

# Comparison of the effectiveness of the XEN microstent in the treatment of different types of glaucoma

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## Research article

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# Abstract

## Purpose

The aim of this study was to compare the efficacy and safety profile of the XEN-microstent in different types of primary and secondary open angle glaucoma.

## Methods

The XEN microstent was implanted in patients with primary open-angle glaucoma (POAG), normal-tension glaucoma (NTG), pseudoexfoliation glaucoma (PEX) and secondary glaucoma (Sec.GI). The intraocular pressure (IOP), the active substances of the applied IOP-lowering drugs, the best corrected visual acuity (BCVA) and the mean deviation (MD) of the perimetry were measured at baseline and at regular follow-ups, scheduled at 2 days and 1, 3, 6 and 12 months after surgery.

## Results

153 eyes were included in this analysis. 113 eyes were affected by POAG (74%), 5 eyes by NTG (3%), 22 eyes by PEX (14%) and 13 eyes by Sec.GI (9%). Mean IOP decreased in all treatment groups during the 12 months of follow-up (complete group:  $23.9 \pm 7.4$  to  $15.4 \pm 5.1$  mmHg ( $p < 0.01$ ); POAG:  $22.8 \pm 6.5$  to  $15.1 \pm 4.6$  mmHg ( $p < 0.01$ ); NTG:  $16.6 \pm 3.4$  to  $11.6 \pm 2.2$  mmHg ( $p < 0.05$ ); PEX:  $28.0 \pm 7.9$  to  $17.1 \pm 6.6$  mmHg ( $p < 0.01$ ); Sec.GI:  $28.9 \pm 13.9$  to  $15.5 \pm 6.9$  mmHg ( $p < 0.05$ )). In the 153 eyes the average number of IOP-lowering drugs applied decreased from  $2.6 \pm 1.2$  to  $0.8 \pm 1.3$  12 months after surgery ( $p < 0.01$ ). BCVA and mean deviation of automated standard perimetry remained stable in all groups during follow-up.

## Conclusion

As in eyes suffering from POAG, IOP and number of IOP-lowering drugs applied can be effectively reduced by XEN implantation in eyes suffering from NTG, PEX and secondary glaucoma while leaving BCVA and visual field unchanged.

## Trial registration

Trial was registered at DRKS (registration number: DRKS00020800, Registered 25.February 2020 - Retrospectively registered, [https://www.drks.de/drks\\_web/navigate.do?navigationId=trial.HTML&TRIAL\\_ID=DRKS00020800](https://www.drks.de/drks_web/navigate.do?navigationId=trial.HTML&TRIAL_ID=DRKS00020800))

## Background

Glaucoma is one of the leading causes of blindness worldwide, with an estimated prevalence of 2-4% in the 40 years and older age group [1,2]. Glaucoma is a very heterogeneous group of diseases characterized by progressive atrophy of the optic disc caused by apoptotic retinal ganglion cell death [3,4]. Known risk factors for the development of glaucoma are an elevated intraocular pressure (IOP), familial history of glaucoma, myopia and thin central corneal thickness [5-7]. Reduction of IOP by means of medication and/or surgery is the only known way to effectively slow down further disease progression [8,9].

Usually, IOP reduction by means of medication is the first-line treatment in glaucoma therapy. Surgical intervention is indicated in cases of insufficient medical IOP reduction, problems with side effects, insufficient adherence and persistence to therapy and further progression of optic nerve damage. [10]. Trabeculectomy (TE) with or without the

use of antimetabolites was first introduced in the mid-1960s and has since remained the “gold standard” for long-term surgical IOP reduction [11,12]. However, TE has numerous risks and unintended side effects that limit its use to advanced disease stages [13-16]. In recent years, various techniques have been developed to minimize surgical trauma and the risk of serious side effects. These newly developed techniques make use of different mechanisms to reduce the resistance of aqueous humor outflow, thereby reducing IOP. These new techniques are summarized under the term minimally invasive glaucoma surgery (MIGS) [17].

A promising MIGS procedure is the XEN microstent. The XEN microstent is approved for the treatment of primary open-angle glaucoma (POAG). The XEN microstent facilitates subconjunctival drainage of aqueous humor from the anterior chamber, which is comparable to the mode of action utilized in TE [18]. The XEN microstent does not comprise a valve mechanism, but maintains a minimum IOP of approximately 8 mmHg through its length and internal lumen [19].

However, subconjunctival drainage of aqueous humor is suitable for more than one type of glaucoma (i.e. POAG). Therefore, the concept of this study was to analyze the IOP-lowering efficacy of the XEN microstent in the treatment of other types of glaucoma. Other glaucoma entities suitable for XEN implantation were pseudoexfoliation glaucoma (PEX), secondary open-angle glaucoma of various causes (Sec.GI) and normal tension glaucoma (NTG). The main objective of the investigations was to analyze whether or not the XEN implant is also suitable for the treatment of these types of glaucoma.

## Methods

For this retrospective analysis, we reviewed the medical records of all patients/eyes scheduled for XEN microstent implantation from January 1, 2017 to December 31, 2018 at the University Eye Hospital in Leipzig.

The study was approved by the local ethics committee of the University Leipzig, Leipzig, Germany. Written informed consent was obtained from all patients. All procedures performed met the ethical standards of the institutional research commission as well as the Helsinki Declaration of 1964 and its later amendments. The trial was registered with the DRKS (registration number: DRKS00020800, Registered 25.February 2020 - Retrospectively registered,[https://www.drks.de/drks\\_web/navigate.do?navigationId=trial.HTML&TRIAL\\_ID=DRKS00020800](https://www.drks.de/drks_web/navigate.do?navigationId=trial.HTML&TRIAL_ID=DRKS00020800)).

Presence of optic disc changes such as an increased cup/disc ratio, optic disc hemorrhages, nerve fiber layer defects and/or indentations of the papillary vessels verified glaucoma diagnosis. Untreated IOP had to be  $\geq 21$  mmHg in POAG, PEX and secondary glaucoma cases. In NTG IOP was by definition lower than 21 mmHg. In the analyzed cases surgical intervention was necessary due to disease progression or medically uncontrollable IOP. This was demonstrated by deterioration of repeated automated standard perimetry results and/or reduction of RNFL thickness on repeated optical coherence tomography (RNFL-OCT) examinations. Topical IOP-lowering therapy was discontinued four weeks prior to surgery in eyes scheduled for XEN implantation and preservative-free steroid eye drops were administered four times daily to achieve an irritation free conjunctiva. Exclusion criteria were a patient age below 40 years and a narrow anterior chamber angle. If both eyes of a single patient required surgical treatment for glaucoma, only the results of the first-operated eye were included into this analysis.

Four weeks prior to surgery, a complete ophthalmological examination was performed with maximum tolerable anti-glaucomatous local medication, which included measurement of best-corrected visual acuity (BCVA) using Snellen charts (transformed into logMAR for statistical analysis), objective refraction, slit-lamp examination of anterior and posterior eye segments with evaluation of the optic disc by indirect ophthalmoscopy and RNFL-OCT

scans; Spectralis, Heidelberg Engineering, Heidelberg, Germany), automated standard perimetry (Twinfield 2, Oculus, Wetzlar, Germany; 24-2 test strategy, 55 targets), IOP measurement with Goldmann applanation tonometry and gonioscopy with the Sussmann four-mirror contact lens. The indication for the planned surgical procedure was re-evaluated, whereby the aim was to lower IOP and/or to reduce the number of necessary IOP-lowering agents. The demographic patient data collected prior to surgery were age, sex and laterality of the operated eye.

#### *Surgical Technique:*

Ocular surface was disinfected using povidone iodine. Two side port paracenteses were laid and the eyes anterior chamber was filled with a dispersive viscoelastic agent. In the superior nasal quadrant a mark 3 mm posterior to the limbus was made. 0.1 ml of 0.01% Mitomycin C (MMC) was administered 6 mm from the limbus through the conjunctiva and into the Tenon's capsule to form a bleb. The MMC was then massaged posteriorly away from the corneal limbus. The XEN microstent was then inserted into the eyes anterior chamber mounted in its applicator. The applicator's tip was aimed at the chamber angle and pierced through the chamber angle anterior to the trabecular meshwork and was directed through the sclera forming a scleral tunnel of approximately 3 mm in length. The outer orifice was targeted so as to lie 3 mm behind the limbus without piercing the overlying conjunctiva. The XEN stent was then released from the applicator. If performed correctly approximately 1 mm of the microstent lay in the anterior chamber, 3 mm in the formed intrascleral tunnel and 2 mm outside the tunnel underneath the conjunctiva. The subconjunctival portion of the XEN stent was then examined and freed from Tenon's capsule if bent (or not moving freely) using a 30G needle.

Postoperative visits were scheduled at day 1 and 2 as well as at month 1, 3 and 6 and 12 after surgery. All local and oral antiglaucoma medications were discontinued. Preservative-free steroid eye drops were given 6 times daily for 4 weeks and then slowly reduced over 3 months. Additionally preservative-free antibiotic eye drops were prescribed four times daily for one week. At each visit BCVA and IOP were measured and the anterior and posterior eye segments were evaluated for adverse events (conjunctival scarring, flat bleb, shallow anterior chamber, choroidal detachment, hypotony maculopathy etc.). The number of glaucoma medications taken was queried. In addition, visual field examinations were performed during the visits 6 and 12 months after the surgery.

For additional necessary post-surgical needling procedures a 27G cannula was used on a syringe with 5-FU (5 mg in 0.1 ml). The needle was inserted under the conjunctiva 3 mm temporal from the XEN stent and needling was performed by sweeping the needle tip posteriorly above and beneath the XEN microstent. Finally 0.1 ml of 5-FU was injected posterior to the end of the XEN microstent.

Clinical success was defined according to the recommendations of the World Glaucoma Association [20]. For complete success (A) an IOP reduction of  $\geq 20\%$  from baseline and resulting IOP of  $< 21$  mmHg without the use of IOP-lowering drugs had to be achieved. For qualified success (A) the same criteria applied as for complete success A with the use of additional IOP-lowering drugs permitted. For complete success (B) an IOP reduction of  $\geq 30\%$  from baseline and resulting IOP of  $< 18$  mmHg without the use of IOP-lowering drugs had to be achieved. For qualified success (B) the same criteria applied as for complete success B with the use of additional IOP-lowering drugs permitted. For complete success (C) an IOP reduction of  $\geq 40\%$  from baseline and resulting IOP of  $< 15$  mmHg without the use of IOP-lowering drugs had to be achieved. For qualified success (C) the same criteria applied as for complete success C with the use of additional IOP-lowering drugs permitted.

Data collection and statistical analysis were performed using Excel (Version 2007, Microsoft; Redmond, USA) and SPSS (IBM Version 22.0; Chicago, Illinois, USA). The tested indices for patient age, BCVA, objective refraction and

visual field are given as mean and standard deviation. The differences between the pre- and postoperative results for IOP, IOP reduction, BCVA, number of active IOP-lowering agents applied and the mean defect of static automated perimetry were analyzed using the Kruskal-Wallis nonparametric test or one-way ANOVA (where applicable) for intergroup comparisons and the Friedman test for intragroup comparisons of results measured in groups of different glaucoma types. A  $p \leq 0.05$  indicated statistical significance.

## Results

For this analysis the clinical course of 153 eyes of 153 patients (80 female and 73 male; 77 right and 76 left eyes) were included. Four groups of eyes suffering from different types of glaucoma were treated. 113 eyes (74%) were treated for POAG, 5 eyes (3%) for NTG, 13 eyes (9%) for secondary glaucoma and 22 eyes (14%) for pseudoexfoliation glaucoma. Of the 13 secondary glaucoma cases, four were due to previous eye trauma, four were due to neovascularization (2 cases of proliferative diabetic eye disease and 2 cases of central retinal vein occlusion, the underlying disease being considered in a stable phase at the time of XEN implantation), three cases were secondary to uveitis and the last two cases were due to steroid-induced glaucoma. In the complete patient group the mean age of patients at the time of surgery was  $70.2 \pm 10.8$  years. The difference in mean patient age was not statistically significant between the four treated patient groups ( $p=0.24$ ). Before surgery the mean IOP of the 153 eyes was  $23.9 \pm 7.4$  mmHg in the 153 eyes. Upon comparison of the mean IOP before surgery between the four treated groups the difference was statistically significant ( $p < 0.01$ ). The mean number of active substances contained in the applied IOP-lowering eye drops was  $2.6 \pm 1.2$  before surgery, and the comparison between the four treated groups showed no statistically significant difference ( $p=0.56$ ). The mean defect tested by standard automated perimetry was  $10.1 \pm 4.3$  dB before surgery, and the comparison between the four treated groups showed no statistically significant difference ( $p=0.96$ ). The exact demographic data are also presented in **Table 1**.

### *IOP results*

In the complete group of eyes analyzed mean IOP before surgery was  $23.9 \pm 7.4$  mmHg. Two days after XEN implantation, mean IOP decreased to  $9.2 \pm 5.2$  mmHg and then increased again to  $15.5 \pm 7.9$  mmHg one month and to  $15.9 \pm 6.1$  mmHg three months after surgery. Thereafter, mean IOP remained stable with a mean value of  $15.4 \pm 5.1$  mmHg one year after XEN implantation, which corresponds to a mean IOP reduction of 31% compared to baseline before surgery. For the complete group of eyes analyzed the difference between the mean IOP results measured at all follow-up examinations and those measured at baseline was statistically significant at all-time points ( $p < 0.01$ ). The exact values and the course of mean IOP during the first 12 months after surgery for the complete group as well as for the four treated subgroups are summarized in **Figures 1 & 2** and **Table 2**.

### *IOP results in different types of glaucoma*

Mean IOP at baseline before XEN implantation in the 113 POAG eyes was  $22.8 \pm 6.5$  mmHg. Two days after surgery mean IOP dropped to  $8.9 \pm 5.1$  mmHg. From the follow-up examination one month after surgery the IOP remained stable at about 15 mmHg and one year postoperatively the mean value was  $15.1 \pm 4.6$  mmHg. This corresponds to an average IOP decrease of 31% compared to baseline. Comparison of mean IOP results before and after surgery showed a difference of statistical significance ( $p < 0.01$ ) at all follow-up examinations.

In the 5 NTG eyes the mean IOP before XEN implantation was  $16.6 \pm 3.4$  mmHg. Mean IOP decreased to  $5.6 \pm 2.7$  mmHg two days after surgery and rose again to  $10.0 \pm 3.0$  mmHg one month after surgery and remained relatively stable thereafter with a mean value of  $11.6 \pm 2.2$  mmHg 12 months after surgery. This corresponds to an IOP

reduction of 29% from baseline. IOP was well regulated, with all five eyes achieving an IOP <15 mmHg 12 months after surgery. Comparison of mean IOP results before and after surgery showed a difference of statistical significance ( $p<0.05$ ) at all follow-up examinations.

In the 22 treated eyes suffering from PEX mean IOP before surgery was  $28.0\pm 7.9$  mmHg. Similarly to the other treatment groups mean IOP decreased to  $11.9\pm 6.4$  mmHg two days after surgery and increased to  $16.5\pm 8.0$  mmHg one month after surgery. Thereafter, IOP remained reasonably stable with a mean value of  $17.1\pm 6.6$  mmHg one year after XEN implantation, which corresponds to a decrease of 38% compared to baseline. The comparison between the average IOP results before and after surgery showed a difference of statistical significance ( $p<0.01$ ) at all follow-up examinations.

In the 13 eyes suffering from secondary glaucoma mean IOP before surgery was  $28.9\pm 13.9$  mmHg. Mean IOP dropped to  $8.7\pm 4.6$  mmHg 2 days after surgery. Thereafter, as in the other treatment groups, mean IOP increased to  $16.7\pm 10.6$  mmHg one month after XEN implantation and remained stable with a mean of  $15.5\pm 6.9$  mmHg at the follow-up examination one year after surgery, which corresponds to a mean IOP decrease of 36% compared to baseline. Comparison of follow-up to baseline results again showed a difference of statistical significance at all-time points ( $p<0.05$ ).

A further statistical analysis before and 12 months after surgery comparing mean IOP results between the four treatment groups revealed differences of statistical significance at baseline ( $p<0.01$ ) as well as 12 months after surgery ( $p<0.01$ ). However, when comparing results for mean IOP reduction from baseline to 12 months after surgery between the four groups, no difference of statistical significance was found ( $p=0.2$ ).

#### *Complete and qualified success*

Taking into account the WGA guidelines and the criteria summarized above defining complete and qualified success levels A to C, in the complete group of 153 eyes 60% achieved a complete success (A) and 74% a qualified success (A). Complete success levels B and C were achieved by 51% and 45% respectively. Qualified success B and C was achieved by 61% and 56% in the complete group of 153 eyes operated. The exact results for complete and qualified success levels A to C achieved in the four subgroups of different glaucoma entities is summarized in **Table 3**.

#### *IOP-lowering medication*

The exact course of the number of IOP-lowering eye drops applied is summarized in **Figure 3** and **Table 4**. The average number of active substances applied in the entire group of 153 eyes fell from  $2.6\pm 1.2$  before to  $0.8\pm 1.3$  12 months after XEN implantation ( $p<0.01$ ). In the four subgroups treated the number of applied drugs decreased from  $2.5\pm 1.2$  to  $0.8\pm 1.3$  in the POAG group ( $p<0.01$ ), from  $2.6\pm 0.9$  to  $0.6\pm 0.9$  in the NTG group ( $p<0.05$ ), from  $2.9\pm 1.2$  to  $1.0\pm 1.3$  in the PEX group ( $p<0.01$ ) and from  $2.7\pm 0.9$  to  $0.7\pm 1.4$  in the group of eyes suffering from secondary glaucoma ( $p<0.01$ ) during the first 12 months after surgery.

#### *Visual Acuity*

In the entire group of 153 eyes treated with the XEN microstent, mean BCVA remained stable and showed no difference of statistical significance during postoperative follow-up. Mean BCVA was  $0.38\pm 0.52$  logMAR before surgery and  $0.36\pm 0.49$  logMAR 6 months and  $0.37\pm 0.49$  logMAR 12 months after surgery ( $p=0.97$  after 6 months and  $p=0.88$  after 12 months). In the four subgroups of the different glaucoma types, changes in mean BCVA over

the postoperative follow-up period also showed no statistical significance (POAG:  $p=0.31$ ; NTG:  $p=0.22$ ; PEX:  $p=0.92$ ; secondary glaucoma:  $p=0.91$ ). (See also **Figure 4** for the exact course). However, the comparison of mean BCVA between the four treatment groups before and 12 months after surgery showed a difference of statistical significance (before surgery:  $p<0.01$ ; 12 months:  $p<0.01$ ).

### *Visual field*

Simultaneously with the drop of mean IOP, mean visual field defect remained stable. In the complete group of 153 eyes treated mean defect was  $10.1\pm 4.3$  dB at baseline, increased slightly to  $10.8\pm 4.3$  dB at 6 months ( $p=0.11$ ) and was  $10.8\pm 4.2$  dB at 12 months after surgery, which was not statistically significant ( $p=0.15$ ). Also in the four subgroups, mean visual field defect showed no difference of statistical significance compared to the baseline (POAG:  $p=0.8$ ; NTG:  $p=0.23$ ; PEX:  $p=0.17$ ; secondary glaucoma:  $p=0.37$ ) (see **Table 5** for details).

### *Complications and needling rate*

To achieve the results described, 64 needling procedures had to be performed in 54 of the 153 eyes (35.3%). 44 eyes needed 1 needling and another 10 eyes needed 2 needlings during the first year after XEN implantation. None of the eyes needed  $>2$  needlings. The needling rate was different between the four subgroups analyzed (see **Table 6**). The lowest needling rate was found in NTG eyes (20%) and the highest rate in PEX glaucoma eyes (55%). In the total group of 153 eyes treated 20 eyes showed benign choroidal detachment during the first postoperative month. All cases responded well to conservative treatment (contact lens and cycloplegia). A large and prominent subconjunctival hemorrhage (to the extent that it was classified as clinically significant) was seen in 12 cases immediately after surgery, but was resorbed after 1 to 4 weeks. Blood in the anterior chamber immediately after surgery was seen in 10 eyes and dissolved in all cases without further consequences after 1 to 4 weeks. Postoperative macular edema was seen in 3 eyes, which all responded well to treatment with carbonic anhydrase inhibitors. Apart from the above described incidents, no serious complications were observed in the treated eyes.

## **Discussion**

Classic TE with or without the use of antimetabolites is the “gold standard” for surgical treatment of a wide range of glaucoma entities. The XEN microstent is designed to bypass the transtrabecular outflow pathway whereby reducing IOP. Since its initial description, a number of reports have been published on the efficacy and safety profile of the XEN microstent for the treatment of POAG [21,18, 22]. In summary, implantation of the XEN microstent can significantly reduce IOP and the amount of IOP-lowering eye drops applied, resulting in acceptable success rates in POAG after 12 and 24 months. Reitsamer and colleagues already showed in their one and two-year multicenter study (APEX study) that IOP and required medication can be reduced effectively by implantation of the XEN microstent either alone or in combination with phacoemulsification and posterior chamber lens implantation [21]. Some groups even reported on achieving lower mean postoperative IOP values of around 12 mmHg when starting from a lower initial mean level at baseline before surgery [23].

Grover et al reported on their 12-month XEN results in a group of 65 eyes with uncontrolled and already pre-operated glaucoma cases (85% of eyes had already been unsuccessfully treated with filtering surgery and/or cilioabative techniques) [24]. The results were similar to the data hereby reported with a qualified success rate of 75%, a reduction of mean IOP from  $25.1\pm 3.7$  mmHg at baseline to  $15.9\pm 5.2$  mmHg 12 months after surgery and a needling rate of about 32%. The patient cohort reported on also included a large percentage of POAG cases and some PEX cases, but no case of secondary glaucoma. Grover et al. also did not report on the efficacy of the XEN microstent in

subgroups of different glaucoma entities. Lenzhofer et al. already demonstrated the long-term effectiveness of the XEN microstent in a group of 64 eyes of 64 POAG patients. It was shown that low mean IOP values and reduced necessity for application of IOP-lowering medication can even be found as long as four years after implantation of the XEN microstent [25]. However, these data were collected in eyes in which the XEN 63 was implanted (with a larger internal lumen of 63  $\mu\text{m}$ ).

Given the mode of action utilized, the XEN microstent should in theory also be applicable in glaucoma entities other than POAG. Although some groups reported on the treatment of different types of glaucoma with the XEN microstent, they so far failed analyzing the efficacy in the treated subgroups [26, 22]. We analyzed the 12-month postoperative follow-up results in NTG, PEX and secondary glaucoma cases and compared the results with those obtained in a medium-sized comparison group of POAG eyes. With the reported postoperative results we could clearly and for the first time demonstrate that IOP and necessary IOP-lowering medication can be lowered with a comparable efficacy in NTG, PEX and secondary glaucoma cases as in POAG. Apart from this visual acuity and visual field indices remained stable without evidence for further postoperative deterioration, although only the first 12 months after surgery were monitored. There was a notable difference in mean BCVA, which was worse but also stable during the postoperative course in the subgroup of treated secondary glaucoma cases. This must be interpreted within the context of the underlying disease process leading to secondary glaucoma, which in most cases has devastating consequences on visual acuity.

Postoperative results after implantation of the XEN microstent other types of glaucoma than POAG have also been described (but not been analyzed in more detail) by other authors. Ibanez-Munoz and colleagues implanted the XEN microstent in 36 eyes with POAG and 37 eyes with secondary glaucoma, 34 of which had PEX glaucoma [27]. The difference in the postoperative results regarding the reduction of IOP and the required medication was not statistically significant in both groups. Apart from that, no difference was found when the XEN microstent was implanted as a solo procedure or in combination with cataract extraction and IOL implantation.

Karimi et al. (like our group) have implanted the XEN microstent in different glaucoma types, including traumatic and neovascular glaucoma, but have not reported on postoperative results in these treated subgroups [28]. They also found no statistically significant differences in their results regarding IOP reduction and medication in cases where the XEN microstent was implanted alone or in combination with cataract extraction. In the 259 eyes treated, 41% required needling during the first 18 months after implantation. However, it should be noted that results originating from only 34% and 12% of eyes were included for analysis of the 12- and 18-month postoperative follow-up.

The higher rate of needling after XEN microstent implantation compared to TE, the “gold standard” in glaucoma surgery, has been the subject of criticism in the past. Schlenker et al. and others reported on further necessary secondary interventions and safety problems when comparing the results following both XEN microstent implantation and TE $\pm$ MMC, which showed a slightly higher needling rate after XEN, but which did not reach statistical significance during further analysis [29]. However, the different rates of necessary postoperative interventions and the rates of postoperative complications were not statistically significant between the groups treated with XEN microstent or TE. In summary, XEN microstent and TE are comparable in terms of postoperative safety. However TE led to more visits, especially in the first 3 months after surgery.

The main strengths of this analysis are the results for glaucoma types other than POAG. In this analysis only one eye per patient was included (even if both eyes were treated). And for all included eyes a full 12-month

postoperative follow-up was available. One limiting factor, concerning the hereby presented data, is that the sizes of the four treatment groups were different. However, the largest group, which comprises POAG patients, should only be regarded as a comparison group for the other, less frequent glaucoma entities, treated under the same conditions. In the entire study group, XEN microstent implantation not only resulted in a reduction of IOP and necessary IOP-lowering drugs, but also had no significant effect on BCVA, neither in the total group of 153 eyes nor in the four subgroups analyzed. Lenzhofer et al. showed similar results in their treated POAG cases [30]. It has also been shown earlier that BCVA in eyes after TE decreases, even when taking into account (and ruling out) the known side effect of cataract formation. [31]. Therefore, our hereby presented data also complement the growing evidence in favor for the XEN microstent in POAG and other types of glaucoma with an unblocked anterior chamber angle.

## Conclusion

Implantation of the XEN microstent was effective in reducing intraocular pressure and the number of drugs applied to reduce intraocular pressure, while BCVA and perimetry results remained unchanged. In conclusion, the data presented here on the efficacy and safety of the XEN microstent in glaucoma types other than POAG are encouraging for the use of this (comparatively new) technique also in the treatment of PEX and other secondary glaucoma cases. Longer follow-up time, a larger number of eyes treated and a comparison group comparing the efficacy of the XEN microstent to the “gold standard” of glaucoma surgery, which remains the TE, are necessary to further demonstrate the usefulness of this technique.

## Declarations

### Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. (Ethics approval: No: 209-18-ek (Ethics committee of medical faculty of University of Leipzig, Leipzig, Germany)) Informed consent was obtained from all individual participants included in the study

### Availability of data and material

The datasets obtained during and/or analyzed during the current study available from the corresponding author on reasonable request.

### Conflicts of interest/Competing interests

The authors declare that they have no conflict of interest.

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### Authors` Contributions

Involved in the design of the study (JDU,MS,MR,TT); conduct of the study (JDU,TT,CBU,CBO); collection, management, analysis of the data (JDU,TT,CBU,CBO); preparation of the manuscript (JDU,TT,MS,CBU,CBO,MR); and

critical revision of the manuscript (JDU,TT,MS,CBU,CBO,MR). All authors read and approved the final manuscript.

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## Tables

Table 1

<b>age [years]</b>	<b>70.2±10.8</b> (p=0.24) <i>POAG: 70.5±8.5</i> <i>NTG: 76.6±3.9</i> <i>PEX: 73.9±5.9</i> <i>Secondary Glaucoma: 68.7±10.7</i>
<b>laterality</b>	77 right; 76 left
<b>gender</b>	80 female; 73 male
<b>diagnosis</b>	POAG: 113 eyes (74%) NTG: 5 eyes (3%) PEX: 22 eyes (14%) Secondary glaucoma: 13 eyes (9%)
<b>number of medications [n]</b>	<b>2.6±1.2</b> (p=0.56) <i>POAG: 2.5±1.2</i> <i>NTG: 2.6±0.9</i> <i>PEX: 2.9±1.2</i> <i>Secondary Glaucoma: 2.7±0.9</i>
<b>mean deviation [dB]</b>	<b>10.1±4.3</b> (p=0.96) <i>POAG: 10.2±3.9</i> <i>NTG: 10.8±2.9</i> <i>PEX: 9.7±4.7</i> <i>Secondary Glaucoma: 10.1±6.8</i>

Patient demographic data for the 153 eyes treated with XEN microstent implantation in uncontrolled glaucoma. Also shown are the glaucoma types and the percentage of each glaucoma type as a proportion of the total treated

eye group.

**Table 2**

	baseline	2 days	1 month	3 months	6 months	12 months	p=	mean reduction [%]
<b>complete group</b>	23.9±7.4	9.2±5.2	15.5±7.9	15.9±6.1	15.7±6.7	15.4±5.1	<b>&lt;0.01</b>	-31.3±23.9
<b>POAG</b>	22.8±6.5	8.9±5.1	15.3±7.6	15.9±6.0	15.3±6.2	15.1±4.6	<b>&lt;0.01</b>	-29.8±23.8
<b>NTG</b>	16.6±3.4	5.6±2.7	10.0±3.0	13.4±2.9	10.8±4.6	11.6±2.2	<b>&lt;0.05</b>	-28.6±18.4
<b>PEX</b>	28.0±7.9	11.9±6.4	16.5±8.0	15.7±6.2	17.1±7.2	17.1±6.6	<b>&lt;0.01</b>	-37.8±17.9
<b>secondary glaucoma</b>	28.9±13.9	8.7±4.6	16.7±10.6	17.7±10.3	17.0±10.4	15.5±6.9	<b>&lt;0.05</b>	-35.7±36.3

Mean IOP (mmHg) measured at baseline and all follow-ups after XEN microstent-implantation. Results are reported for the whole group of eyes treated and for the four subgroups of eyes with different glaucoma types. The indicated P-values and mean reduction represent the comparison between the results of the baseline examination and the 12-month results of the respective group.

**Table 3**

	Complete success (A)	Qualified success (A)	Complete success (B)	Qualified success (B)	Complete success (C)	Qualified success (C)
<b>complete group</b>	60%	74%	51%	61%	45%	56%
<b>POAG</b>	54%	71%	45%	57%	29%	38%
<b>NTG</b>	60%	60%	60%	60%	20%	20%
<b>PEX</b>	86%	91%	77%	82%	50%	59%
<b>secondary glaucoma</b>	75%	75%	58%	58%	50%	50%

Clinical Success defined as complete (without the use of IOP-lowering drugs) and qualified (with the use of additional IOP-lowering drugs) success for the complete treated group of eyes and the four subgroups of the different glaucoma types (A) IOP reduction of  $\geq 20\%$  from baseline and resulting IOP of  $< 21$  mmHg; complete success (B) IOP reduction of  $\geq 30\%$  from baseline and resulting IOP of  $< 18$  mmHg; complete success (C) IOP reduction of  $\geq 40\%$  from baseline and resulting IOP of  $< 15$  mmHg)

**Table 4**

	baseline	2 days	1 month	3 months	6 months	12 months	p=
<b>complete group</b>	2.6±1.2	0.1±0.5	0.8±1.4	1.0±1.4	0.9±1.4	0.8±1.3	<b>&lt;0.01</b>
<b>POAG</b>	2.5±1.2	0.1±0.5	0.7±1.4	0.9±1.4	0.9±1.4	0.8±1.3	<b>&lt;0.01</b>
<b>NTG</b>	2.6±0.9	0±0	0.7±1.2	0.7±1.0	0.3±0.6	0.6±0.9	<b>&lt;0.05</b>
<b>PEX</b>	2.9±1.2	0.1±0.4	0.9±1.4	1.1±1.4	0.9±1.4	1.0±1.3	<b>&lt;0.01</b>
<b>secondary glaucoma</b>	2.6±0.9	0±0	0.9±1.8	0.8±1.5	0.5±1.0	0.6±1.5	<b>&lt;0.01</b>

Examination values for the number of applied IOP-lowering agents at the beginning of the treatment as well as for all follow-ups after XEN implantation for the whole treated group of eyes and the four subgroups of the different glaucoma types. The P-values given represent the comparison between the baseline and 12-month results for each group.

**Table 5**

	baseline	6 months	12 months	p=
<b>complete group</b>	10.1±4.3	10.8±4.3	10.8±4.2	0.11
<b>POAG</b>	10.2±3.9	10.6±3.9	10.5±3.9	0.08
<b>NTG</b>	10.9±2.9	10.8±2.3	10.8±2.5	0.23
<b>PEX</b>	9.7±4.7	9.8±4.5	9.6±4.7	0.17
<b>secondary glaucoma</b>	10.0±4.9	10.7±5.0	10.7±5.0	0.37

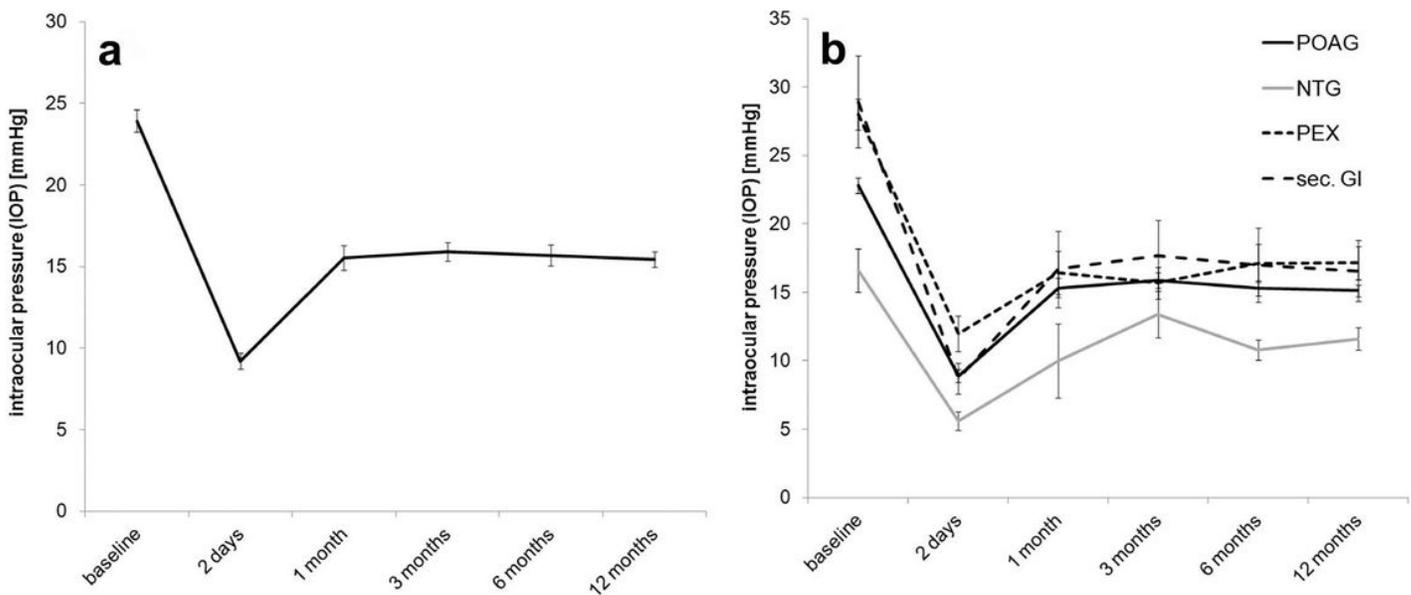
Examination values for mean deviation (in decibels) of automated standard perimetry at baseline and follow-up 6 and 12 months after XEN implantation for the entire patient population and the four subgroups of different glaucoma types. The P-values given represent the comparison between the results at baseline and at 12 months for each group and do not show any statistically significant difference for any of the groups analyzed.

**Table 6**

needling procedures	64 in 54 eyes POAG: 38 of 113 (34%) NTG: 1 of 5 (20%) PEX: 12 of 22 (55%) Sec. Gl.: 3 of 13 (23%)
choroidal detachment	20 of 153 (13%)
prominent or large subconjunctival hemorrhage	12 of 153 (8%)
hyphaema	10 of 153 (7%)
shallow anterior chamber	3 of 153 (2%)
macular edema	3 of 153 (2%)
conjunctival erosion	2 of 153 (1%)
uveitis	1 of 153 (<1%)
keratitis	1 of 153 (<1%)
corneal erosion	1 of 153 (<1%)

Needling rate for the whole group of patients (as well as for the four subgroups of the different types of glaucoma treated) and the rate of other complications observed during the first 12 months of follow-up after XEN microstent implantation in uncontrolled glaucoma in all groups together.

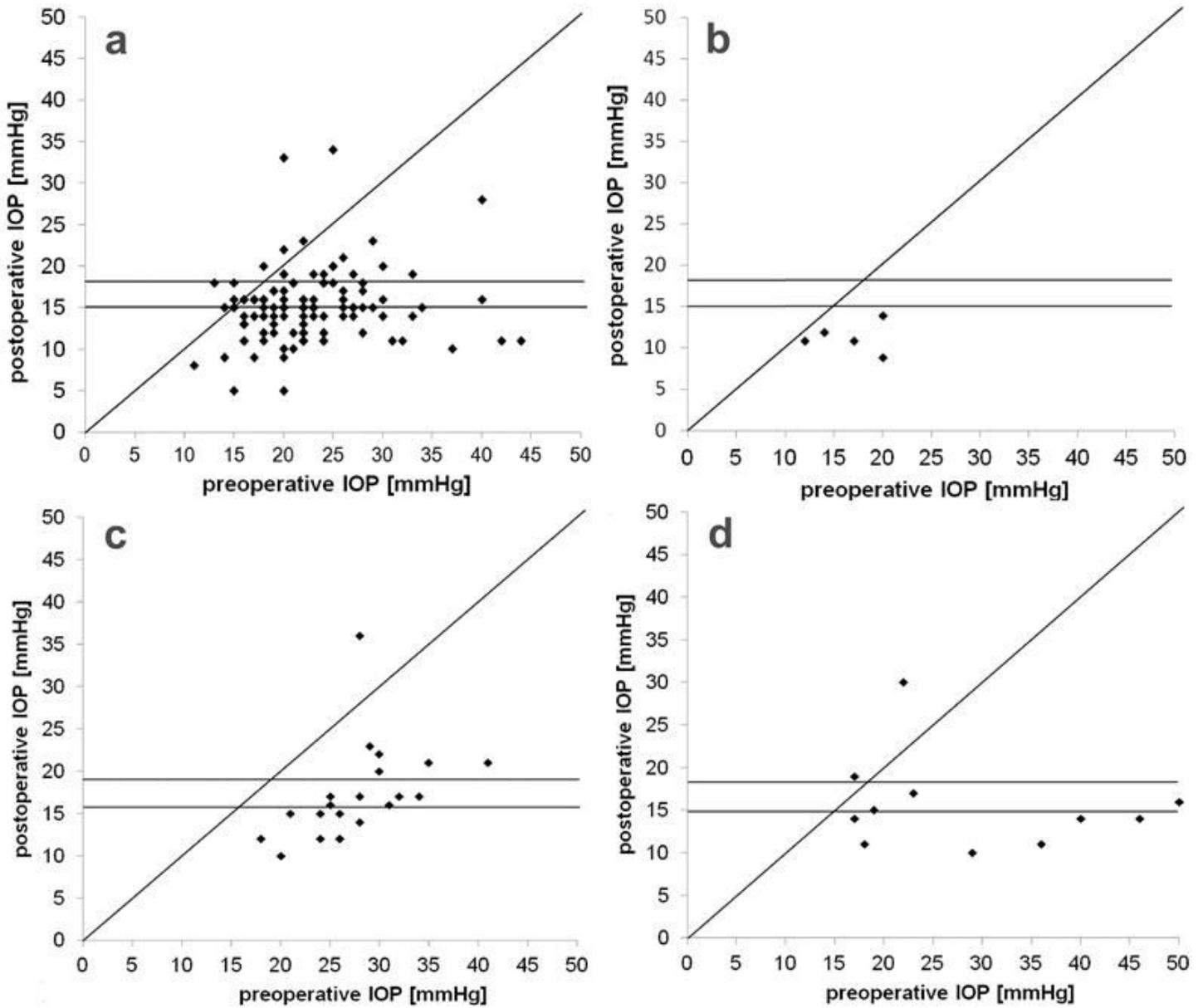
## Figures



**Figure 1**

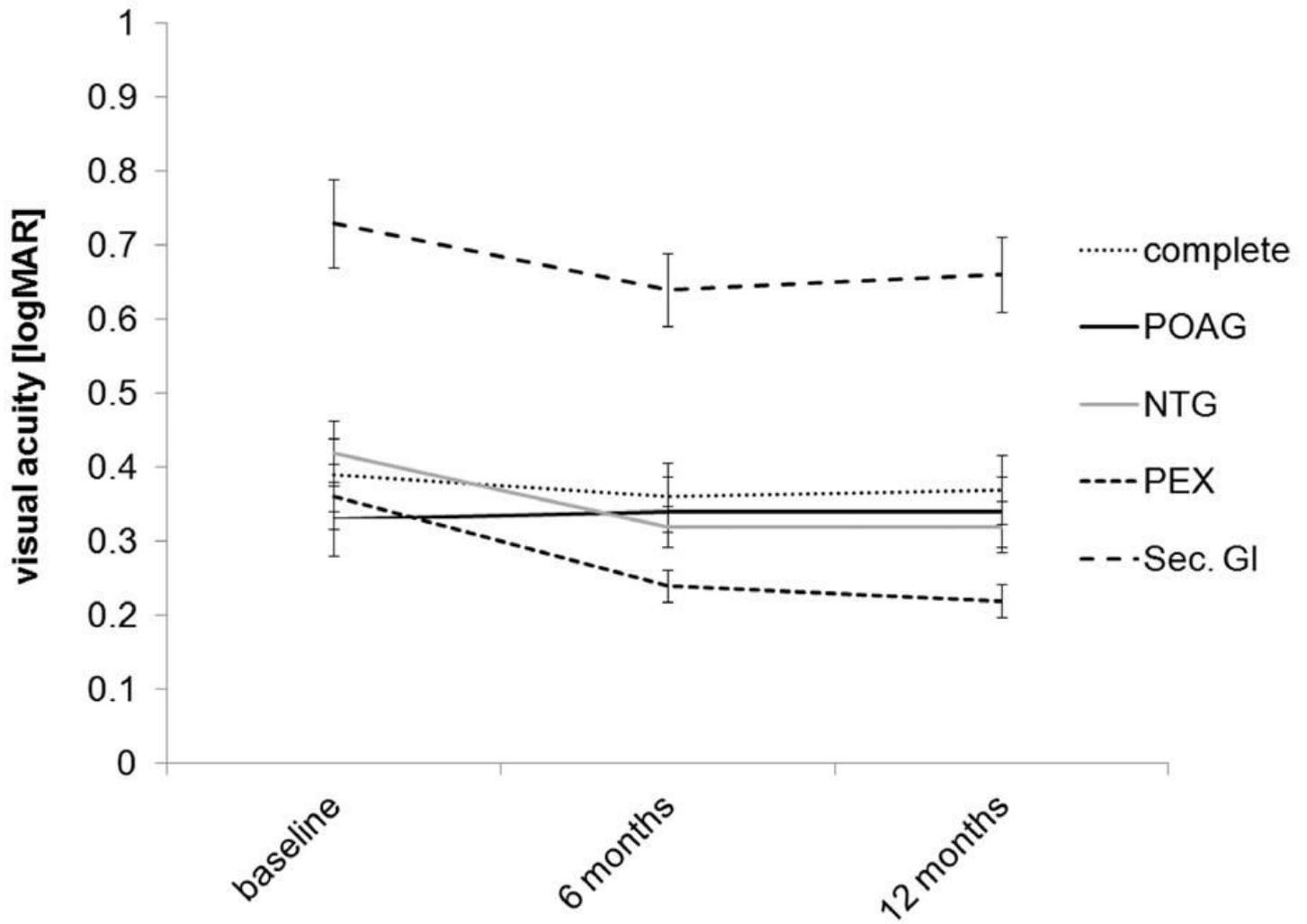
Course of mean IOP (in mmHg) for the whole group (a) as well as the subgroups (b) according to glaucoma type, i.e. primary open angle glaucoma (POAG), normal pressure glaucoma (NTG), pseudoexfoliation glaucoma (PEX)

and secondary glaucoma of different etiology (see eq.).



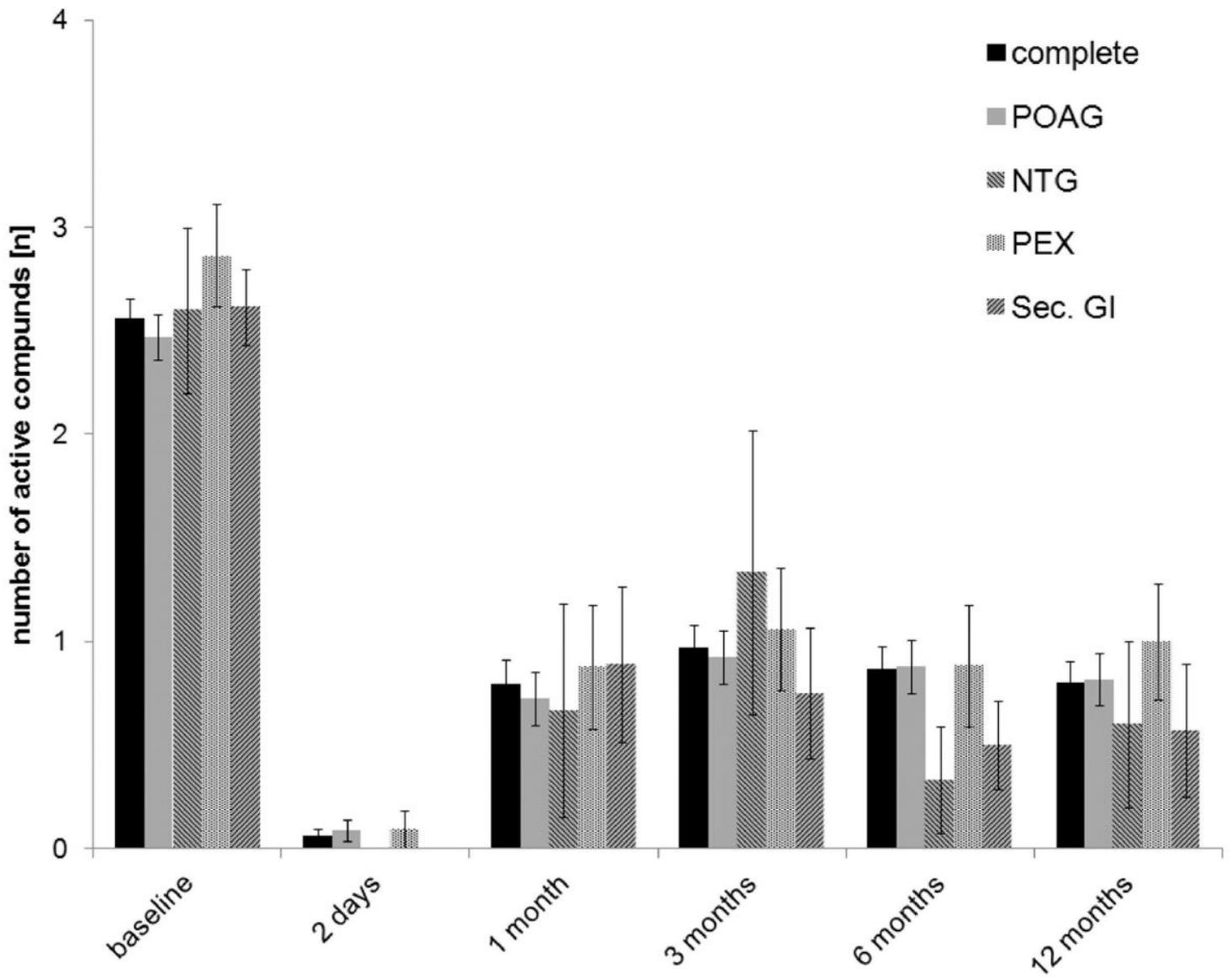
**Figure 2**

Scattergram of pre- and 12-month postoperative IOP (in mmHg) in the four subgroups of glaucoma treated with XEN-microstent-implantation in a) primary open angle glaucoma, b) normal pressure glaucoma, c) pseudoexfoliation glaucoma, d) secondary glaucoma.



**Figure 3**

Progression of the number of mean IOP-lowering agents (number) used in the entire XEN Microstent patient group and in the subgroups depending on glaucoma type during the first 12 months of postoperative follow-up. (primary open angle glaucoma (POAG); normal pressure glaucoma (NTG); pseudoexfoliation glaucoma (PEX); secondary glaucoma (sec. Gl)).



**Figure 4**

Course of BCVA in the entire group of eyes treated with XEN microstent implantation and in subgroups depending on the type of glaucoma in the first 12 months of postoperative follow-up. (primary open angle glaucoma (POAG); normal pressure glaucoma (NTG); pseudoexfoliation glaucoma (PEX); secondary glaucoma (sec. Gl))