoic spaces were noted to be significantly higher on AS-OCT in functioning blebs. Further, at 1 year follow-up, the bleb wall reflectivity noted was significantly higher in the failure group. In a long-term study on blebs post-XEN63 stent, Lenzhofer *et al.* classified the blebs into four categories, according to the internal bleb characteristics.[33] They noted that microcystic multiform morphology (multiple cystic hyporeflective areas in deep layer separated by thin septae and having thicker bleb wall which makes the bleb appears encapsulated) at month 3 and uniform bleb morphology (no fluid-filled hyporeflective spaces in

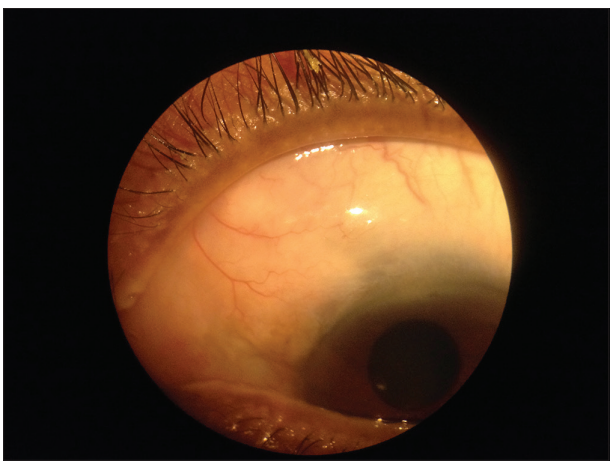

Figure 2: Slit-lamp photograph of a XEN gel stent bleb

Table 2: Complications and adverse events post-XEN gel stent surgery

???	Intraoperative complications while implantation	Bleb intervention (needling, injection and revision) (%)	Additional glaucoma surgeries needed (%)	Hypotony and related choroidal effusion (%)	Device explant or exposure (%)	Infection and Endophthalmitis (%)	Iris obstruction of the internal ostium and iritis (%)
Grover *et al.*[11]	Implant malpositioning – 2%	32	12	25	<2	0	Iritis – 3
Mansouri *et al.*[12]	Several cases (% N/A)	37	6	<1	<1	<1	0
De Gregorio *et al.*[13]	Subconjunctival bleeding – 37% Implant malpositioning – 12%	2	2	2	2	0	0
Galal *et al.*[14]	0	31	15	15	8	0	0
Pérez-Torregrosa *et al.*[15]	Implant malpositioning – 23%	23	0	0	0	0	0
Tan *et al.*[16]	0	51	3	21	0	0	Iris obstruction – 8
Fea *et al.*[17]	0	50	8	0	0	0	0
Karimi *et al.*[18]	0	41	11	37	2	<1	Iris obstruction – 4
Heidinger *et al.*[26]	Implant malpositioning/ malfunction – 8%	22	14	8	0	<1	0
Hengerer *et al.*[25]	Subconjunctival bleeding – 5%	28	6	4	0	0	0
Smith *et al.*[27]	Hyphema – 10%	43	3	9	2	0	0
Widder *et al.**[19]	Intraoperative bleeding – 9%	34	10	5	<1	0	Iritis – <1

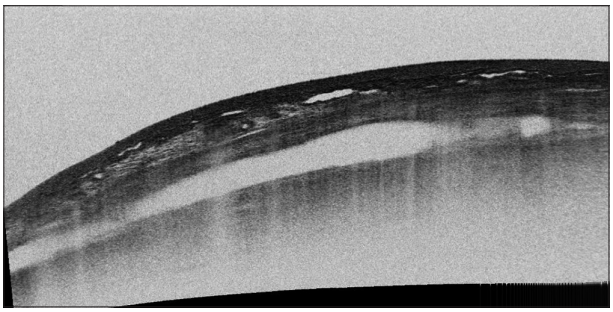

Figure 3: Anterior segment optical coherence tomography image of a XEN bleb showing the subconjunctival separation morphology

subconjunctival space) at month 9 were associated with greater risk of failure at the 1 year follow-up. The authors also note that the subconjunctival separation morphology (multiple small spaces in more superficial layers) was associated with a lower IOP [Figure 3]. A time series analysis further showed a strong negative correlation between the timelines of subconjunctival separation morphology prevalence in the AS-OCT and the mean IOP during the 1st year postoperatively.

Cost Analysis

Current literature is limited in terms of cost analysis studies for XEN gel stent implantation. A study done by Martinez-de-la-Casa *et al.* to assess the economic impact of including XEN gel stent into glaucoma surgical care for the treatment of open-angle glaucoma in Spain, noted this to result in economic savings for the Spanish National Health System. The cost reductions were more marked in patients with mild glaucoma associated with cataracts or uncontrolled glaucoma not associated with cataracts. An expert panel provided proportions of use and resource consumption for various combinations of glaucoma surgical interventions, and the unitary costs were derived from a national database. They concluded that the current cost for surgical treatment of glaucoma was €4,665.41 per patient, and the inclusion of the XEN gel stent into standard care would generate savings of €465.24 in the 1st year and €618.82 by the 3rd year.[34] The authors' experience is limited with regard to cost savings in the United States. The cost of the actual device (around $2000) must be weighed in association with the potential cost savings from less frequent follow-up visits, less frequent reoperation rates for serious complications, and a quicker return to work for the patients.

Conclusion

The XEN gel stent has shown effective IOP lowering along with a favorable safety profile in primary open angle and pseudoexfoliative glaucoma. It is also a safe and reasonable surgical alternative in patients with uveitic glaucoma. Although post-operative bleb interventions like needling, have been reported to be higher compared to trabeculectomy, various modifications of the surgical procedure are being currently contemplated, which may enhance outcomes.

References

1. Kerr NM, Wang J, Barton K. Minimally invasive glaucoma surgery as primary stand-alone surgery for glaucoma. Clin Exp Ophthalmol 2017;45:393-400.
2. Yu DY, Morgan WH, Sun X, Su EN, Cringle SJ, Yu PK, *et al.* The critical role of the conjunctiva in glaucoma filtration surgery. Prog Retin Eye Res 2009;28:303-28.
3. Gedde SJ, Schiffman JC, Feuer WJ, Herndon LW, Brandt JD, Budenz DL. Treatment outcomes in the Tube Versus Trabeculectomy (TVT) study after five years of follow-up. Am J Ophthalmol 2012;153:789-803.e2.
4. Gedde SJ, Herndon LW, Brandt JD, Budenz DL, Feuer WJ, Schiffman JC. Postoperative complications in the Tube Versus Trabeculectomy (TVT) study during five years of follow-up. Am J Ophthalmol 2012;153:804-140.
5. Vera VI, Horvath C. XEN Gel stent: The solution designed by AqueSys®. In: Samples JR, Ahmed II, editors. Surgical Innovations in Glaucoma. New York: Springer New York; 2014. p. 189-98.
6. Lewis RA. Ab interno approach to the subconjunctival space using a collagen glaucoma stent. J Cataract Refract Surg 2014;40:1301-6.
7. Sheybani A, Reitsamer H, Ahmed II. Fluid dynamics of a novel micro-fistula implant for the surgical treatment of glaucoma. Invest Ophthalmol Vis Sci 2015;56:4789-95.
8. Green W, Lind JT, Sheybani A. Review of the xen gel stent and innFocus microShunt. Curr Opin Ophthalmol 2018;29:162-70.
9. Sheybani A, Lenzhofer M, Hohensinn M, Reitsamer H, Ahmed II. Phacoemulsification combined with a new ab interno gel stent to treat open-angle glaucoma: Pilot study. J Cataract Refract Surg 2015;41:1905-9.
10. Sheybani A, Dick HB, Ahmed II. Early clinical results of a novel ab interno gel stent for the surgical treatment of open-angle glaucoma. J Glaucoma 2016;25:e691-6.
11. Grover DS, Flynn WJ, Bashford KP, Lewis RA, Duh YJ, Nangia RS, *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.
12. Mansouri K, Guidotti J, Rao HL, Ouabas A, D'Alessandro E, Roy S, *et al.* Prospective evaluation of standalone XEN gel implant and combined phacoemulsification-XEN gel implant surgery: 1-year results. J Glaucoma 2018;27:140-7.
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. Int Ophthalmol 2018;38:1129-34.
14. Galal A, Bilgic A, Eltanamly R, Osman A. XEN glaucoma implant with mitomycin C 1-year follow-up: Result and complications. J Ophthalmol 2017;2017:5457246.
15. Pérez-Torregrosa VT, Olate-Pérez Á, Cerdà-Ibáñez M, Gargallo-Benedicto A, Osorio-Alayo V, Barreiro-Rego A, *et al.* Combined phacoemulsification and XEN45 surgery from a temporal approach and 2 incisions. Arch Soc Esp Oftalmol 2016;91:415-21.
16. Tan SZ, Walkden A, Au L. One-year result of XEN45 implant for

glaucoma: Efficacy, safety, and postoperative management. Eye (Lond) 2018;32:324-32.
17. Fea AM, Spinetta R, Cannizzo PM, Consolandi G, Lavia C, Aragno V, *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.
18. Karimi A, Lindfield D, Turnbull A, Dimitriou C, Bhatia B, Radwan M, *et al.* A multi-centre interventional case series of 259 ab-interno Xen gel implants for glaucoma, with and without combined cataract surgery. Eye (Lond) 2019;33:469-77.
19. Widder RA, Dietlein TS, Dinslage S, Kühnrich P, Rennings C, Rössler G. The XEN45 gel stent as a minimally invasive procedure in glaucoma surgery: Success rates, risk profile, and rates of re-surgery after 261 surgeries. Graefes Arch Clin Exp Ophthalmol 2018;256:765-71.
20. Reitsamer H, Sng C, Vera V, Lenzhofer M, Barton K, Stalmans I, *et al.* Two-year results of a multicenter study of the ab interno gelatin implant in medically uncontrolled primary open-angle glaucoma. Graefes Arch Clin Exp Ophthalmol 2019;257:983-96.
21. Mansouri K, Gillmann K, Rao HL, Guidotti J, Mermoud A. Prospective evaluation of XEN gel implant in eyes with pseudoexfoliative glaucoma. J Glaucoma 2018;27:869-73.
22. Ibáñez-Muñoz A, Soto-Biforcos VS, Chacón-González M, Rúa-Galisteo O, Arrieta-Los Santos A, Lizuain-Abadía ME, *et al.* One-year follow-up of the XEN® implant with mitomycin-C in pseudoexfoliative glaucoma patients. Eur J Ophthalmol 2019;29:309-14.
23. Sng CC, Wang J, Hau S, Htoon HM, Barton K. XEN-45 collagen implant for the treatment of uveitic glaucoma. Clin Exp Ophthalmol 2018;46:339-45.
24. Karimi A, Hopes M, Martin KR, Lindfield D. Efficacy and safety of the Ab-interno xen gel stent after failed trabeculectomy. J Glaucoma 2018;27:864-8.
25. Hengerer FH, Kohnen T, Mueller M, Conrad-Hengerer I. Ab interno gel implant for the treatment of glaucoma patients with or without prior glaucoma surgery: 1-year results. J Glaucoma 2017;26:1130-6.
26. Heidinger A, Schwab C, Lindner E, Riedl R, Mossböck G. A retrospective study of 199 xen45 stent implantations from 2014 to 2016. J Glaucoma 2019;28:75-9.
27. Smith M, Charles R, Abdel-Hay A, Shah B, Byles D, Lim LA, *et al.*1-year outcomes of the Xen45 glaucoma implant. Eye (Lond) 2019;33:761-6.
28. Arnljots TS, Kasina R, Bykov VJN, Economou MA. Needling with 5-fluorouracil (5-FU) after XEN gel stent implantation: 6-month outcomes. J Glaucoma 2018;27:893-9.
29. Midha N, Rao HL, Mermoud A, Mansouri K. Identifying the predictors of needling after XEN gel implant. Eye (Lond) 2019;33:353-7.
30. Rooney DM, Shadid HR, Siegel LI, Watnick RL, Lesser GR, Obertynski T, *et al.* Postoperative complications of ab interno gelatin microstent. J Glaucoma 2019;28:e77-81.
31. Schlenker MB, Gulamhusein H, Conrad-Hengerer I, Somers A, Lenzhofer M, Stalmans I, *et al.* Efficacy, safety, and risk factors for failure of standalone ab interno gelatin microstent implantation versus standalone trabeculectomy. Ophthalmology 2017;124:1579-88.
32. Olate-Pérez Á, Pérez-Torregrosa VT, Gargallo-Benedicto A, Neira-Ibáñez P, Cerdà-Ibáñez M, Osorio-Alayo V, *et al.* Prospective study of filtering blebs after XEN45 surgery. Arch Soc Esp Oftalmol 2017;92:366-71.
33. Lenzhofer M, Strohmaier C, Hohensinn M, Hitzl W, Sperl P, Gerner M, *et al.* Longitudinal bleb morphology in anterior segment OCT after minimally invasive transscleral ab interno glaucoma gel microstent implantation. Acta Ophthalmol 2019;97:e231-7.
34. Martínez-de-la-Casa JM, Amaro-Barra A, Teus M, Vila-Arteaga J, Oyagüez I, Martínez C. Budget impact analysis of the XEN gel stent implant for glaucoma treatment. Expert Rev Ophthalmol 2018;14. [Doi: 10.1080/17469899.2018.1560264].

How to cite this article: Dangda S, Castanos MV, Do A, Panarelli JF. XEN gel stent: A review. Cli Exp Vis Eye Res J 2019;2(1):30-37.