Automated Gonioscopy Assessment of XEN45 Gel Stent Angle Location After Isolated XEN or Combined Phaco-XEN Procedures: Clinical Implications

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Glaucoma is the leading cause of blindness in the world.1,2 Intraocular pressure (IOP) remains the only modifiable risk factor for the disease, which is why IOP reduction is the mainstay of glaucoma therapy. Topical treatment is an effective strategy in most cases, but medication-related symptoms and a high treatment burden are common problems in achieving optimal disease control. The advent of MIGS (minimally invasive glaucoma surgery) led to the development of faster, less invasive, and safer surgical procedures offering a change in the paradigm of glaucoma treatment.3 MIGS offers the possibility of early intervention delaying classical, more aggressive, glaucoma surgery, and works as drop-sparing procedures, reducing treatment burden.

The XEN45 Gel Stent (Allergan, Dublin, Ireland) is a small hydrophilic porcine gelatin stent 6 mm long with a 45 µm luminal diameter, designed to work as an anterior chamber (AC) shunt to the subconjunctival space, allowing aqueous humor drainage, thus lowering IOP.4,5 This device belongs to the MIGS group of procedures and has a registered indication for the treatment of refractory open-angle glaucomas (OAGs, including pigmentary and pseudoxfoliative forms), with a favorable IOP-lowering performance and safety profile, and has also shown promising results in the treatment of uveitic glaucoma.6–14

Despite the availability of ab interno and ab externo XEN placement approaches, the former is the preferred approach as it is less invasive, less traumatic, and less prone to conjunctival bleb scarring and failure.5 Using the ab interno route, the implant is delivered into the iridocorneal angle (ICA), passing through the sclera, ending in the subconjunctival space, where a filtration bleb develops. Most authors use an antiscarring drug such as mitomycin C (MMC), which is injected into the subconjunctival space in the selected quadrant before the XEN insertion.5,7,15 Ab interno placement of the XEN depends on the use of a preloaded injector introduced into the AC, inserting stent at the level of the scleral spur (SS) or pigmented trabecular meshwork, preferably in the superior nasal quadrant.7,13,16 To ensure proper placement of the stent, several authors advocate the use of an intraoperative gonioscopy lens to avoid hitting the iris root or Schlemm canal, but also concede that its use is not mandatory. Furthermore, some authors admit using an intraoperative gonioscopy lens to avoid hitting the iris root or Schlemm canal, but also concede that its use is not mandatory. However, it remains unknown whether the XEN position in the ICA influences its performance or safety profile.

The combination of XEN implantation with cataract surgery (phaco-XEN) has a favorable safety and success profile, and has been shown to be a reasonable approach in
glaucoma patients with cataract. Studies have also demonstrated that cataract surgery results in AC-deepening and a widening of the ICA. However, knowledge on how these changes in perception of AC parameters by the cataract surgeon might affect XEN placement in the ICA is still lacking. 

The primary purpose of this study was to assess the placement of the XEN45 gel stent in the ICA and analyze surgical and safety outcomes according to XEN position in patients who had undergone XEN placement in a setting without intraoperative gonioscopy. Furthermore, secondary objectives included the comparison of XEN position in the angle in isolated and combined phaco-XEN placement, and also analysis on the surgical outcomes of both isolated and combined phaco-XEN surgeries.

**METHODS**

This study was a cross-sectional analysis of a group of consecutive adult glaucoma patients with OAG at a Glaucoma Clinic in tertiary referral hospital center. Patients in whom an XEN45 stent had been implanted underwent postoperative automated gonioscopy on study visit between January and August 2019 and all relevant clinical data were retrieved from patient clinical files on previous observations at our department. Inclusion criteria were as follows: patients 18 years of age and older; diagnosed with OAG; and previously subjected to XEN surgery. Exclusion criteria were as follows: history of previous laser procedures for glaucoma or ocular surgical procedures other than cataract surgery; inability or unwillingness to cooperate with automated gonioscopy; and patients whose gonioscopy photographs were of poor quality or the XEN and the angle were not adequately visible. An informed consent was obtained from all the patients included. This study was approved by the local ethical committee and adhered to the tenets of the Declaration of Helsinki and good clinical practice guidelines.

Surgical indication criterion for XEN placement in this group was either IOP above the target level despite maximum tolerated medical therapy or unwillingness to undergo that level of topical therapy or intolerance to that level of topical therapy. Patients were eligible for combined surgery if they also had a visually significant cataract. All XEN were implanted ab interno in the superior nasal quadrant, with the injection of 0.1 mL of MMC (0.2 mg/mL; 20 µg absolute dose) in the subconjunctival space before XEN insertion. A preloaded injector with a bevelled retractable 27G needle tip was introduced into a viscoelastic-filled AC through a clear corneal incision and the needle was introduced into the angle without gonioscopic control. After advancing the needle through the sclera up to the subconjunctival space, the stent was deployed as the needle was retracted, to guarantee adequate positioning of the stent. In combined phaco-XEN surgery, the stent was placed at the end of the phacoemulsification and intraocular lens insertion.

Per protocol, patients in whom XEN is implanted at our center stop all hypotensive drops and are started on antibiotic and steroid drops 4 times a day over 4 weeks with subsequent tapering. Information on needling or bleb revision procedures was retrieved from patient files. In our department, needling procedures of XEN implants use a bent 30 G needle to dissect fibrotic tissue within the bleb, followed by an injection of 0.1 mL MMC (0.2 mg/mL; 20 µg absolute dose) in the bleb.

The main outcome was surgical success. Absolute success was defined as an IOP reduction of ≥ 20% from baseline at last follow-up and an unmedicated IOP ranging from 6 to 21 mm Hg, whereas qualified success allowed for hypotensive medication. Failure to meet qualified success criteria at last follow-up and loss of light perception attributable to glaucoma or the surgical procedure and cases that needed additional drainage surgery were considered failures, but bleb revision or needling procedures were allowed. Kaplan-Meier survival curves were used to assess cumulative success probability for both absolute and qualified success at 24 months. Survival analysis also included the Manthel-Cox log-rank test to compare the probability of success.

Information on complications was retrieved from patient files and divided into intraoperative, early (within 1 wk postoperative), late (after 1 mo postoperative), and other complications. Intraoperative complications included visible AC bleeding upon XEN insertion. Early complications included seidel-positive sign; significant corneal edema, defined as increased stromal thickness, Descemet folds, and hazy iris details; hyphema, defined as blood pooling in the inferior AC on slit-lamp examination; shallow or flat AC; transient hypotony, defined as IOP < 6 mm Hg in the absence of hypotony-related complications; and choroidal effusion or folds. Late complications included sweating bleb, defined as necrotic and avascular walled bleb with seidel positivity. Other complications, unconstrained by time frame, included malignant glaucoma; endophthalmitis; blebitis; retinal detachment; visual acuity loss ≥ 2 lines at last follow-up; macular edema; and IOP spikes defined as IOP ≥ 30 mm Hg. XEN-related findings, such as occlusion, migration into or out of AC, iris touch, subconjunctival implant folding/kinking, and implant exposure, were also retrieved.

Automated gonioscopy was performed on study visit. Images were taken with the GS-1 automated gonioscope (NIDEK, Gamagori, Japan) to perform a 360-degree analysis of the ICA and to assess the location of the XEN stent in the angle. Before automated gonioscopy, topical oxybuprocaine hydrochloride 0.4% was administered to the eye intended for examination. The machine-attached gonio prism coupled with a lubricating gel was then manually operated with a joystick to contact the cornea and further adjustments were made to ensure proper centering and visualization of the ICA. When adequate focus was attained, the machine automatically took 16 sequential sets of high-resolution photographs of all ICA quadrants. Image analysis was carried out by 2 independent and masked observers and interrater agreement analysis was carried out with Cohen κ statistical model for rating the position of the XEN implant, where a κ of <0.00 indicated poor agreement, a κ of 0.00 to 0.20 indicated slight agreement, a κ of 0.21 to 0.40 indicated fair agreement, a κ of 0.41 to 0.60 indicated moderate agreement, a κ of 0.61 to 0.80 indicated substantial agreement, and a κ of 0.81 to 1.00 indicated almost perfect agreement. Image grading followed the Shaffer ICA Classification System. XEN insertion was classified as being anterior when at the level of the SS or anterior to it, or posterior insertion, when the insertion was posterior to the SS. Angle changes, both XEN-related and unrelated, such as peripheral anterior synchiae (PAS), were recorded.

Statistical analysis was carried out using GraphPad Prism 8 (San Diego, CA). Normality of distributions was assessed using the Shapiro-Wilk test. Continuous variables were
described as mean ± SD in parametric distributions or median and interquartile range in nonparametric ones. Group comparisons of continuous variables were performed using the Student \( t \) test or the Kolmogorov-Smirnov test according to normality, and using Fisher exact test in categorical variables. \( P < 0.05 \) was considered statistically significant.

**RESULTS**

Forty-six eyes of 37 patients were originally enrolled in this study, but 4 patients were subsequently excluded due to poor gonioscopy image quality and poor cooperation with the examination. Therefore, the remaining analyzed sample consisted of 42 eyes of 33 patients, two thirds (\( n = 22 \)) of patients being female. Our sample had a mean age of 71.6 ± 12 years, and all patients had completed at least 6 months of follow-up, with an average follow-up time of 17.7 ± 9.4 months after surgery. Fourteen eyes (33%) were pseudophakic and underwent isolated XEN placement, with the remaining 28 eyes having undergone a combined procedure. Apart from cataract surgery, there was no other concomitant surgical history at the time of XEN surgical implant in any of the eyes. Thirty-two eyes (76%) had POAG, with the remaining 10 eyes having secondary forms of OAG (8 eyes pseudoexfoliative and 2 uveitic). Most patients had moderate to advanced glaucoma damage, with an overall mean deviation of sensitivity of \(-13 ± 6.9 \)dB, similar for all compared groups (\( P > 0.05 \)). The demographic and clinical characteristics of our sample are detailed in Table 1. The Cohen \( \kappa \) for interrater agreement for the XEN position in the ICA was 0.903 (95% confidence interval: 0.772-1.000), indicating almost perfect agreement.

**XEN Implant Location**

After automated gonioscopy image analysis, a slight majority (60%) of the XEN implants were found to be inserted at SS or anterior to it (Figs. 1, 2) rather than posterior (Fig. 3). Nine eyes (64%) of the isolated XEN stents and 16 eyes (57%) of the combined surgery stents were placed anteriorly (\( P = 0.75 \)) (Table 2). None of the anteriorly placed stents were inserted anterior to Schwalbe line. Similar clinical characteristics were found after comparing cases according to XEN insertion location in the ICA (Table 1). The absolute success rate for anteriorly placed XEN was 32% and 35% in posteriorly placed stents (\( P > 0.99 \) and qualified success was 44% and 65% (\( P = 0.22 \)), respectively (Table 2). Survival analysis comparison of anterior and posterior XEN placements yielded similar survival curves.

**TABLE 1. Demographic and Clinical Characteristics of Our Sample According to Surgery and XEN Position**

|                          | Total          | Anterior XEN (at SS or Anterior) | Posterior XEN (Posterior to SS) | \( P \) | Isolated XEN | Combined XEN | \( P \) |
|--------------------------|---------------|----------------------------------|--------------------------------|--------|-------------|-------------|--------|
| Total number of eyes     | 42 (100)      | 25 (60)                          | 17 (40)                         | NA     | 14 (33)     | 28 (67)     | NA     |
| Age (mean ± SD) (y)      | 71.7 ± 12     | 70.2 ± 13                        | 73.7 ± 11                       | 0.55   | 73.4 ± 6.0  | 70.8 ± 9.8  | 0.19   |
| Female                   | 30 (71)       | 20 (80)                          | 10 (59)                         | 0.17   | 12 (86)     | 18 (64)     | 0.28   |
| White                    | 42 (100)      | —                                | —                               | —      | —           | —           | —      |
| Diagnosis                |               |                                  |                                 |        |             |             |        |
| POAG                     | 32 (76)       | 17 (68)                          | 15 (88)                         | 0.16   | 10 (71)     | 22 (79)     | 0.71   |
| SOAG                     | 10 (24)       | 8 (32)                           | 2 (12)                          | 0.16   | 4 (29)      | 6 (21)      | 0.71   |
| PEXG                     | 8 (19)        | 7 (28)                           | 1 (6)                           | 0.11   | 3 (21)      | 5 (18)      | > 0.99 |
| Uveitic                  | 2 (5)         | 1 (4)                            | 1 (6)                           | > 0.99 | 1 (7)       | 1 (4)       | > 0.99 |
| MD (mean ± SD) (dB)      | −13 ± 6.9     | −14 ± 6.8                        | −12 ± 7.2                       | 0.52   | −14 ± 5.6   | −13 ± 7.6   | 0.31   |
| Follow-up (mean ± SD) (mo)| 17.7 ± 9.4    | 18.1 ± 8.7                       | 17.2 ± 11                       | 0.77   | 20.1 ± 9.4  | 16.5 ± 9.3  | 0.79   |

Data is expressed as number of eyes (%), unless otherwise specified.
MD indicates mean deviation; NA, not applicable; PEXG, pseudoexfoliative glaucoma; POAG, primary open-angle glaucoma; SOAG, secondary open-angle glaucoma; SS, scleral spur.

FIGURE 1. A gonioscopy image of an XEN implanted at the level of the scleral spur. Figure 1 can be viewed in color online at www.glaucomajournal.com.

FIGURE 2. A XEN stent piercing a densely pigmented trabecular meshwork. Figure 2 can be viewed in color online at www.glaucomajournal.com.
(P = 0.84 for absolute success and 0.60 for qualified). The median survival for absolute success was 10 months for anterior placements and 16 months for posterior placements, whereas the median survival to failure was 21 months for both groups. For anteriorly placed XEN, the probability of survival of absolute success at 12 and 24 months was 51% and 33%, respectively, and for posterior placements, it was 53% and 34%. Accounting for qualified success, survival at 12 and 24 months was 74% and 41% for anterior placements and 80% and 50% for posterior placements (Fig. 4).

The mean (±SD) preoperative and last-visit IOP was 22.8 (± 9.09) and 19.4 (± 11.7) mm Hg (P = 0.15) for anteriorly placed XEN and 22.9 (± 7.61) and 16.4 (± 5.30) mm Hg (P < 0.01) for posterior placements (Fig. 5). Mean (±SD) number of medications preoperative and at last visit was 2.36 (± 1.04) and 0.68 (± 0.95) drugs for anterior placements (P < 0.01), and 2.77 (± 1.17) drugs for posterior placements (P = 0.02) (Fig. 6).

**Combined Versus Standalone XEN Surgery**

The overall absolute success rate was 33% and the qualified success rate was 52% at last follow-up. Both isolated XEN and combined phaco-XEN groups showed similar success rates, IOP-lowering, and drop-sparing performances. In combined phaco-XEN, absolute success was 36%, whereas in standalone XEN surgery, it was 29%, with no significant difference between groups (P = 0.74). Mean (±SD) preoperative and last-visit IOP was 21.6 (± 7.05) and 16.9 (± 8.40) mm Hg (P < 0.03) for combined surgery and 25.0 (± 10.6) and 20.9 (± 11.6) mm Hg (P = 0.06) for isolated XEN. Mean (±SD) number of medications preoperative and at last visit was 2.46 (± 1.20) and 0.74 (± 0.81) drugs for combined surgery and 2.93 (± 0.95) and 1.00 (± 1.17) drugs for isolated surgery. There were no significant differences between preoperative IOP and number of medications comparing combined and isolated surgery groups (P = 0.93). See Table 2 for further details.

**Complications**

Our sample recorded 20 cases of failure (48%). This outcome was not associated with type of surgery or location of the XEN, with 14 cases of failure in anteriorly placed XEN and 6 in posterior placements (P = 0.22). The mean time of failure was 19 ± 10 months after surgery, with only 4 cases (20% of failures) occurring before year 1 of follow-up.

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**FIGURE 3.** A XEN inserted posterior to the scleral spur. Figure 3 can be viewed in color online at www.glaucomajournal.com.

**TABLE 2.** Comparison of Success Outcomes and Clinical Measurements Between Surgical Groups and XEN Location

|                | Total | Anterior XEN (at SS or Anterior) | Posterior XEN (Posterior to SS) | Isolated XEN | Combined XEN |
|----------------|-------|----------------------------------|----------------------------------|--------------|--------------|
| Preoperative IOP [mean (± SD)] (mm Hg) | 22.8 (± 9.09) | 22.8 (± 9.43) | 25.0 (± 10.6) | 21.6 (± 7.05) | 25.0 (± 10.6) |
| Last visit IOP [mean (± SD)] (mm Hg) | 19.4 (± 11.7) | 16.9 (± 8.40) | 16.4 (± 5.30) | 19.4 (± 11.7) | 16.4 (± 5.30) |
| P for preoperative vs. last visit IOP | <0.01* | <0.01* | <0.01* | <0.01* | <0.01* |
| IOP drop rate from baseline to last follow up [mean (± SD)] (%) | 18 (± 28) | 14 (± 27) | 23 (± 29) | 2.46 (± 1.20) |
| Preoperative Meds [mean (± SD)] | 2.62 (± 1.13) | 2.83 (± 1.64) | 2.76 (± 1.63) | 2.46 (± 1.20) |
| Last visit Meds [mean (± SD)] | 0.83 (± 0.74) | 0.88 (± 0.75) | 0.80 (± 0.77) | 0.74 (± 0.81) |
| P for preoperative vs. last visit Meds | <0.01* | <0.01* | <0.01* | <0.01* |
| Absolute success (%) | 33 | 25 | 26 | 29 | 36 |
| Relative success (%) | 52 | 44 | 65 | 50 | 54 |
| Anteriorly placed XEN (at SS or anterior) | 25 (60) | 18 (36) | 33 | 25 (60) | 18 (36) |
| Posteriorly placed XEN (posterior to SS) | 65 | 44 | 32 | 65 | 44 |
| IOP indicates intraocular pressure; Meds, number of medication classes; NA, not applicable; SS, scleral spur.

*P < 0.05 is considered statistically significant.
all of them representing early bleb failures by month 3, and 3 of them were implanted with a new XEN stent in a different quadrant. The rest of the failures occurred on average at 23 months after surgery.

Overall, the most common complications were intraoperative AC bleeding (24%; n = 10), early hypotony (24%; n = 10), IOP spikes (19%; n = 8), and hyphema (12%; n = 5). We recorded a higher rate of intraoperative and early postoperative complications in the group with posteriorly placed XEN (Table 3). The number of eyes with an intraoperative or an early complication was significantly higher in posterior placements (40% vs. 76%; anterior vs. posterior; P = 0.03). Most of these complications were hemorrhagic in nature, such as intraoperative AC bleeding and hyphema. There was no association between intraoperative AC bleeding or hyphema and overall or early failure (P > 0.05).

Hypotony cases were numerical only (IOP < 6 mm Hg), with no association with XEN level of insertion (P > 0.99), and all resolved spontaneously within the first week after surgery, with no ensuing vision-threatening complications such as choroidal effusion, folds, or macular edema. Two of the patients with hypotony showed visibly narrow or flat AC, which also resolved within the first week after surgery. Eyes in three patients (7%) had small temporal choroidal effusions that spontaneously resolved without specific treatment. There were no cases of persistent hypotony.

IOP spikes occurred within the first 6 months after the surgery, more than half of those (n = 5) within the first month. IOP spike rates were similar in both anterior and posterior XEN placement groups (P > 0.99). The presence of an IOP spike resulted in failure in 50% of cases and needling in 38%. It was not associated with overall failure (P > 0.99), but was associated with cases of early failure (<6 mo after the surgery; P < 0.01) and with needling (P = 0.02).

No eyes suffered from loss of light perception or other serious, sight-threatening complications. Needling was performed in 4 eyes (10%). Of these, 3 patients underwent needling under 6 months after surgery and the other at 17 months of follow-up. No patient underwent needling more than once. Two cases that had been subjected to needling early eventually failed late in the follow-up. Late complication and needling rates were similar between both anterior and posterior XEN placement groups (Table 3).

Almost half of the stents in both groups (48% and 47% in anterior and posterior placements, respectively; total n = 20) showed XEN-related complications or abnormal gonioscopic findings, such as stent kinking/folding, migration out of or into the AC, iris touch, and adjacent PAS

FIGURE 4. Kaplan-Meier survival curves for anterior and posterior XEN groups according to absolute (A) and qualified (B) success criteria at 24 months. Censored patients include those who completed follow-up without failure and patients followed under 24 months, but did not fail at last follow-up. Figure 4 can be viewed in color online at www.glaucomajournal.com.

FIGURE 5. Mean (±SD) changes in the intraocular pressure (IOP) profile over time during 24-month follow-up according to XEN location. Figure 5 can be viewed in color online at www.glaucomajournal.com.
There was no significant difference in success outcomes between patients with XEN-related findings and those without \( (P > 0.99) \), as was the case when specifically comparing patients with or without XEN-related PAS \( (P > 0.05) \).

Complication rates were similar between both combined and isolated XEN procedures, including needling rates (Table 3). All phacoemulsification procedures were uncomplicated, except for 2 cases with significant but transient corneal edema in the first week after surgery.

**DISCUSSION**

The XEN45 gel stent has been recognized as a safe and effective MIGS procedure for several forms of OAG, including advanced and refractory glaucoma.\(^6,7\) Its need for minimal conjunctival manipulation allows for combination with cataract surgery.\(^6,12,15,19,20\) To the best of our knowledge, ours is the first study on XEN location assessment in the ICA and its possible clinical implications, either in standalone or in combined surgeries.

The main purpose of this study was to determine whether different levels of XEN insertion in the ICA could result in different success or safety profiles. Our results show similar absolute (32% vs. 35%; \( P > 0.99 \)) and qualified (44% vs. 65%; \( P = 0.22 \)) success rates for both anterior and posteriorly placed XEN, respectively. Both groups also showed similar IOP-lowering and drop-sparing performances, although the anterior XEN group failed to show a statistically significant IOP drop from baseline to last follow-up \( (P = 0.15) \). This difference in IOP reduction from baseline between both XEN location groups suggests an overall better IOP reduction profile for posteriorly placed XEN. As can be seen in Table 2, the IOP drop rate in the anterior XEN group is slightly lower than that

**TABLE 3. Complications and Needling Rates Comparing XEN Position and Surgical Approach**

| Intraoperative       | Total | Anterior (at SS or Anterior) | Posterior (Posterior to SS) | \( P \)   | Isolated XEN | Combined XEN | \( P \)   |
|----------------------|-------|-------------------------------|-----------------------------|------|-------------|-------------|------|
| AC bleeding          | 10 (24) | 4 (16)                        | 6 (35)                      | 0.27 | 3 (21)      | 7 (25)      | > 0.99 |
| Early (first week)   | 16 (38) | 8 (35)                        | 9 (53)                      | 0.34 | 6 (43)      | 10 (36)     | 0.74 |
| Seidel positive      | 0 (0)   | 0 (0)                         | 0 (0)                       | > 0.99 | 0 (0)      | 0 (0)      | > 0.99 |
| Hyphema              | 5 (12)  | 1 (4)                         | 4 (24)                      | 0.14 | 2 (14)      | 3 (11)      | > 0.99 |
| Hypotony             | 10 (24) | 6 (24)                        | 4 (24)                      | > 0.99 | 3 (21)     | 7 (25)      | > 0.99 |
| Shallow or flat AC   | 4 (10)  | 2 (8)                         | 2 (12)                      | > 0.99 | 2 (14)     | 2 (7)       | 0.59 |
| Choroidal effusion   | 3 (7)   | 2 (8)                         | 1 (6)                       | > 0.99 | 2 (14)     | 1 (4)       | 0.25 |
| Corneal edema        | 2 (5)   | 1 (4)                         | 1 (6)                       | > 0.99 | 0 (0)      | 2 (7)       | 0.54 |
| Intraoperative+early | 22 (53) | 10 (40)                       | 13 (76)                     | 0.03* | 7 (50)     | 15 (54)     | > 0.99 |
| Late (> 1 mo)        | 3 (7)   | 1 (4)                         | 2 (12)                      | 0.56 | 0 (0)      | 3 (11)      | 0.54 |

Other complications

- Sweating bleb
  - 3 (7) | 1 (4) | 2 (12) | 0.56 | 0 (0) | 3 (11) | 0.54

- Malignant glaucoma
  - 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | > 0.99

- Endophthalmitis
  - 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | > 0.99

- Blebitis
  - 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | > 0.99

- Retinal detachment
  - 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | > 0.99

- VA loss ≥ 2 lines
  - 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | > 0.99

- Macular edema
  - 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | > 0.99

- IOP spikes
  - 8 (19) | 5 (20) | 3 (18) | > 0.99 | 4 (29) | 4 (14) | 0.41

- Needling
  - 4 (10) | 3 (12) | 1 (6) | 0.64 | 2 (14) | 2 (7) | 0.59

Data is expressed as number of eyes (%) for each type of complication.

AC indicates anterior chamber; IOP, intraocular pressure; SS, scleral spur; VA, visual acuity.

*\( P < 0.05 \) is considered statistically significant.
in posterior XEN (14±27% vs. 23±29%; P=0.24), and despite similar mean baseline IOP, measurements at last follow-up are slightly higher in the anterior group. Survival curves for both groups resulted in similar success probabilities at 12 and 24 months and similar median times to failure, although the posterior placement group had a slightly higher median survival time for absolute success (16 vs. 10 mo in the anterior stents; Fig. 4).

Safetywise, our results point toward a higher proportion of complications within the first week of the surgery, including intraoperative complications, in XEN stents that have been placed posterior to the SS (40% vs. 76%; P=0.03). This difference is largely due to the higher rates of intraoperative AC bleeding (16% vs. 35%; P=0.34) and hyphema within the first week after the procedure (4% vs. 24%; P=0.14). All the remaining complications were similar in number in both groups (Table 3).

It could have been expected that the AC pressures involved in cataract surgery could have a temporary effect on the angle and in deepening the AC compared with a more stable pseudophakic eye. This effect could theoretically make room for a more posterior placement of the stent in a setting without intraoperative gonioscopy. However, we found no significant difference in XEN placement in the ICA comparing combined and standalone procedures, with the majority of the stents being placed in the SS or anterior to it in both groups (P=0.75). It should be stated that this conclusion is hindered by a small sample and by the fact that we analyzed twice as many combined surgeries as we did standalone procedures.

The use of a gonio lens to aid in the procedure has been suggested, but many glaucoma surgeons do not use it routinely after the initial learning curve, nor is it deemed strictly necessary. Most authors have advised proper placement of the XEN with direct visualization of the angle to avoid hitting the iris root, ciliary body band, or the Schlemm canal, fearing intracameral bleeding or postoperative hypotony.13,16 Our results seem to support the hypothesis that early complications and bleeding rates may be higher in XEN placed posterior to the spur (Table 3). Interestingly, these early complications did not seem to influence long-term final outcomes in a significant manner. Although it may be prudent to use a gonio lens in a patient with a high bleeding risk or in the case of a more inexperienced surgeon, it is not mandatory, as the level of XEN placement does not seem to be a critical factor in determining surgical success. It would be interesting to see a prospective randomized trial comparing XEN surgery outcomes between intraoperative gonioscopy and no-gonioscopy groups.

Our study discloses overall, standalone, and combined XEN surgery absolute success rates of 33%, 29%, and 36% and qualified rates of 52%, 50%, and 54%, respectively. These results are slightly lower than those reported in most studies at 12 months (37.4% to 76.5%11,13,15,18), although definitions of success varied widely among these reports. Some factors may account for this difference, such as a longer follow-up in our series (average: 18 vs. 12 mo in most studies), and a lower needling rate in our study (10%) versus reported rates of 32.3% to 41.1%.11,13,15,18 At our center, we are precluded from performing needling procedures with MMC outside the operating room due to hospital pharmacy rules, and it is our experience that most of our patients would rather have 1 drop added to their therapeutic regimen than go back to the operating table, which might partially explain this difference in needling rates. Moreover, most of our failures (80%) occurred after 1 year of follow-up (average: 23 mo). Two large studies have shown greater success rates at 2 years of follow-up than ours, albeit with less stringent success criteria.6,12 The presence of IOP spikes was associated with stent failure within the first 6 months (P=0.01) and with the need for needling procedures (P=0.02), possibly indicating early bleb failure.

Combined XEN surgery could, theoretically, take advantage of the IOP-lowering effect of both cataract surgery27 and glaucoma surgery. However, most published studies do not support this idea, and have shown comparable results between both isolated and combined XEN surgery techniques.11-13,18,19 Nevertheless, our study shows a trend toward better results in the combined phaco-XEN group (Table 2). In fact, the IOP difference from baseline to last visit was statistically significant in the combined surgery group (P<0.03), but not in the standalone XEN group (P=0.06). These results are in disagreement with previous reports.11-13,18,19

Automated gonioscopy is a promising and recently developed technique for ICA analysis that has shown good results for ICA grading, pigmentaion analysis, and the ability to demonstrate proper positioning of angle devices and postsurgical angle changes.28-30 Similarly, anterior segment optical coherence tomography may prove to be an interesting approach to evaluate angle surgical devices.
and bleb changes. Accumulation of hyperreflective material within the lumen of XEN stents with anterior segment optical coherence tomography was recently described and it was posited that this phenomenon may be responsible for late XEN failure cases, particularly in combined surgery.31 In our study, automated gonioscopy proved to be a valuable tool in documenting angle changes after surgery and throughout patient follow-up. It allowed for a post hoc analysis of a picture rather than a fleeting image at the slit lamp. The masked observers were thus able to assess all angle features in a systematic and similar way, decreasing observer bias. These magnified views of the angle permitted both angle classification and XEN location, and documentation of the development of some XEN-related angle changes, such as synechiae formation, XEN migration, and displacement. Gonioscopic identification and documentation of these changes may, in some settings, allow for more careful vigilance of at-risk implants and help develop subsequent interventions. Furthermore, although we did not analyze endothelial cell count and postoperative loss, XEN movements in the AC may be linked to localized and significant endothelial cell loss.32,33 Although endothelial cell density loss of the XEN stent has been shown to be comparable to that of standard cataract surgery,34 it would be interesting to assess whether endothelial cell density loss could be directly related to the implant’s position in the ICA and length in the AC.

This study has several limitations. First and foremost, a small and imbalanced sample hindered the statistical power of some comparisons between groups. Furthermore, given its cross-sectional design, there was no predefined time-frame for evaluations and consequently follow-up times varied among our patients. Considering that gonioscopy was performed at study visit, the time from surgery to registering the angle findings in angle pictures (i.e., the follow-up time) varied among the patients. This may be particularly important for the parameter of stent length in the AC, as there have been reports of late movement of the XEN.32,33 and other angle findings that may be dynamic and time dependent, such as the formation of PAS or stent occlusion. However, because it is unlikely that the stent location in the angle itself would change over time, our main gonioscopic analysis should stand independent of follow-up time. Also, there was no medication washout period, which means that we never measured the patient’s nonmedicated IOP. Some patients had different IOP targets due to their disease stage, which allowed for a higher tolerance in some patients toward medication prescription.

In conclusion, the location of the stent in the ICA did not seem to impact late success outcomes and was not associated with a higher risk of serious complication, although posterior placements did show a tendency toward a higher rate of early postoperative complications, particularly of a hemorrhagic nature. Moreover, in our sample, the combined phaco-XEN procedure did not seem to influence the location of the XEN in the ICA versus an isolated XEN placement. The authors believe that the angle location of the stent is not a determining factor of success in XEN surgery and that further investigation is warranted to clarify positive and negative predictive factors for this type of surgical procedure.

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