DIPLOMA THESIS

A Retrospective Study of 199 Xen45 Stent Implantations from 2014-2016

submitted by

Astrid Heidinger

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under the Supervision of

Priv.-Doz. Dr. Georg Mossböck

and

Priv.-Doz. DDr. Christoph Schwab

Graz, November 22nd, 2018

Statutory Declaration

I hereby formally declare that I have written the submitted thesis independently and without any outside support except for the quoted literature and other sources mentioned in the paper. I clearly marked and separately listed all of the literature and all of the other sources which I employed when producing this academic work, either literally or in content.

Graz, November 22nd, 2018 *Astrid Heidinger eh.*

Foreword

This work* has been accepted by the Journal of Glaucoma and is expected to be published in Volume 28, January 2019, Issue 1. As first author of this peer-reviewed publication I collected and prepared clinical data to investigate the postoperative course after Xen45 implantation performed at the Department of Ophthalmology, Medical University Graz. Follow-up examinations were conducted by Priv.-Doz. DDr. Christoph Schwab, Priv.-Doz. Dr. Ewald Lindner and Priv.-Doz. Dr. Georg Mossböck. Complex statistical analysis were conducted by Dipl.-Ing. Dr. Regina Riedl, Institute for Medical Informatics, Statistics and Documentation, Medical University of Graz. To give a better representation of the outcome, I compared our results with recently published Xen studies.

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I am also grateful for the untiring statistical effort of Dipl.-Ing. Dr. Regina Riedl, without whom I would not have been able to write this thesis.

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And, last but not least, I would like to say thank you to my wonderful friends, who made my years of study memorable.

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Abbreviations

AC	anterior chamber
BCVA	best corrected visual acuity
IOP	intraocular pressure
MD	mean defect
MIGS	minimally invasive glaucoma surgery
MMC	mitomycin C
n.a.	not available
PE	phacoemulsification
PEX-G	pseudoexfoliative glaucoma
POAG	primary open-angle glaucoma
SD	standard deviation
TSCPC	transscleral cyclophotocoagulation

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Zusammenfassung

Einleitung:

Das Ziel dieser Studie ist die Ermittlung des postoperativen Verlaufes nach Xen45 Gel Stent Implantation an der Medizinischen Universität Graz zwischen 2014-2016.

Methoden:

Es handelt sich um eine monozentrische retrospektive Studie, wobei alle PatientInnen mit Xen-Implantation im Zeitraum 2014-2016 inkludiert wurden. Klinische Aufzeichnungen, wie auch erhaltene Berichte von niedergelassenen AugenärztInnen wurden für die Evaluation herangezogen. Folgende Parameter wurden untersucht: intraokulärer Druck (IOD), drucksenkende Therapie, Visus, Anzahl der Voroperationen, IOD-Follow-Up, intra- und postoperative Komplikationen, Interventionsrate (Needling), zusätzlich indizierte Glaukomoperationen.

Ergebnisse:

Xen wurde in 199 Augen von 160 PatientInnen implantiert. Der mittlere präoperative IOD lag bei 22.8 ± 6.9 mmHg unter einer mittleren drucksenkenden Therapie von 2.9 ± 1.0. Nach 12 Monaten war der mittlere IOD bei 17.1 ± 5.9 mmHg (n=89, $p < 0.0001$; 22.7% mittlere Senkung) unter einer mittleren drucksenkenden Therapie von 1.8 ± 1.4 (n=87, $p < 0.0001$). Es gab keine intraoperativen Komplikationen. Zwei Fälle (1.0%) von schweren postoperativen Komplikationen sind aufgetreten (malignes Glaukom und late-onset Endophthalmitis). Postoperatives Needling war in 44 Fällen (22.1%) indiziert, während in 28 Fällen (14.1%) eine weitere sekundäre Glaukomoperation durchgeführt wurde.

Fazit:

Unsere Ergebnisse zeigen, dass die Xen-Implantation ein effektiver chirurgischer Eingriff ist, der zu einer signifikanten Reduktion des IOD sowie der drucksenkenden Medikation bei einer niedrigen Komplikationsrate führt. Ein aufmerksames postoperatives Management scheint unerlässlich zu sein.

Abstract

Purpose:

The aim of this study is to determine the postoperative course after Xen45 Gel Stent implantation at the Medical University of Graz from 2014-2016.

Methods:

Single-center, retrospective study. All patients with Xen implantation between 2014-2016 were included. Clinical records and reports received from supervising ophthalmologists were used for evaluations. Investigated parameters were intraocular pressure (IOP), number of medications, visual acuity and number of previous operations, IOP-follow-up, intra- and postoperative complications, rate of interventions (needling), and additionally performed surgeries.

Results:

Xen was implanted in 199 eyes of 160 patients. Mean preoperative IOP was 22.8 ± 6.9 mmHg on 2.9 ± 1.0 IOP-lowering medication. After 12 months follow-up, mean IOP was 17.1 ± 5.9 mmHg (n=89, $p < 0.0001$; mean reduction of 22.7%) on 1.8 ± 1.4 (n=87, $p < 0.0001$) IOP-lowering medications. There were no intraoperative complications and in two cases (1.0%) severe postoperative adverse events occurred (aqueous misdirection and late-onset endophthalmitis). Postoperative needling was indicated in 44 cases (22.1%), while in 28 cases (14.1%) an additional glaucoma surgery was performed.

Conclusion:

Our results indicate that Xen implantation is an effective surgical intervention leading to a significant reduction of IOP and number of medications with a low rate of complications. An attentive postoperative management seems to be mandatory.

1 Introduction

Glaucoma remains the second leading cause of blindness in the world [1]. At present, the reduction of intraocular pressure (IOP) remains the only effective treatment of glaucoma with the aim of preventing additional optic nerve damage [2]. IOP reduction might be achieved by topical therapy, or operation in case of insufficient effect or intolerance, whereas trabeculectomy remains the most effective IOP lowering operation. However, trabeculectomy is an invasive treatment method with potential sight-threatening postoperative complications (e.g. hypotony or endophthalmitis).[3] Minimally invasive glaucoma surgery (MIGS) is a relatively new development in glaucoma care aiming faster recovery, less impact to eye structures, less refractive and visual changes, and a lower risk of complications compared to trabeculectomy.

The Xen-Implant represents a new minimally invasive glaucoma treatment method. Xen is a small tube made of gelatine with a lumen of 45µm, which is placed in the iridocorneal angle draining the aqueous humour into the subconjunctival tissue. The principle of the Xen is based on the Hagen-Poiseuille equation allowing the calculation of the aqueous outflow resistance [4]. These considerations reduce the risk of postoperative hypotony. Xen insertion is done through a 1.5mm incision which theoretically reduces the risk for postoperative endophthalmitis.

Since Xen is a relatively new device only few long-term data are available at the moment.

In this study we present the postoperative course of IOP, number of medications, adverse events and interventions up to 18 months in patients receiving Xen.

2 Material and Methods

In this single-center study we retrospectively investigated the course of eyes after Xen implantation (Xen45, Allergan, CA, USA) between 2014 and 2016. All patients who received a Xen implant within this time period were included in this study. No further exclusion criteria were defined. All implantations were performed at the University Hospital of Graz, Department of Ophthalmology. The study was conducted in accordance with the Declaration of Helsinki, and the study protocol was approved by the local ethics committee.

Data were acquired from clinical records, both analog and digital as well as reports received from supervising ophthalmologists. Ocular examination in the preoperative visit included Goldmann Applanation Tonometry, best corrected visual acuity (BCVA), slit lamp biomicroscopy and gonioscopy. Furthermore, number of medications were recorded. Visual field testing was performed using Octopus 900 (Haag Streit, Switzerland).

Postoperatively, intraocular pressure, number of glaucoma medications and number of interventions (i.e. needling) as well as adverse events were noted at day 1 (1-3 d), week 1 (4-14d), month 1 (15-60d), month 3 (61-122d), month 6 (123-272d), month 12 (273-456d) and month 18 (457-639d) [5]. For multiple measurements per eye within each time window, mean values were calculated for IOP and maximum values were used for medication. Best corrected visual acuity was examined up to 12 months. Follow-up data for reoperation was available up to about 30 months. If a secondary glaucoma surgery was indicated, patients' follow-up discontinued.

Complete success was defined as an IOP reduction ≥ 20% from baseline with an IOP < 18mmHg without glaucoma medications at 12 months. Qualified success was defined as an IOP reduction ≥ 20% from baseline with an IOP < 18mmHg with glaucoma medications at 12 months. Failure was defined as an IOP reduction ≤ 20% from baseline, IOP ≥ 18mmHg and need of additional glaucoma surgery.

2.1 Surgical Technique

Surgeries were performed in topical or retrobulbar anesthesia. After povidone iodine skin disinfection patients' eyelashes and the surroundings were covered with sterile foil and eyelids were kept in position with a lid speculum. 0.1ml of mitomycin C (MMC) 0.1mg/ml was applied under the conjunctiva at the superior nasal conjunctiva and was not washed out. The peripheral corneal incision was done at the contralateral side of the desired implant position. After the anterior chamber (AC) was filled with a cohesive viscoelastic device (Healon Ophthalmic Viscoelastic Device, Abbott Medical Optics, CA, USA) the XEN preloaded injector was inserted and directed across the AC to penetrate the iridocorneal angle. Passing through the sclera the needle exited approximately 3 mm post-limbal into the subconjunctival space, where the implant was then released. After the injector was removed, the AC was cleared from the cohesive viscoelastic and cefuroxim was applied. No sutures were needed for the incision. At the end a combination of dexamethasone and gentamicinsulfate eye ointment (Dexagenta, Ursapharma, Austria) were applied to the eye. The postoperative management included topical steroid and antibiotics for five weeks. In case the implantation was combined with a cataract surgery, phacoemulsification was done first. All surgeries were done by the same surgeon (G.M.).

2.2 Statistical Analysis

To evaluate the postoperative course of IOP and number of postoperative medications over time, a mixed-effects model was performed as recommended by Fan et. al. [6]. To account for the correlated structure in the data (i.e. inclusion of both eyes for 39 patients and the repeated measurements over time), a random intercept for patient and for eye was included in the model. The repeated measurements over time were included in the categories: pre-OP, 1 day (only for IOP), 1 week, 1, 3, 6, 12 and 18 months after implantation, as fixed effect. A banded main diagonal covariance matrix (UN(1), no covariance and heterogeneous variances between the time windows) was modeled for the repeated measurements over time. Postoperative complications and interventions were analyzed descriptively. Continuous variables are presented as mean ±

standard deviation, minimum and maximum, categorical data frequencies and percentages, unless otherwise stated. Statistical analyses were performed using SAS software (version 9.4, SAS Institute, Cary, NC).

3 Results

Preoperative clinical data are presented in Table 1. 199 eyes of 160 glaucoma patients of both sexes (115 female; 84 male) were included in this study. The mean age at implantation was 74.8 ± 10.5 (33-93) years. Primary open-angle glaucoma (POAG) was the most common diagnosis with 113 eyes (56.8%), followed by 72 (36.2%) cases with pseudoexfoliation glaucoma. Another eleven secondary glaucoma were noted as follows: three pigmentary glaucoma, two traumatic glaucoma, two steroid glaucoma, one uveitic glaucoma, one aphakic glaucoma, one post-penetrating keratoplasty glaucoma and one glaucoma after retinal detachment. Further two eyes were diagnosed with angle-closure glaucoma and one with normal-tension glaucoma.

Table 1: Preoperative Clinical Data

Sex, n (%) Female Male	 115 (57.8) 84 (42.2)
Age, years mean ± SD (range)	74.8 ± 10.5 (33-93)
Type of glaucoma, n (%) POAG PEX-G Other secondary glaucoma Angle-closure glaucoma Normal-tension glaucoma	 113 (56.8) 72 (36.2) 11 (5.5) 2 (1.0) 1 (0.5)
IOP-Baseline, mmHg mean ± SD (range)	22.8 ± 6.9 (9 - 46)
Number of IOP-lowering medication, mean ± SD (range) Total number, n (%) 0 1 2 3 4 5	2.9 ± 1.0 (0 - 5) 1 (0.5) 18 (9.1) 45 (22.6) 76 (38.2) 55 (27.6) 4 (2.0)
Visual acuity, logMAR mean ± SD (range)	0.5 ± 0.5 (0.0 - 2.1)
MD, dB, mean ± SD (range)	12.0 ± 5.6 (1.8 - 23.5)

POAG = Primary open angle glaucoma; PEX-G = Pseudoexfoliative Glaucoma; IOP = Intraocular pressure; MD = Mean defect, SD = Standard deviation

In 89 cases (44.7%) a previous ocular surgery was performed (Table 2): 61 eyes (30.7%) had at least one glaucoma surgery, 45 (22.6%) underwent a previous cataract surgery and in 13 cases (6.5%) other ocular surgeries were previously performed. Preoperative, mean baseline IOP was 22.8 ± 6.9 (9 - 46) mmHg, while mean IOP-lowering medication was 2.9 ± 1.0 (0 - 5), including 22 (11.1%) cases requiring oral IOP-lowering medications. Mean visual acuity was 0.5 ± 0.5 (0.0 - 2.1) logMAR, while mean visual field mean deviation was 12.0 ± 5.6 (1.8 - 23.5) dB.

Table 2: Previous Ocular Surgeries

Surgery	n (%)
Number of cases with previous ocular surgeries	*89 (44.7)*
One or more previous glaucoma surgery	*61 (30.7)*
Laser trabeculoplasty	33 (16.6)
Trabeculectomy	28 (14.1)
Iridotomy	5 (2.5)
TSCPC	2 (1.0)
Goniotomy	2 (1.0)
Gold shunt	1 (0.5)
Cyclocryotherapy	1 (0.5)
Previous cataract surgery	*45 (22.6)*
Phacoemulsification	44 (22.1)
Lentectomy	1 (0.5)
One or more other previous ocular surgery	*13 (6.5)*
Vitrectomy	5 (2.5)
Intravitreal injection	3 (1.5)
Encircling band	3 (1.5)
Penetrating keratoplasty	3 (1.5)

TSCPC = Transscleral cyclophotocoagulation

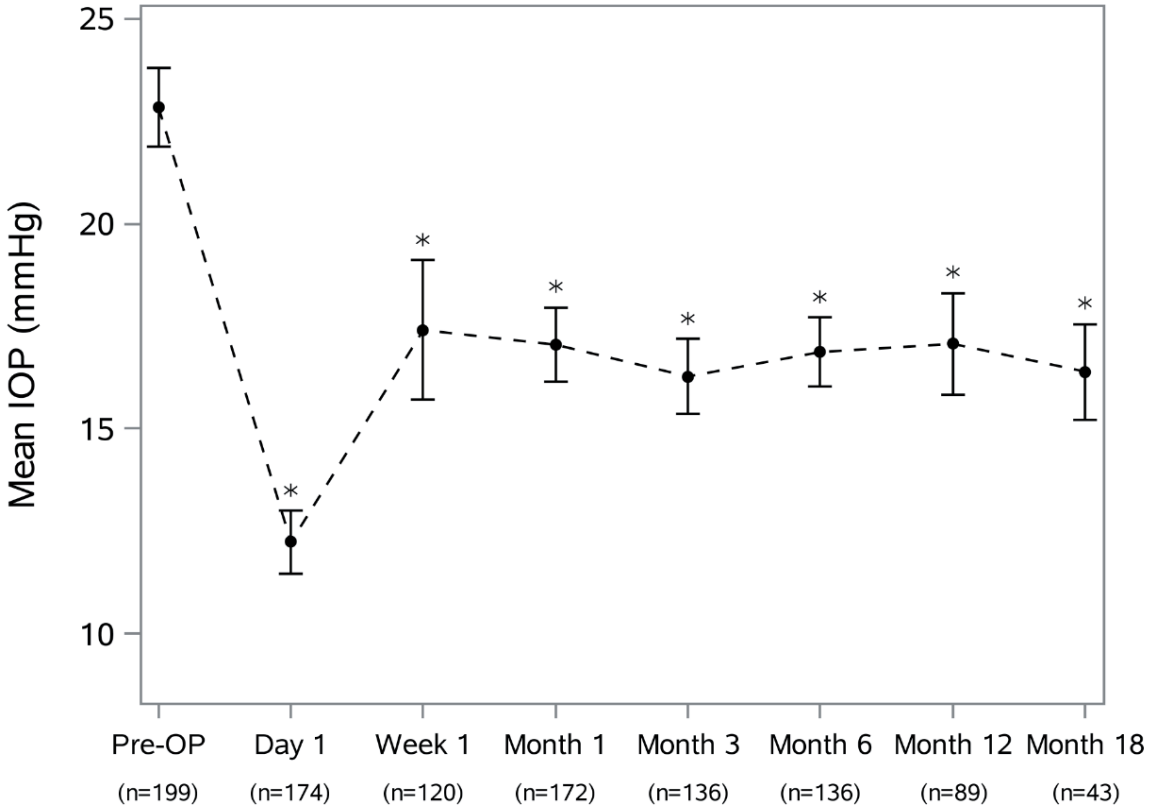
In 92 cases (46.2%) the right eye and in 107 cases (53.8%) the left eye was stented. In 138 operations (69.3%) the implantation was combined with a phacoemulsification, whereas the other 61 (30.7%) operations were done as a standalone procedure. MMC was applied in 188 procedures (94.5%). In 183 (92.0%) procedures only one Xen injector was used. In 14 (7.0%) cases two and

in 2 (1.0%) cases three Xen injectors were required due to malpositioning (n=14) and device malfunctions (n=2).

3.1 Follow-up Data

The mean preoperative IOP of 22.8 ± 6.9 mmHg dropped significantly after XEN implantation in all investigated time windows (p<0.0001, respectively) (Figure 1). During follow up, mean IOP of 17.1 ± 6.1 mmHg (n=172), 17.1 ± 5.9 mmHg (n=89) and 16.4 ± 3.8 mmHg (n=43) were observed after 1, 12 and 18 months, corresponding to an IOP-reduction of 22.3%, 22.7% and 20.1% from baseline, respectively.

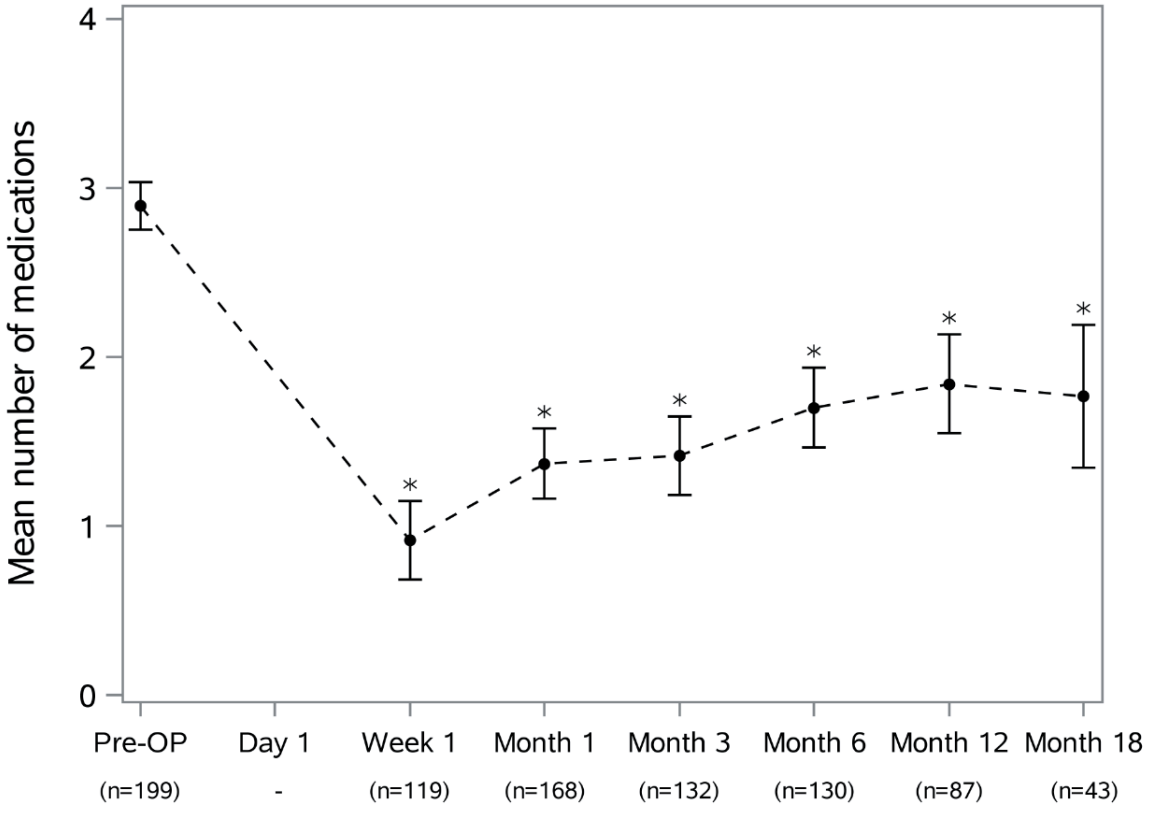
Figure 1: Mean Intraocular Pressure (IOP) with 95% Confidence Intervals Over Time



** indicates statistical significance compared with pre-OP (p<.0001)*

Statistically significant changes in the mean number of medications from baseline to the follow-up measurements were observed (p<0.0001, respectively) (Figure 2). After one month, the mean number of medications decreased from 2.9 ± 1.0 at baseline to 1.4 ± 1.4 (n=168), which increased to 1.8 ± 1.4 (n=87) after one year. Furthermore, 18 months postoperative number of medications was 1.8 ± 1.4 (n=43).

Figure 2: Mean Number of Glaucoma Medications with 95% Confidence Intervals Over Time



** indicates statistical significance compared with pre-OP (p<.0001)*

Mean visual acuity was 0.4 ± 0.5 logMAR (n=166) at last measurement within 365 days postoperatively, with a median follow-up of 186 days (1 – 365 days). An improvement was seen in 90 cases (54.2%) whereas a decrease was seen in 40

cases (24.1%), of which 22 cases (55.0%) were done in Xen standalone procedure. In 36 cases (21.7%) visual acuity remained stable.

Performing a descriptive follow-up stratified by age (categories: <60, 60-79, >79 years), sex, type of glaucoma, type of operation (combined versus standalone) and cases with previous ocular surgeries, a similar postoperative course of IOP and number of postoperative medications over time were observed within the strata (Supplemental Table 1).

Supplemental Table 1: Stratified analyses of IOP and number of medication follow-up

	Category	*n* at baseline	*n* at 12 months	Baseline IOP ± SD (mmHg)	IOP at 12 months ± SD (mmHg)	Baseline medication ± SD (number)	Medication at 12 months ± SD (number)
Sex	Female	115	49	22.7 ± 6.8	17.3 ± 6.8	3.0 ± 1.0	1.8 ± 1.3
	Male	84	40	23.0 ± 7.0	16.8 ± 4.6	2.8 ± 1.0	1.9 ± 1.4 *n=38*
Age	< 60	19	12	25.1 ± 8.9	18.5 ± 4.3	3.5 ± 0.9	1.7 ± 1.6
	60-79	109	50	23.2 ± 6.9	16.8 ± 3.9	2.9 ± 1.0	1.8 ± 1.4 *n=48*
	≥ 80	71	27	21.6 ± 6.1	17.0 ± 9.0	2.7 ± 1.0	2.0 ± 1.3
Type of Glaucoma	POAG	113	48	21.2 ± 6.1	17.2 ± 6.7	2.8 ± 1.0	2.0 ± 1.3
	PEX-G	72	31	24.5 ± 6.9	16.5 ± 4.4	3.0 ± 1.0	1.7 ± 1.3 *n=29*
	Other Types*	14	10	27.7 ± 8.3	18.3 ± 5.7	2.9 ± 0.9	1.5 ± 1.6
Type of Operation	Xen	61	30	25.8 ± 6.5	19.5 ± 8.5	3.1 ± 1.0	1.9 ± 1.3
	Xen + PE	138	59	21.5 ± 6.7	15.8 ± 3.5	2.8 ± 1.0	1.8 ± 1.4 *n=57*
Previous Ocular Surgeries	Glaucoma Surgery						
	Yes	61	29	25.2 ± 6.8	17.4 ± 3.8	3.0 ± 1.0	2.1 ± 1.2
	No	138	60	21.8 ± 6.7	16.9 ± 6.7	2.9 ± 1	1.7 ± 1.0 *n=58*
	Cataract Surgery						
	Yes	45	21	26.1 ± 6.1	20.5 ± 9.5	3.2 ± 0.9	1.9 ± 1.3
	No	154	68	21.9 ± 6.8	16.0 ± 3.7	2.8 ± 1	1.8 ± 1.0 *n=66*
	Other Ocular Surgery						
	Yes	13	7	28.1 ± 7.6	19.3 ± 6.7	2.9 ± 1.0	1.6 ± 1.5
	No	186	82	22.5 ± 6.7	16.9 ± 5.8	2.9 ± 1	1.9 ± 1.0 *n=80*

** Secondary Glaucoma: n=11, Angle-closure Glaucoma: n=2, Normal-tension Glaucoma: n=1;*
IOP = intraocular pressure, SD = Standard deviation, *POAG = Primary open-angle glaucoma, PEX-G = pseudoexfoliation glaucoma, PE = phacoemulsification*

3.2 Adverse Events

There were no reports of intraoperative complications. Postoperative adverse events are shown in Table 3. In 16 cases (8.0%) hypotony (≤6 mmHg) occurred at day 1, albeit replenishment with viscoelastic device was performed only in one case. In the immediate postoperative course 7 (3.5%) hyphemas were recorded, which regressed spontaneously. No choroidal detachment was seen. Aqueous misdirection developed in one patient 5 days after Xen implantation necessitating vitrectomy and in one case a late-onset postoperative endophthalmitis four months after Xen implantation was suspected leading to intravitreal injection of antibiotics, albeit microbial cultures remained negative.

Table 3: Postoperative Complications

Events	n (%)
Hypotony (≤6 mmHg) at day 1	16 (8.0)
Hyphema	7 (3.5)
Choroidal detachment	0 (0.0)
Aqueous misdirection	1 (0.5)
Late-onset endophthalmitis	1 (0.5)

In 44 cases (22.1%) postoperative interventions (needling and/or revision) were indicated (Table 4). In total 65 needlings were performed to remove tissue adhesions. 5-Fluorouracil was used in 44 needlings (67.7%), while dexamethasone was used in 12 needlings (18.5%) and 2 needlings (3.1%) were performed without medication. YAG laser was used in 7 cases (10.8%). Time to first needling ranged between 6 and 582 days, median was 59.5 days. Furthermore, 3 revisions (1.5%) were indicated due to stent exposure.

Table 4: Postoperative Interventions

Events	n (%)
Number of cases requiring postoperative interventions	44 (22.1)
Needling	
1 time	25 (12.6)
2 times	14 (7.0)
3 times	4 (2.0)
Revision	3 (1.5)
Needling procedure	
5-Fluorouracil	44 (67.7)
Dexamethasone	12 (18.5)
Without medication	2 (3.1)
YAG laser	7 (10.8)

In 28 cases (14.1%) an additional glaucoma surgery was performed due to insufficient IOP reduction (Table 5): 15 trabeculectomies (53.6%), 8 implantations of a second Xen implant (28.6%), 4 transscleral cyclophotocoagulations (14.3%), 1 laser trabeculoplasty (3.6%). Time to reoperation ranged between 8 and 916 days, median was 196 days.

Table 5: Secondary Glaucoma Surgeries

Surgery	n (%)
Total number of cases	28 (14.1)
Trabeculectomy	15 (53.6)
Second Xen	8 (28.6)
TSCPC	4 (14.3)
Laser trabeculoplasty	1 (3.6)

TSCPC = Transscleral cyclophotocoagulation

Complete success was achieved in 15.4% (n=16) at 12 months, qualified success in 25.0% (n=26). A failure was noted in 59.6% (n=62) at 12 months, from which 23 cases needed an additional glaucoma surgery.

4 Discussion

In this retrospective, single-center study the course of 199 Xen-implanted eyes was evaluated. The implantations were performed between 2014 and 2016. We observed a significant IOP-reduction of 22.3% from baseline after one month (n=172), which remained stable until 12 months (n=89) postoperatively.

In reference to other published studies, we saw comparable outcomes. An overview of recently published data is given in Table 6.

Mansouri et al [7] compared 40 Xen standalone implantations with 109 combined phacoemulsification-Xen implantations. In their prospective study, they reported a larger IOP-lowering effect in the Xen alone group (40% vs. 22.9%) which was not seen in our study (17.8% vs. 25.2%). The difference in the study by Mansouri et al [7] (IOP reduction of 31% and reduction of medications from 1.9 to 0.5) and our results (IOP-reduction of 22.3% and reduction of number of medications from 2.9 to 1.8) after 12 months may be explained by a higher rate of needling (37% Mansouri et al vs. this study 22.6%). However, the rate of reoperation was lower in their cohort (6.0%).

The aim of the study by Widder et al [8] was to achieve an adequate IOP reduction without any glaucoma medications. Following this strategy, all patients with insufficient reduction (34%) underwent a surgical revision with opening of the conjunctiva, scar tissue removal and refixation with two absorbable sutures. Regarding the invasiveness of this revision technique in comparison to our less invasive intervention technique, the rates are not directly comparable. Although, Widder et al [8] achieved a significant IOP reduction from 24.3 mmHg at baseline to 13.9 mmHg (without revision) and 13.5 mmHg (one revision allowed) after 12 months.

In reference to the prospective, multicenter study by Grover et al [9] with 65 implanted eyes with refractory glaucoma, they reported an IOP-reduction of 35.6% compared to our 22.7% reduction. Number of medications was similar at 12 months of follow-up, although their baseline was higher. Our surgical technique

varied from that described by Grover et al [9]: They pretreated the target area with MMC saturated sponges for 2 minutes, whereas we injected 0.1ml MMC subconjunctival without rinsing it. However, secondary glaucoma surgery was indicated in 14.1% in our study and in 13.8% in the study of Grover et al [9].

A prospective study by De Gregorio et al [10] including 41 procedures reported an IOP-reduction of 41.8%, with a low rate of needling (2.4%) and secondary glaucoma surgery (2.4%).

Yet another prospective study by Galal et al [11] including 13 procedures showed similar IOP-reduction (23%) compared to our study (22.7%), although they reported of a lower number of medication at 12 months.

Table 6: Comparison of Outcomes with Recently Published Xen Studies

	Study design	*n* at baseline	*n* at 12 months	Baseline IOP ± SD (mmHg)	IOP at 12 months ± SD (mmHg, -%)	Baseline medication ± SD (number)	Medication at 12 months ± SD (number)	Rate of needling/revision	Rate of reoperation
Current Study	Retrospective single-center	199	89	22.8 ± 6.9	17.1 ± 5.9 *-22.7*	2.9 ± 1.0	1.8 ± 1.4*	22.1%	14.1%
Mansouri et al [7] (February 2018)	Prospective single-center	149	87	20.0 ± 7.1	13.9 ± 4.3 *-31*	1.9 ± 1.3	0.5 ± 0.8	37%	6.0%
Widder et al [8] (January 2018)	Retrospective single-center	233	65** 82***	24.3 ± 6.6	13.9 ± 3.8** *n.a.* 13.5 ± 3.3*** *n.a.*	2.6 ± 1.1	*n.a.*	34%	10%****
Grover et al [9] (November 2017)	Prospective multicenter	65	52	25.1 ± 3.7	15.9 ± 5.2 *-35.6*	3.5 ± 1.0	1.7 ± 1.5	32.3%	13.8%
De Gregorio et al [10] (May 2017)	Prospective single-center	41	40	22.5 ± 3.7	13.1 ± 2.4 *-41.8*	2.5 ± 0.9	0.4 ± 0.8	2.4%	2.4%
Galal et al [11] (March 2017)	Prospective single-center	13	13	16 ± 4	12 ± 3 *-23*	1.9 ± 1	0.3 ± 0.49	30.7%	15.4%

** n=87, ** without revision, *** one revision allowed, **** more than one surgical revision or with another pressure-lowering surgical method after the first revision*
IOP = intraocular pressure, SD = Standard deviation, n.a.=not available

It should be noted again, as evident in Figure 1 and 2, that the IOP remained stable in the later follow-up, while at the same time number of medications increased. Therefore the later time windows should be interpreted with caution.

Our study has several limitations: due to the retrospective design with no regular follow-up visits fewer observations, especially for later time windows, were available compared to baseline. However, we took great effort to obtain as much routinely documented follow-up data as possible by investigating clinical records as well as reports received from supervising ophthalmologists. Furthermore, there was no standardized protocol for postoperative management concerning reinitiation of IOP-lowering medications, date of needling or reoperation but were at each ophthalmologists' discretion.

5 Conclusion

Our results indicate that Xen implantation is a safe and effective surgical intervention leading to a significant IOP and medication reduction with a low rate of complications. However, severe adverse events may occur and needling was indicated in almost every fifth case, demanding an attentive postoperative management.

6 Bibliography

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