



# MIGS: therapeutic success of combined Xen Gel Stent implantation with cataract surgery

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## Abstract

**Purpose** Glaucoma, a common disease in the elderly population, is frequently coexistent with cataract. While the combination of filtration surgery and cataract surgery is a challenging topic with limited success, minimal invasive glaucoma surgery (MIGS), such as Xen Gel Stents, seems to provide promising results. The aim of this study was to investigate the complete and qualified therapeutic success of Xen Gel Stent implantation with (XenPhaco) and without cataract surgery.

**Methods** One hundred and eleven open-angle glaucoma eyes underwent implantation of Xen45 Gel Stent (AqueSys, Inc.) with or without cataract operation. Complete therapeutic success was defined as target intraocular pressure (IOP) < 18 mmHg at any time point within 6 months of follow-up without local antiglaucomatous therapy or further surgical interventions. Qualified success was defined as target IOP < 18 mmHg with additional 1–2 local antiglaucomatous eye drops. Failure included all cases with the necessity of at least three local antiglaucomatous eye drops or additional glaucoma surgery.

**Results** Combined implantation of Xen Gel Stent with cataract surgery was performed in 30 eyes and stand-alone Xen Gel Stent implantation was performed in 81 eyes. A complete therapeutic success was achieved in 46.9% of single Xen Gel Stent implantation, whereas 53.3% was reached with combined XenPhaco. Qualified success was seen in 2.5% in the eyes of the single Xen Gel Stent implantation group and in 3.3% of the combined surgery group. Therapeutic failure rate was 49.4% in the stand-alone group vs 46.7% in the combined group. Data were not significantly different for group and subgroup analyses.

**Conclusions** Complete and qualified therapeutic success is similar for the combination of Xen Gel Stent implantation with and without cataract surgery in open-angle glaucoma patients. MIGS using Xen Gel Stent can be recommended in situations if glaucoma surgery is indicated besides coexisting cataract.

**Keywords** Xen gel stent · Minimal invasive glaucoma surgery · MIGS · Open-angle glaucoma · Ab interno

## Introduction

Glaucoma therapy is mainly based on lowering intraocular pressure (IOP) to an individual target level in order to decelerate glaucoma progression. As glaucoma is a common disease of elderly persons, ocular comorbidities are common. A special challenging topic is the coexistence of cataract and the ‘ideal’ time-point for each operation. Previous glaucoma surgery may accelerate cataract formation [1]. Otherwise, subsequent cataract surgery can increase bleb scarring after

glaucoma surgery [2]. Even primary cataract surgery can impair therapeutic success of subsequent glaucoma operations [3]. New techniques of MIGS (minimal invasive glaucoma surgery) permit new possibilities of combined surgery. The gold standard in glaucoma therapy is the trabeculectomy (TE). However, adverse events after TE are not rare, and postoperative care is very intensive in the following months. Thus, novel less invasive methods have been developed with the aim of reducing the risk of postoperative adverse events and the intensive follow-up care. One new development of MIGS is the Xen45 Gel Stent (AqueSys, Inc., Aliso Viejo, CA, USA). Consisting of collagen-based gelatine, the 6 mm long and 45 µm wide tube is rigid without contact to liquids. When the tube is inserted ab interno by a clear cornea incision subconjunctivally, it becomes soft due to the hydrophilic characteristics of the material. The Xen Gel Stent adapts well to the surrounding tissue. Similarly to TE, Xen Gel Stents shunt

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aqueous humor into the subconjunctival space. Thus, Xen Gel Stents offer the opportunity of avoiding all outflow resistances by a minimally invasive technique creating a filtering bleb without surgical opening of the conjunctiva. Even in difficult conditions, this ab-interno stent seems to provide promising results in the regulation of IOP. In addition to good postoperative visual acuity, intraoperative trauma is much less and postoperative management is easier in the early postoperative period [4].

However, no data investigating the therapeutic success of combined Xen45 Gel Stent implantation with cataract surgery are available in literature up to now. This study was performed to investigate the complete and qualified therapeutic success of combined MIGS (Xen45 Gel Stent implantation) and cataract surgery (XenPhaco) in comparison to stand-alone Xen45 Gel Stent implantation in a large patients' group of open-angle glaucoma patients.

## Material and methods

One hundred and eleven eyes of open-angle glaucoma patients (64 male, 47 female) of the Department of Ophthalmology, University of Erlangen and from the Erlangen Glaucoma Registry (EGR; ClinicalTrials.gov Identifier: NCT00494923; ISSN 2191-5008, CS-2011 [5]) underwent implantation of Xen45 Gel Stent (AqueSys, Inc., Aliso Viejo, CA, USA) due to a non regulated IOP under maximal local and/or systemic antiglaucomatous therapy or insufficient toleration of the medication. Seventy-two of the patients were primary open-angle glaucoma (POAG) and 39 were secondary open-angle glaucoma patients (SOAG, especially, 31 pseudoexfoliation glaucoma, PEXG). Mean age was  $68 \pm 14$  years (range 22–94 years). All patients underwent a complete ophthalmological examination including slit-lamp biomicroscopy, funduscopy, Goldmann applanation tonometry, corneal pachymetry, standard white-on-white full-field perimetry (Octopus 500, G1 protocol, Interzeag, Schlieren, Switzerland) and Spectralis Optical Coherence Tomography (Spectralis® OCT Version 1.9.10.0, Heidelberg Engineering, Heidelberg, Germany).

## Surgical technique

The surgery was performed after topical anesthesia. After insertion of the eyelid retractor, the target sector was marked in the nasal upper quadrant with 3 mm limbal distance using a pair of compasses. Mitomycin 10  $\mu$ g (0.03 mg, pharmacy of University of Erlangen, Erlangen, Germany) in 0.1 ml was subconjunctivally injected adjacent to the target sector. A clear cornea self-sealing incision (1.5 mm) was done at the 7 o' clock position as well as a further small paracentesis at the 11 o' clock position of the right eye (and vice versa for the left

eye). After injection of viscoelasticum (Dispasan® Plus, Ciba Vision, Ophthalmics, Germany) in the anterior chamber, the eye was stabilized with a Hirschmann spatula over the superior paracentesis. The Xen implantation system was entered into the anterior chamber via the corneal incision at 7 o' clock position (right eye; 5 o' clock position for the left eye). As the Xen implantation bevel was visible in the previously marked area, the system was rotated to the 12 o' clock position and the Xen Gel Stent was injected. The Xen implantation system was removed and the position of the Xen Gel Stent was checked. After extraction of the viscoelastic substance by a bimanual hand piece, the corneal incisions were hydrated and the eyelid retractor was removed.

All local and systemic antiglaucomatous medications were stopped after the surgery and local anti-inflammatory (prednisolone acetat, Prednifluid eye drops, Dermapharm AT, Germany; five times a day, reduced by one drop per week) and antibiotics (ofloxacin, floxal EDO eye drops, Bausch & Lomb GmbH, Germany; three times a day for 1 week) were applied.

## Bleb needling

The surgery was performed under topical anesthesia using an eyelid retractor. After penetration of the conjunctiva near the bleb by a 27-gauge needle, subconjunctival scaring was dissected by moving the needle. Afterwards 1.00 mg anti-VEGF (Avastin®, bevacizumab, pharmacy of University of Erlangen, Erlangen, Germany) was injected and the 27-gauge needle was removed. Local anti-inflammatory (prednisolone acetate, Prednifluid eye drops, Dermapharm AT, Germany; five times a day, reduced by one drop per week) and antibiotics (ofloxacin, floxal EDO eye drops, Bausch & Lomb GmbH, Germany; three times a day for 1 week) were applied.

## Statistical analysis

The target point of this study was complete therapeutic success after 6 months follow-up period. Complete therapeutic success was defined as target intraocular pressure (IOP) < 18 mmHg at any time point within 6 months of follow-up without local antiglaucomatous therapy or further surgical interventions. Qualified therapeutic success was defined as target IOP < 18 mmHg with 1–2 local antiglaucomatous eye drops. Therapeutic failure was defined as the necessity for at least three local antiglaucomatous eye drops or additional glaucoma surgery. Data analysis was done by SPSS, version 21.0. Data were presented as descriptive mean  $\pm$  standard deviation (SD), counts and percentages.

## Results

Combined Xen Gel Stent implantation with cataract surgery was performed in 30 eyes. Stand-alone Xen Gel Stent implantation was performed in 81 eyes. Fifty-two of the 81 eye were already pseudophakic at the time of the stand-alone Xen Gel Stent implantation. A complete therapeutic success was achieved in 46.9% in single Xen Gel Stent implantation group. Combined Xen Gel Stent and cataract operation showed a complete therapeutic success in even 53.3%. Qualified therapeutic success was achieved in 2.5% in the single Xen Gel Stent group and in 3.3% in the XenPhaco group. Failure rate was 49.4% in the single Xen Gel Stent group and 46.7% in the XenPhaco group (Fig. 1). However, 50% of the eyes in the failure group (single Xen Gel Stent group and XenPhaco group) showed a target IOP < 18 mmHg after one single bleb needling during the follow-up period, yet without local antiglaucomatous therapy.

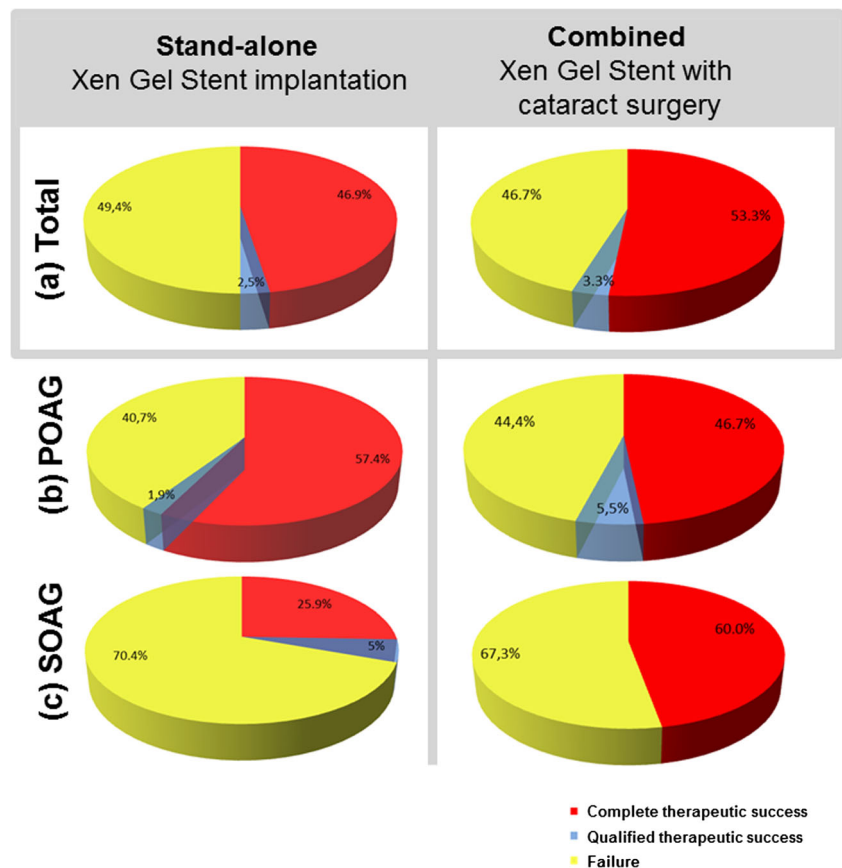
Subgroup analysis yielded a complete therapeutic success in 57.4% (POAG), 25.9% (SOAG), and 20% (PEXG) in the stand-alone group. Combined Xen Gel Stent Implantation and cataract surgery showed a complete therapeutic success in 46.7% (POAG), 60% (SOAG) and 57.1% (PEXG). A qualified therapeutic success was allocated in 1.9% (POAG), 5.0% (SOAG) and 5.0% (PEXG) in the stand-alone Xen Gel Stent

group vs 5.5% (POAG), 0% (SOAG) and 0% (PEXG) in the combined XenPhaco group. Therapeutic failure was 40.7% (POAG), 70.4% (SOAG) and 75.0% (PEXG) in the single Xen Gel Stent group, whereas in the XenPhaco group percentages of 44.4% (POAG), 67.3% (SOAG) and 67.3% (PEXG) were observed (Fig. 1). Data were not significantly different for group and subgroup analyses ( $p > 0.05$ , Qui-Quadrat after Pearson).

## Discussion

Coexistence of cataract and not regulated intraocular pressure is a challenge for every ophthalmologist. As data were not available regarding therapeutic success of Xen45 Gel Stent in combination with cataract surgery, this study investigated the complete and qualified therapeutic success as well as failure rate in open-angle glaucoma patients in comparison to stand-alone Xen45 Gel Stent implantation. In a large cohort of 111 patients we observed an IOP decrease of < 18 mmHg without any medications in 46.9% (stand-alone) and 53.3% (XenPhaco) of the patients even after 6 months follow-up (complete therapeutic success). A qualified therapeutic success was achieved in 2.5% (stand-alone) and 3.3% (XenPhaco). Therapeutic failure rate was 49.4% (stand-

**Fig. 1** Therapeutic outcome of stand-alone Xen45 Gel Stent implantation (*left side*) and combined Xen45 Gel Stent implantation with cataract surgery (*right side*) in all patients (a) and subdivided into primary open-angle glaucoma (POAG, b) and secondary open-angle glaucoma (SOAG, c). Complete therapeutic success — red; therapeutic success with IOP <18 mmHg without any local antiglaucomatous therapy or further surgical interventions after 6 month follow-up. Qualified therapeutic success — blue; target IOP <18 mmHg with additional 1–2 local antiglaucomatous eye drops during the follow-up period. Therapeutic failure — yellow; i.e., necessity of at least three local antiglaucomatous eye drops or additional glaucoma surgery



alone) and 46.7% (XenPhaco). No significant differences were seen for group and subgroup analyses.

A recent study reported about a therapeutic success of 80.4% (33 of 41 eyes) in open-angle glaucoma after combined Xen Gel Stent implantation and cataract surgery [6]. In this study therapeutic success was defined as IOP range between 6 and 18 mmHg without glaucoma medications after 1 year of follow-up. The same IOP range with the need of glaucoma medications was found to be 97.5% (40 of 41 eyes); thus, a total of seven of 41 eyes of the previous study had a demand of postoperative glaucoma medication (i.e., 17.1%). One eye underwent further glaucoma surgery (trabeculectomy, 1 of 41; 2.4%) [6]. In the only further study of combined Xen Gel Stent implantation with phacoemulsification in 30 open-angle glaucoma patients, an IOP decrease of 29.34% (in relation to the preoperative IOP) was described after 1 year of follow-up. Additionally, the number of medications were reduced by 94.57% [7]. However, there were no control groups in those two prospective studies; thus, a direct comparison of those data to our ones cannot be done, even as the number of patients was lower in the recent two studies.

Subdividing the patients into primary and secondary open-angle glaucoma, therapeutic success differed between the two groups, yet not significantly. In POAG patients, a complete therapeutic success was 57.4% in the stand-alone group vs 46.7% in the XenPhaco group. SOAG patients showed a reduction of IOP <18 mmHg without any medications in 60.0% after XenPhaco, however, only 25.9% in the stand-alone group. Therefore, qualified therapeutic success (1.9%) and failure rate (70.4%) were higher in the stand-alone group than in the XenPhaco in SOAG patients (qualified therapeutic success 0%, failure rate 67.3%). No study is available right now, investigating the therapeutic success of a combination of XEN Gel Stents and cataract surgery in PEXG patients compared to a stand-alone Xen Gel Stent implantation. Thus, a comparison to phacotrabeculectomy or ab-interno trabeculectomy (Trabectome) with and without cataract surgery was done. PEXG patients seemed to benefit of combined phacoemulsification and trabeculectomy in the postoperative IOP decrease more than of single cataract surgery [8]. Landa et al. observed a similar IOP decrease after phacotrabeculectomy in POAG and PEXG [9]. After ab-interno trabeculectomy, open-angle glaucoma patients (chronic open-angle glaucoma  $n=7$ ; PEXG  $n=2$ ) showed a 38.56% IOP decrease with a drop to a number of 0.8 medications (preoperative 2.4) [10]. It would be of interest if the two PEXG included in the study would vary in any postoperative course. Unfortunately, no special data are given. It seemed that IOP reduction after ab-interno trabeculectomy is greater in PEXG than in POAG, and therapeutic success is improved when combined with phacomemulsification [11].

Damji et al. stated that IOP decreases more in patients with than without exfoliation syndrome after phacoemulsification due to several hypothetical mechanisms [12]. These assumptions might also be relevant for the improved therapeutic success of the combined XenPhaco in PEXG: a more deep anterior chamber with consecutive more open iridocorneal angle and the reduced friction of the iris at the lens with reduced release of pseudoexfoliation (PEX) material. Further on, there is a washout phase during cataract surgery, which might lead to a washout of the PEX material.

Xen Gel Stents seems to be an effective tool in glaucoma surgery to lower IOP, even in difficult situations [4]. The surgical procedure is minimally invasive, which can use the same corneal dissections as the cataract surgery when the operation is combined. Thus, no subconjunctival incision is necessary — a fact which preserves the conjunctiva and enables potential required additional glaucoma filtration surgeries to work. In animal models, no foreign body reaction was observed [13].

The ab-interno implantation of the Xen45 Gel Stents is the only surgical technique of MIGS, up to now, which allows filtration directly into the subconjunctival space with protection of the conjunctiva and good clinical therapeutic success. A combination with cataract surgery is possible with a complete therapeutic success in even 46.7% of POAG patients. If Xen45 Gel Stent implantation is planned to be performed in PEXG, the data of the present study seem to suggest a surgical procedure in combination with cataract surgery to increase therapeutic success.

## Conclusion

Complete and qualified therapeutic success is similar for the combination of Xen Gel Stent implantation with cataract surgery when compared to Xen Gel Stent implantation alone in POAG patients. Even in PEXG eyes, a combination of MIGS using Xen45 Gel Stent implantation is recommended in situations if glaucoma surgery is indicated besides coexisting cataract formation to increase therapeutic success.

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## Compliance with ethical standards

**Conflict of interest** All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

For this type of study, formal consent is not required.

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