



The STARflo™ glaucoma implant: a single-centre experience at 24 months

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Abstract

Purpose To evaluate the 24-month outcomes following STARflo™ implantation in patients with moderate or advanced open-angle glaucoma.

Methods We enrolled 32 patients (40 eyes) with high intraocular pressure (IOP) resistant to topical and systemic medical therapy. After baseline assessments, patients were implanted with STARflo™ implants with the goal of IOP reduction and long-term maintenance. Patients were followed for 24 months. Complete success of implantation was defined as a restoration of normal IOP without topical glaucoma medications, while qualified success was defined as a restoration of normal IOP with implantation and topical glaucoma medications.

Results STARflo™ did not satisfactorily reduce IOP at 24 months. Twenty-eight eyes (70%) had elevated IOP at least once during the 24 months post-implantation period. Five eyes (12.5%) developed corneal decompensation. The average IOP 24 months after the surgery was 13.42 ± 6.03 mmHg and was not significantly different than IOP at 12 months (13.2 ± 5.59 mmHg). Moreover, 45% of treated eyes needed additional glaucoma procedures after 1 year and 2 years to achieve these IOPs. STARflo™ did reduce the average number of topical glaucoma medications from 2.7 pre-implantation to 1.17 at 24 months postoperatively in the rest 55% of the eyes.

Conclusions The STARflo™ implantation did not meet success criteria and so appears to be an ineffective alternative to filtering surgical procedures for patients with treatment-refractory open-angle glaucoma.

Keywords STARflo™ implant · Intraocular pressure · Glaucoma · Loss of corneal endothelial cells · Corneal decompensation

Introduction

The aim of all glaucoma treatments, either conservative or surgical, is to reduce the intraocular pressure (IOP). The rationale for this aim is to avoid a rapid progression of optic neuropathy and resultant visual field defects. Many conventional glaucoma surgeries have satisfactory mid-term results. The fibrotic changes and the subsequent failure to drain aqueous humour after conventional glaucoma surgery often leave patients needing various stents and/or shunts to achieve long-term control of IOP. While most current implants include a draining tube, some implants are solid and promote the flow

of the aqueous humour along the surface of the implant [1, 2]. Regardless of design, all implants are intended to decrease IOP by increasing outflow of aqueous humour [1, 2].

The STARflo™ implant is produced by the iSTAR company in Belgium. A detailed description of its structure and its function is presented in our previous publication [3]. We previously reported that the implant met sufficient safety standards and satisfactorily reduced IOP within the first 12 months after implantation [3]. We are currently presenting the 24-month outcomes after implantation of STARflo™ glaucoma implant in patients with treatment-refractory open-angle glaucoma.

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Materials and methods

The prospective STARflo™ implantation study was conducted in the Department of Ophthalmology in St. Johannes Hospital in Dortmund from October 2016 to January 2018.

Table 1 Demographic data of the patients included in the study

Sex	Age		Starflo™ implants		
Male	14	Min	30	Right eye	13
Female	18	Max	82	Left eye	13
		Average	63.2	Both eyes	7
		Standard deviation	12.8	Total	40
		Median	64		

A total of 32 patients (40 eyes) with POAG, PEX and congenital glaucoma underwent implantation of STARflo™ because of high intraocular pressure. Our patient cohort, the largest in the literature so far, consisted of 14 men and 18 women with an average age of 63.2 ± 12.8 years (Table 1). All patients in this study were treated with at least one glaucoma surgery prior to this clinical study.

The key inclusion criteria are the diagnosis of moderate to advanced therapy-resistant open-angle glaucoma and intraocular pressure above 20 mmHg. Using the Hodapp-Parrish-Anderson classification system, moderate glaucoma was defined as median deviation (MD) of the Humphrey visual fields $-6 \text{ dB} < \text{MD} < -12 \text{ dB}$ and advanced glaucoma was $\text{MD} > -12.00 \text{ dB}$. The secondary inclusion criteria were the following: cup-to-disc ratio 0.9–1.0, Shaffer gonioscopy system grade 3 or 4 (i.e. “wide open”), too little response either to the maximal topical therapy (3 to 4 glaucoma eye drops) or to systemic therapy (acetazolamide) for the target IOP to be reached. All 32 patients included in the study fulfilled the above criteria and no patient was withdrawn during the 24-month study period (Table 2).

The postoperative follow-up visits were conducted at 1 week, 1 month, 2 months, 3 months, 6 months, 1 year and 2 years after implantation. Patients who could not come to our clinic due to poor general health ($n = 3$) were evaluated by

ophthalmologists in their private practices. Thirteen patients (13 eyes) are completing the 24-month follow-up at the end of 2019.

Our criterion for complete success was the achievement of target IOP after the implantation of STARflo™ without topical glaucoma medications. A qualified success was defined as the achievement of target IOP with the additional use of topical medications.

Statistical calculations were carried out with R: A language and environment for statistical computing (R Foundation for Statistical Computing, Vienna, Austria). Normality of the data was assessed using a histogram as a graphical method. Because the examined parameters did not follow a normal distribution, we used the nonparametric Wilcoxon sign rank test for all analyses. Statistical significance was set at 5% ($p = 0.05$).

Results

The preoperative IOP fluctuated between 16 and 39 mmHg; the mean preoperative IOP was 21.78 ± 7.58 mmHg. The average IOP after 1-month follow-up was 15.4 ± 7.09 mmHg, and after 3 months postoperatively was 16.85 ± 6.03 mmHg. The average IOP after 24 months (13.42 ± 6.03 mmHg) was not significantly lower than the IOP values measured at 12 months (13.2 ± 5.59 mmHg). IOP values at 1 and 2 years were not the sole result of STARflo™ implantation, however, and could only be achieved through additional ocular surgical procedures (Fig. 1).

Complications in the early postoperative period included anterior chamber inflammation, hyphema, hypotony and blurred vision, all of which were transient and resolved completely within one or two weeks (Table 3).

The average number of topical medications that were administered at 24 months after STARflo™ implantation

Table 2 Preoperative findings and history of the patients and eye surgeries before the STARflo™ implantation

Preoperative findings			Eye surgeries before the STARflo™ implantation		
	Average	Standard deviation (SD)	Type of surgery	Eyes in %	Eyes (n)
Vision	0.41	0.35	Phacoemulsification/PC-IOL	77.5	31
IOP (mmHg)	21.78	7.58	Trabeculectomy + mitomycin	17.5	7
CDR	0.97	0.05	Canaloplasty	7.5	3
Pachymetry (μm)	563.2	39.86	Transscleral Cyclophotocoagulation	20.0	8
Gonioscopy (Shaffer Grad)	3.63	0.57	Cypass implant	2.5	1
Visual fields Humphrey MD	-17.27	8.31	Ahmed valve implant	–	–
Visual fields Humphrey PSD	7.88	4.13	ALT/SLT	5.0	2
			Goniotomy/trabeculotomy	12.5	5

IOP intraocular pressure, CDR cup-to-disc ratio, MD mean deviation, PSD pattern standard deviation, PC-IOL posterior chamber intraocular lenses, ALT argon laser trabeculoplasty, SLT selective laser trabeculoplasty

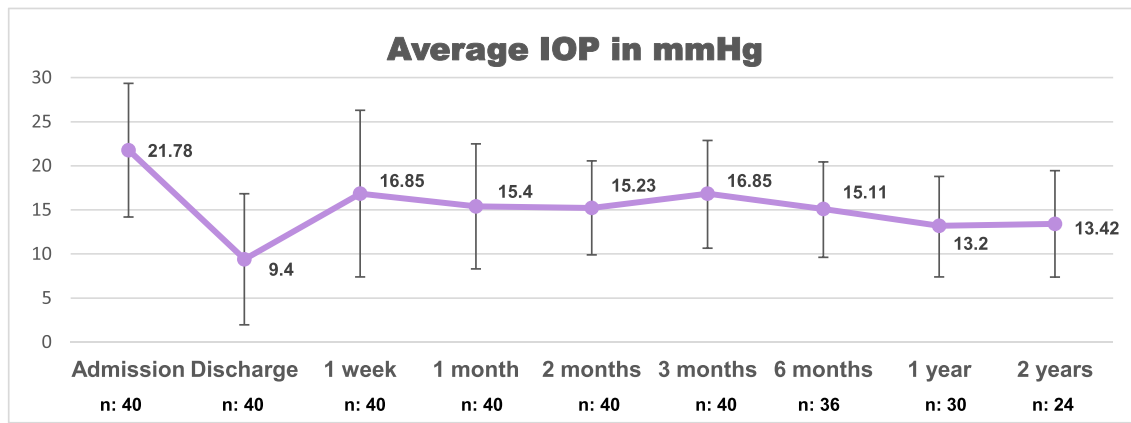


Fig. 1 Average IOP curve (mmHg) with the standard deviation up to 24 months

was 1.17, which is 56.3% lower than the 2.7 medications on average required prior to implantation. This represents a reduction of the topical glaucoma therapy of 56.3% (Fig. 2). In 19.4% of patients, oral acetazolamide was added to treat a significant increase of IOP after the third postoperative month. After 24 months, IOP control was achieved in 31 of the 32 patients without any systemic administration of acetazolamide.

We observed a stable, best-corrected visual acuity average of 0.3 (decimal values) in the postoperative period between 3 months and 1 year. Visual acuity decreased dramatically to 0.12 after 24 months, because of the corneal decompensation in 5 cases (12.5%) (Fig. 3).

Twenty-eight eyes (70%) that received the STARflo™ implant developed increased postoperative IOP at least once during the 24-month follow-up despite maximal topical glaucoma therapy. IOP was persistently elevated in 8 eyes (29.60%) after 24 months. The IOP elevation was successfully treated by optimizing the topical glaucoma therapy.

Due to unsatisfactorily high postoperative IOP, we pursued additional operative measures within the first 12 postoperative

months in 18 cases (45.0%), which eliminated the need for additional surgical procedures in the second year after STARflo™ implantation. In 11 cases, we performed transscleral cyclophotocoagulation. In 3 cases, we implanted an Ahmed valve drainage mechanism at 1 month, 3 months and 12 months. In 1 case, we performed a trabeculectomy combined with mitomycin C 0.02 mg/ml and a biodegradable collagen matrix (Ologen) because of persistent ocular hypertony. In 2 cases of unsatisfactory postoperative IOP at 6 months, we performed canaloplasty. The remaining 12 eyes (30%) achieved the target IOP after the implantation of STARflo™ during the follow-up of 24 months (Fig. 4, Tables 3 and 4).

Three patients (3 eyes) with congenital glaucoma were treated with STARflo™ implantation. Two patients failed to reach the target IOP on topical glaucoma medication in the 2-year follow-up period. In two cases, a transscleral cyclophotocoagulation (after 6 months and after 2 years in each case, respectively) was performed to stabilize the intraocular pressure on a topical therapy with two IOP-lowering glaucoma agents. The third patient developed a suprachoroidal haemorrhage during

Table 3 Postoperative complications in the follow-up of 24 months after the STARflo™ implantation

	Discharge	1 week	1 month	2 months	3 months	6 months	1 year	2 years
IOP elevation	0.00%	27.50%	25%	22.50%	37.50%	55.00%	0%	29.60%
Oc. hypotony	17.50%	17.50%	10%	0%	0%	0%	0%	0%
Choroidal oedema (clinical diagnosis documented also with B-scan echography)	0.00%	2.50%	0%	0%	0%	0%	0%	0%
Hyphema	7.50%	2.50%	0%	0%	0%	0%	0%	0%
Vitreous haemorrhage	2.50%	2.50%	0%	0%	0%	0%	0%	0%
Fibrin in the AC	2.50%	2.50%	0%	0%	0%	0%	0%	0%
Uveitis	0%	0%	0%	0%	2.50%	0%	0%	0%
Macular edema	2.50%	0%	0%	0%	2.50%	0%	0%	0%
Expulsive haemorrhage	2.50%	0%	0%	0%	0%	0%	0%	0%
Corneal decompensation	0%	0%	0%	3%	5%	0%	5.00%	18.50%
Phthisis bulbi	0%	0%	0%	0%	2.50%	0%	0%	0%

AC anterior chamber

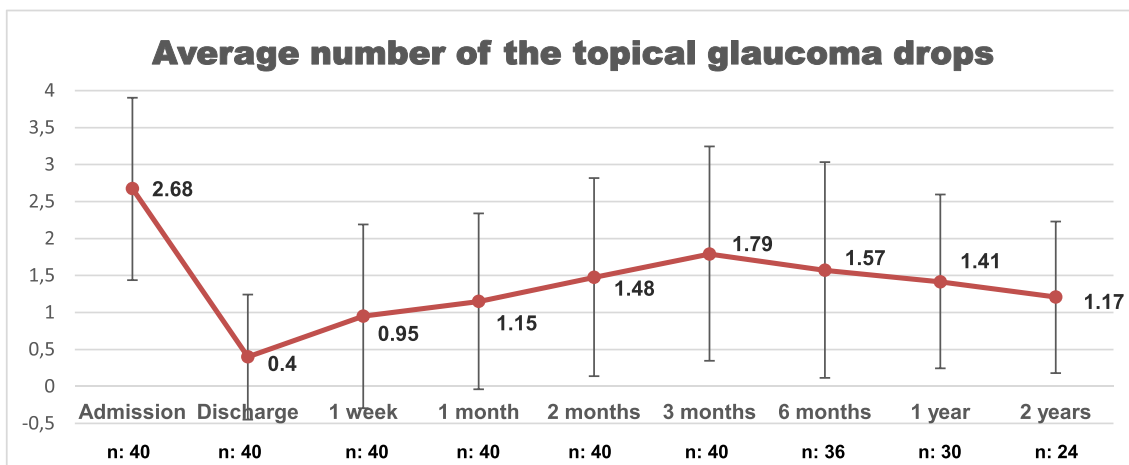


Fig. 2 Average IOP (mmHg) after STARflo™ implantation as well as additional glaucoma surgeries and on topical medical therapy during the follow-up of 2 years. Error bars indicate standard deviation

the second postoperative day with a reported phthisis bulbi after the incident.

The corneal endothelial cell density (ECD) was modestly though not statistically significantly reduced at 6 months postoperatively (2.10%; $p > 0.05$). At 24 months, treatment with the STARflo™ implant significantly reduced corneal ECD by 41.5% (preoperative ECD 2098 cell/mm²; 24 months postoperative ECD 1227 cell/mm²; $p < 0.05$). This reduction in corneal ECD was associated with another important complication after STARflo™ implantation, corneal decompensation. We observed corneal decompensation in 5 cases (12.5%) at 24 months compared with only 3 cases (7.5%) at 12 months. Three of the 5 eyes with corneal decompensation showed no improvement after intensive conservative therapy and needed either penetrating keratoplasty or Descemet membrane endothelial keratoplasty (DMEK) (Fig. 5).

Summarizing the above results, a failure of fulfilling the complete success criterion was shown in 35 cases (87.5%).

Topical medical glaucoma therapy was added during the follow-up after the STARflo™ implantation because of an unsatisfactory postoperative reduction of the intraocular pressure (Fig. 6). However, we observed a qualified success in 24 cases (60%) as the target IOP was achieved after the re-administration of topical medical glaucoma therapy with a reduced number of eye drops (Fig. 7).

Because the intervention did not sufficiently reduce IOP and many patients experienced a substantial reduction in corneal ECD, our team decided in January 2018 to terminate the study and not to enroll additional patients.

Discussion

STARflo™ implantation was largely ineffective at 24 months and potentially led to specific complications, namely a reduction in corneal ECD. It should be noted that this patient

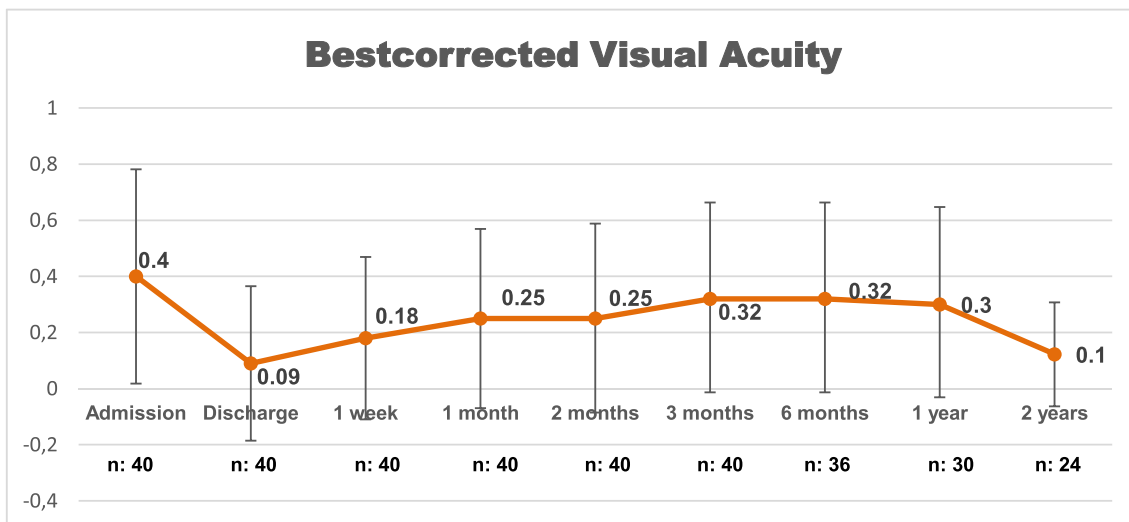


Fig. 3 Average visual acuity with the standard deviation up to 24 months

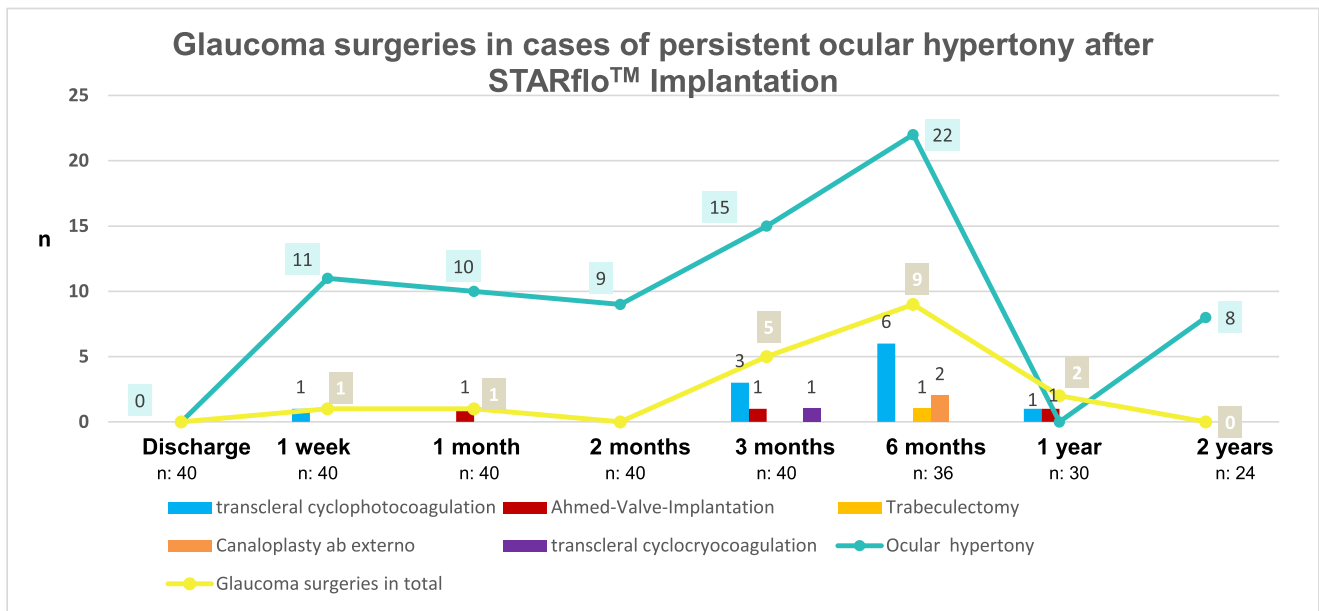


Fig. 4 The number of glaucoma surgeries in cases of persistent ocular hypertony after the STARflo™ implantation

population was treatment-refractory. Each of the 40 eyes did not reach target IOP with maximal tolerated therapy or conventional surgical procedures including trabeculectomy, canaloplasty ab externo, transcleral cyclophotocoagulation and cyclocryocoagulation. Twenty-eight of the implanted eyes had further increases in IOP, which could not be managed with topical or systemic medical therapy. Additional glaucoma surgery was necessary to stabilise IOP at target levels.

We believe that the enlargement of the suprachoroidal space does not sufficiently increase outflow of aqueous humour and therefore cannot lower IOP in eyes with moderate or advanced glaucoma. The excessive fibrotic reaction around the STARflo™ implant possibly reduced aqueous humour outflow in the suprachoroidal space. Figus et al. reported a common cause of failure of the gold micro shunt (SOLX implant) was the formation of an inflammatory membrane in the anterior end of the shunt, obstructing inflow from the anterior chamber [4].

Three patients (3 eyes) with congenital glaucoma were treated with STARflo™ implantation. Two patients failed to reach the target IOP with topical glaucoma medication in the

2-year follow-up period and were treated with a transcleral cyclophotocoagulation. The third patient developed a suprachoroidal haemorrhage during the second postoperative day with a reported phthisis bulbi after the incident. No other reports of implantation of other shunts of the group of MIGS (micro-invasive glaucoma surgery) or BAGS (blebless ab-externo glaucoma surgery) in the suprachoroidal space in cases of congenital glaucoma were found in the literature.

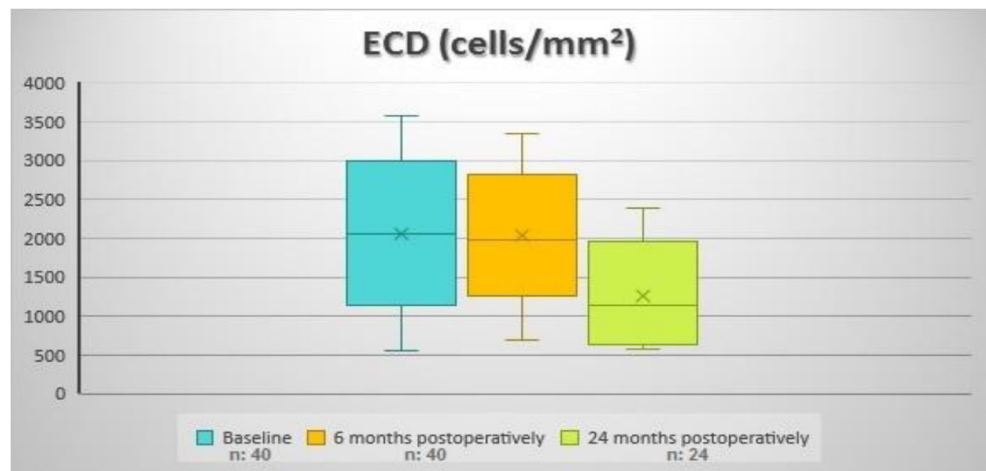
Another important observation during the 24-month follow-up period was the gradual reduction of the ECD in most patients. In 5 cases, the reduced ECD was so severe that it led to corneal decompensation, which was treated with dexamethasone and sodium chloride 5% eye drops. In 3 cases, the corneal decompensation was medically irreversible. These patients were treated with either penetrating keratoplasty or DMEK with excellent results.

The explantation of the STARflo™ implant was a tremendously traumatic procedure. The microporous material becomes integrated with the surrounding tissues making separation from the surrounding tissues impossible. Even the

Table 4 Surgical procedures in the follow-up of 24 months after the STARflo™ implantation (n)

	Discharge	1 week	1 month	2 months	3 months	6 months	1 year	2 years
Transcleral cyclophotocoagulation	0	1	0	0	3	6	1	0
Ahmed valve implantation	0	0	1	0	1	0	1	0
Trabeculectomy	0	0	0	0	0	1	0	0
Canaloplasty ab externo	0	0	0	0	0	2	0	0
Transcleral cyclocryocoagulation	0	0	0	0	1	0	0	0
Penetrating keratoplasty or DMEK	0	0	0	0	2	1	1	0

Fig. 5 Average corneal endothelial cell density (ECD) up to 24 months



removal of the head of the STARflo™ implant from the anterior chamber distorts the anatomy of the angle of the anterior chamber by more than 30°, which could negatively influence IOP. For these reasons, our team did not perform any total or partial explantation of the STARflo™ shunt.

In this study, STARflo™ was associated with a severe reduction of the average ECD of 41.5% at 2 years. In the COMPASS-XT Study, the CyPass implant was associated with a loss of ECD of 12.0% and 20.4% at 2 and 5 years, respectively [5]. Omatsu et al. reported that the mean corneal ECD was 2505 cells/mm² at baseline and 2277 cells/mm² 2 years after trabeculectomy (9.1% decrease) [6]. Another study from Japan showed a significant 9.4% decrease in mean ECD of 2 years after the ExPRESS® implantation (2008 ± 482 cell/mm² at baseline and 1846 ± 537 cells/mm² at 2 years) [7]. Glaucoma drainage implants also lead to a significant

decrease in ECD, which has been shown in many studies. Lee et al. reported a statistically significant reduction of the central corneal ECD of 18.6% 2 years after the implantation of Ahmed glaucoma valve. The supratemporal area—the closest site to the tube—showed the greatest decrease in ECD (22.6%), whereas the central cornea showed the smallest decrease (15.4%) at 24 months postoperative [8]. Similar results were published by Iwasaki et al. showing a 9.2% reduction in ECD by 12 months after Baerveldt glaucoma implantation.

Regarding the anterior chamber, the Baerveldt glaucoma implantation group documented a 13.1% decrease of ECD at 12 months at the tube insertion quadrant. In contrast, the pars plana Baerveldt glaucoma implantation group found no significant loss of corneal ECD in any corneal areas at any post-surgery follow-up visits. Iwasaki et al. showed that the tube-

Fig. 6 Kaplan-Meier survival curve presenting the number of patients that failed to meet complete success criterion after the STARflo™ implantation

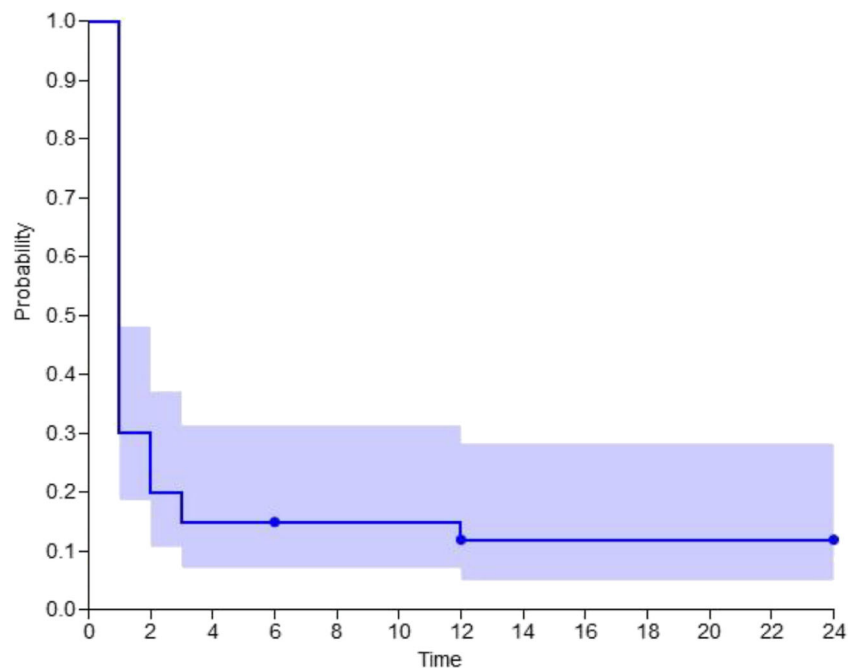
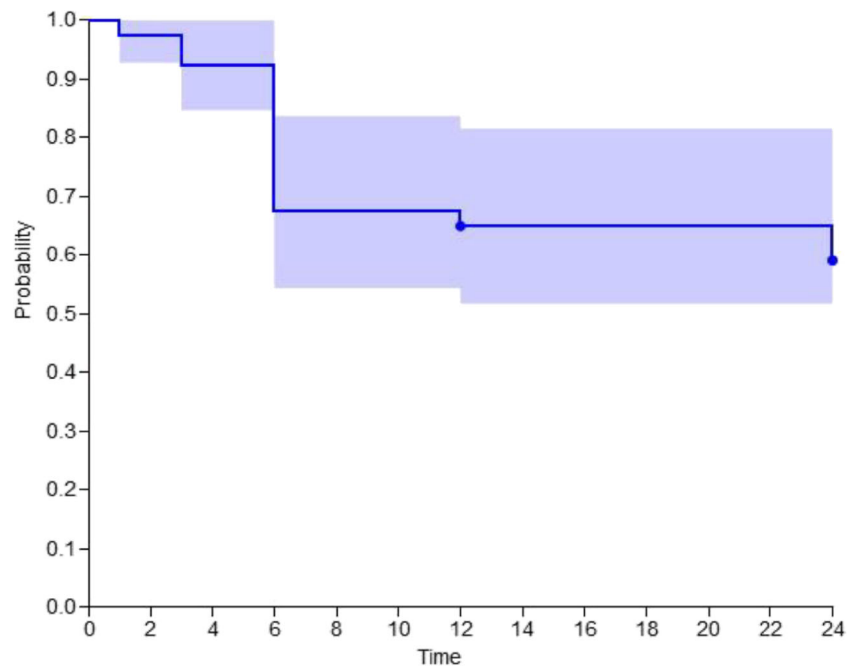


Fig. 7 Kaplan-Meier survival curve presenting the number of patients that failed to meet the qualified success criterion after the STARflo™ implantation



cornea angle was negatively correlated with the rate of corneal ECD loss at the tube insertion quadrant [9]. The exceedingly large, 41.5% loss of the corneal endothelial cells 2 years after the STARflo™ implantation observed in our study can be explained by the partial contact of the head of the implant with the corneal endothelium at the site of insertion of the implant in the anterior chamber over an extended area of 5 mm. This can be induced by the occasional flattening of the upper angle chamber through blinking. Our aforementioned hypothesis is in line with Naoki et al., who believe that a possible endothelial touch of ExPRESS implant through blinking could induce the reported endothelial cell loss [10]. Another explanation would be that altered aqueous humour flow around the head of the STARflo™ in the anterior chamber provokes an increased endothelial cell loss. This possibility is supported by the study of Yamamoto et al., who reported serious corneal endothelial dysfunction because of unusual streaming of the aqueous flow present after filtration surgery or laser iridectomy [11].

The failure of STARflo™ implantation to lower IOP to target levels in 70% of patients along with a 41.5% average loss of ECD and some cases of corneal decompensation led to our decision to terminate the study and not to implant any more shunts. The patients who did receive implants will be followed and treated as needed. While initially promising for bleb-free reduction of IOP, the STARflo™ implant failed to provide a safe and effective long-term alternative to conventional glaucoma surgeries.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee of St. Johannes Hospital in Dortmund, Germany, and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was freely given and obtained from all participants in this study.

Abbreviations ALT, argon laser trabeculoplasty; BAGS, blebless ex-externo glaucoma surgery; CDR, cup-to-disc ratio; DMEK, Descemet membrane endothelial keratoplasty; ECD, corneal endothelial cell density; MD, mean deviation; MIGS, micro-invasive glaucoma surgery; PC-IOL, posterior chamber intraocular lenses; PEX, pseudoexfoliation; POAG, primary open-angle glaucoma; PSD, pattern standard deviation; SLT, selective laser trabeculoplasty

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