# Postoperative RNFL-Changes after Successful Trabeculectomy: 2-Year Outcomes

Zwei-Jahres-Ergebnisse postoperativer RNFL-Entwicklung nach erfolgreicher Trabekulektomie

# Authors

Caroline Bormann<sup>10</sup>, Catharina Busch<sup>1</sup>, Matus Rehak<sup>2</sup>, Christian Thomas Scharenberg<sup>3</sup>, Olga Furashova<sup>4</sup>, Focke Ziemssen<sup>1,5</sup>, Jan Darius Unterlauft<sup>6</sup>

# Affiliations

- 1 Klinik und Poliklinik für Augenheilkunde, Universitätsklinikum Leipzig, Deutschland
- 2 Klinik und Poliklinik für Augenheilkunde, Universitätsklinikum Innsbruck, Österreich
- 3 Augenheilkunde, Smile Eyes, Augen- und Laserzentrum, Leipzig, Deutschland
- 4 Klinik für Augenheilkunde, Klinikum Chemnitz gGmbH, Deutschland
- 5 Department für Augenheilkunde, Eberhard-Karls-Universität Tübingen, Universitätsklinikum Tübingen, Deutschland
- 6 Universitäts-Augenklinik Bern, Inselspital Bern, Schweiz

#### Key words

trabeculectomy, peripapillary retinal nerve fiber layer, optical coherence tomography, primary open-angle glaucoma

#### Schlüsselwörter

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# Correspondence

Dr. Caroline Bormann Klinik und Poliklinik für Augenheilkunde, Universitätsklinikum Leipzig Liebigstraße 10–14, 04103 Leipzig, Deutschland Phone: + 49 (0) 34 19 72 16 50, Fax: + 49 (0) 34 19 72 16 59 caroline.bormann@medizin.uni-leipzig.de

# ABSTRACT

**Background** The most important tool in glaucoma therapy is to lower the intraocular pressure to slow down the apoptosis of retinal ganglion cells. Trabeculectomy (TE) is considered the gold standard in glaucoma surgery. The aim of this study was to analyse the postoperative changes in retinal nerve fibre layer (RNFL) using optical coherence tomography (OCT) after TE.

**Material and Methods** We examined 40 patients naïve to prior glaucoma surgery retrospectively, who received a TE for medically uncontrolled primary open-angle glaucoma (POAG). Intraocular pressure (IOP), IOP-lowering medication, mean deviation of perimetry, visual acuity and peripapillary RNFLthickness using OCT were evaluated during the first 24 month after TE.

**Results** In total 40 eyes from 40 patients were treated with TE. Mean IOP decreased from  $25.0\pm0.9$  to  $13.9\pm0.6$  (p < 0.01), and the mean number of IOP-lowering eye drops from  $3.3\pm0.2$  to  $0.5\pm0.2$  (p < 0.01). Visual acuity and mean deviation in perimetry remained stable while mean global RNFL-thickness decreased from  $67.8\pm2.9$  to  $63.7\pm2.9$  (p < 0.01) and  $63.4\pm2.9\,\mu m$  (p < 0.01) 12 and 24 months after TE.

**Conclusion** The TE is an effective method to reduce the IOD and the amount of IOP-lowering medication. Nevertheless, a significant further loss in RNFL thickness was observed in the first 12 months after TE. Thus, RNFL changes seem to stabilise only after a protracted period.

#### ZUSAMMENFASSUNG

**Hintergrund** Die Senkung des intraokularen Druckes (IOD) gilt als Hauptziel der Glaukomtherapie, um die zunehmende Apoptose retinaler Ganglienzellen zu verhindern. Die Trabekulektomie (TE) gilt als Goldstandard der chirurgischen Glaukomtherapie. Ziel dieser Studie war es, die postoperative Entwicklung der peripapillären retinalen Nervenfaserschichtdicke (englisch: Retinal Nerve Fiber Layer; RNFL) nach TE mittels optischer Kohärenztomografie (OCT) zu untersuchen.

**Material und Methoden** Es erfolgte eine retrospektive Analyse von 40 OP-naiven Augen, die eine TE aufgrund eines medikamentös nicht einstellbaren primären Offenwinkelglaukoms (POWG) erhielten. Innerhalb der ersten 24 Monate nach TE wurde der IOD, die Anzahl applizierter Antiglaukomatosa, der Visus, die statisch-automatische Perimetrie (SAP) und die peripapilläre RNFL-Dicke (gemessen mittels SD-OCT) bestimmt.

**Ergebnisse** Insgesamt wurden 40 Augen von 40 Patienten mittels TE behandelt. Neben der Reduktion des mittleren IOD von  $25,0\pm0,9$  auf  $13,9\pm0,6$  mmHg (p < 0,01), sank die mittlere Anzahl applizierter Antiglaukomatosa von  $3,3\pm0,2$ 

# Introduction

Glaucoma is an umbrella term for a widespread and very heterogeneous group of eye diseases which, in the worst case, can lead to blindness in one or both eyes if not adequately treated [1]. Intraocular pressure (IOP) that remains too high over a prolonged period – to be considered separately for each eye – leads to destruction of the retinal ganglion cells and their axons [2, 3]. In the later stages of the disease, this eventuates in the development and exacerbation of visual field defects, which are initially relative but later become absolute [4].

Various studies, some multicentric, have already demonstrated that lowering IOP can slow the progression of glaucoma [5, 6]. Often, medication is used as the primary strategy for lowering IOP; surgical intervention is only considered if the disease progresses in spite of the medication, if the patient cannot tolerate the medication, or if an adequate reduction in pressure cannot be achieved despite the use of medication. Trabeculectomy (TE), with or without intraoperative use of mitomycin C (MMC), has long been the gold standard for surgical lowering of IOP [7]. Important criteria for assessing the success of a TE procedure include the postoperative reduction in IOP, as well as a reduction in the use of antiglaucoma medications.

Glaucoma progression, with the development of a new scotoma or exacerbation of existing defects, is usually assessed by means of repeated visual field testing. Despite ongoing developments in perimetry methods, which make the tests quicker to perform and lead to earlier detection of defects caused by glaucoma, this is still an arduous examination for patients to undergo. Accordingly, perimetry results are under a subjective influence and often show strong fluctuations; this needs to be taken into account when assessing these results. Moreover, it is currently assumed that morphological progression (RNFL thinning) can precede functional progression (exacerbation of visual field defects); however, this cannot be definitively assessed [8,9].

Modern imaging techniques used to assess the optic disc and thickness of the peripapillary retinal nerve fiber layer (RNFL), such as optical coherence tomography (OCT), could provide an additional objective examination method for the assessment of disease progression [10, 11]. Taking into account the floor effect that occurs in advanced glaucoma, OCT examination of the peripapillary RNFL in the mild and moderate stages of glaucoma seems more likely to produce meaningful findings. auf 0,5 ± 0,2 (p < 0,01) nach 2 Jahren. Der Visus und der mittlere Defekt der SAP blieben stabil; die mittlere globale RNFL-Dicke nahm von 67,8 ± 2,9 auf 63,7 ± 2,9 (p < 0,01) und 63,4 ± 2,9  $\mu$ m (p < 0,01) 12 und 24 Monate nach TE ab.

**Schlussfolgerung** Trotz erfolgreicher postoperativer Senkung von IOD und Anzahl applizierter Antiglaukomatosa nahm die mittlere RNFL-Dicke vor allem während der ersten 12 Monate nach TE weiter statistisch signifikant ab. Die RNFL-Entwicklung nach operativer IOD-Senkung scheint sich erst mit einer gewissen Verzögerung nach TE zu stabilisieren.

Some individual studies on this topic have described a measurable decrease in RNFL after successful glaucoma surgery or druginduced pressure reduction; however, other working groups have been unable to confirm this observation [12 - 14]. The goal of this study was to investigate postoperative changes in the RNFL following TE, using OCT, over an average period of two years.

# Materials and Methods

In this monocentric study we performed a retrospective evaluation of 40 patients who underwent TE, performed by the same ophthalmic surgeon (JDU), at the Ophthalmology Clinic and Outpatient Clinic of the University of Leipzig between January 2017 and March 2019. The study was approved by the local ethics committee of the University of Leipzig Medical Center (209/18-ek) and complied at all times with the Declaration of Helsinki.

Inclusion criteria were the presence of POAG which could not be controlled by drug therapy, featuring optic disc excavation typical for glaucoma (pathological increase in cup-to-disc ratio of > 0.4, depending on the optic disc surface area, and definite thinning of the nerve fiber tissue visible at the edge of the optic disc), as well as a static automated perimetry (SAP) deviation typical of glaucoma. Cataract operations performed via corneal access did not represent an exclusion criterium, as in order to achieve the most successful outcome after TE, the conjunctiva should ideally not have been altered by previous surgery at the time of TE. Patients were excluded in all cases if they had a glaucoma entity other than POAG, had undergone previous glaucoma surgery, or were aged under 40. Patients with non-glaucomatous optic disc atrophy were also excluded.

In all cases, the indication for TE was determined during an outpatient consultation in which the full range of antiglaucoma treatment was applied. The decision-making criteria included demonstrable progression of visual field defects (> 2 dB per year, based on at least 3 visual field examinations per year), intolerance of antiglaucoma medication, decrease in RNFL thickness with corresponding increase in visual field defects (measured using OCT > 5  $\mu$ m/year), as well as an increase in IOP, measured by applanation tonometry, exceeding the target pressure determined individually for each eye and each patient.

Prior to the indication for TE being determined and in the context of follow-up appointments at 6, 12, and 24 months after the operation, the patients underwent a complete ophthalmological examination. This included an assessment of the antiglaucoma treatment, slit lamp microscopy examination of the anterior and posterior eye segments, and IOP measurement using Goldmann applanation tonometry (defined as the initial pressure value under complete IOP-lowering therapy; Haag-Streit, Köniz, Switzerland). In addition, best corrected visual acuity (BCVA) was measured using Snellen charts (converted into logMAR for better statistical analysis), and SAP (Twinfield 2, Oculus, Wetzlar, Germany; 24–2 test strategy, 55 target positions) and optic disc OCT (Spectralis, Heidelberg-Engineering, Heidelberg, Germany; ring scan 3.5 mm in diameter centered around the optic nerve, 100 repeat measurements). For further analysis, we used Garway-Heath sector analysis. Furthermore, prior to the operation, every patient underwent an iridocorneal angle examination using a Sussmann lens to confirm their diagnosis of POAG.

# Surgical Procedure

The individual surgical steps in the TE procedure, as performed by us, have already been set out in another publication [15]. In brief, TE is performed using a fornix-based technique with a  $4 \times 4$  mm scleral flap, with 2 to 4 nonresorbable flap sutures (Ethilon 10/0), and with readaptation of the conjunctiva using 4 simple interrupted sutures made from resorbable material (Vicryl 10/0). After making an incision in the conjunctiva, a  $3 \times 3$  mm sponge soaked in mitomycin C (0.2 mg/mL) for 2 minutes is applied in order to inhibit postoperative scarring. Depending on the postoperative IOP, bleb function, and the conjunctival configuration, a decision was made to perform either suturolysis or subconjunctival application of 5-fluorouracil (5-FU).

As standard after the operation, patients were treated with local antibiotics (gentamicin POS 5 mg/mL eye drops, Ursapharm, Saarbrücken, Germany) and cycloplegics (atropine POS 1% eye drops, Ursapharm, Saarbrücken, Germany) for 2 weeks. To minimize scarring, dexamethasone eye drops (Dexa EDO 1.3 mg/mL eye drops, Bausch + Lomb, Laval, Canada) were applied with tapering frequency over a period of eight weeks.

The surgical TE success was assessed according to the criteria published by the World Glaucoma Association (see also: Guidelines on Design & Reporting Glaucoma Trials https://wga.one/ wga/guidelines-on-design-reporting-glaucoma-trials). To achieve complete success, the reduction in IOP without additional application of IOP-lowering medication had to be greater than 20% compared to the initial pressures, and the IOP measurement had to be <21 mmHg (A), <18 mmHg (B), <15 mmHg (C), or <12 mmHg (D). Limited success was considered to be achieved if IOP-lowering medications were still used, but not in greater number than before the operation. If these criteria were not met, the operation was considered a failure.

The collected data were captured and analyzed using Excel (version 2007, Microsoft; Redmond, USA) and SPSS (IBM version 22.0; Chicago, Illinois, USA). Patient age, IOP, number of antiglaucoma medications used, visual acuity, average visual field abnormality, and RNFL thickness are reported as mean values with standard deviation. In the statistical analysis we used the Wilcoxon test, the Mann-Whitney U test, and the ANOVA analysis of variance test. In addition, the preoperative mean deviation (MD), the preoperative glaucoma stage, and the postoperative RNFL loss **Table 1** Preoperative characteristics of the patient cohort (n = 40).

Age (years)	69.9±1.5
Gender	♀: 23/♂ <sup>*</sup> : 17
Side	Right: 21; Left: 19
Diagnosis	POAG: 40
Visual acuity (logMAR)	$0.14 \pm 0.03$
IOP (mmHg)	25.0 ± 0.9
Number of IOP-lowering medications (n)	3.3 ± 0.2
Mean perimetry deviation at the time of operation (MD in dB)	8.5 ± 0.8
Global peripapillary RNFL thickness (um)	$67.8 \pm 2.9$

POAG: primary open-angle glaucoma; IOP: intraocular pressure; n: number; MD: mean deviation; dB: decibels; RNFL: retinal nerve fiber layer

were tested for correlations (Pearson test). A p-value of  $\leq$  0.05 was considered statistically significant.

# Results

This study included 40 eyes (21 right eyes and 19 left eyes) in 40 patients (23 women, 17 men) who had undergone TE + MMC due to a POAG which could not be controlled with medication. A complete postoperative follow-up assessment over a period of at least 24 months was performed for all 40 eyes. The preoperative characteristics of the patient group are presented in **Table 1**.

# IOP and Number of Antiglaucoma Medications

The mean IOP was reduced from a preoperative value of  $25.0 \pm 0.9$  mmHg to  $14.0 \pm 0.7$  mmHg at 12 months and  $13.9 \pm 0.6$  mmHg at 24 months after the operation; this corresponds to an IOP reduction of 44% or 45% with respect to the initial pressure value. The difference in IOP compared to the preoperative measured value was statistically significant in all cases (p < 0.01 at 12 months; p < 0.01 at 24 months). The lowest postoperative IOP value was 8 mmHg at 24 months after TE. After TE, the mean number of antiglaucoma medications applied was  $0.6 \pm 0.2$  at 12 months (p < 0.01 compared to baseline) and  $0.5 \pm 0.18$  at 24 months (p < 0.01 compared to baseline) (see **> Table 2** and **Fig. 1a** and **1b**).

# Visual Acuity, Perimetry

The mean visual acuity of the study population was  $0.14 \pm 0.03 \log$ MAR before the operation; after the operation, this value increased to  $0.17 \pm 0.03 \log$ MAR at 12 months and  $0.23 \pm 0.08 \log$ MAR at 24 months. Neither comparison with the initial preoperative values was statistically significant (p = 0.17 at 12 months; p = 0.24 at 24 months). Analysis of the preoperative visual field testing according to disease stage showed early deviation in 16 eyes (0 to – 6 dB), moderate deviation in 13 eyes (– 6 to – 12 dB), and advanced deviation in 11 eyes (>–12 dB). SAP



• Fig. 1 Changes in IOP (a) and use of antiglaucoma medications (b) over a period of 24 months following TE (n = 40).

showed a mean deviation of  $8.5 \pm 0.8$  dB prior to TE. In the postoperative follow-up, this value was  $8.0 \pm 0.8$  dB at 12 months and  $8.1 \pm 0.8$  dB at 24 months; again, the difference compared to initial preoperative values was not statistically significant (p = 0.45 at 12 months; p = 0.53 at 24 months, see **Table 2**). No cases of central visual field loss (wipe-out) were observed following the operation. In addition, we considered the possibility of a correlation between preoperative glaucoma stage and postoperative RNFL loss. Again, no statistically significant correlation was observed at any examination timepoint (6 months r = -0.24, p = 0.14; 12 months: r = -0.18, p = 0.26; 24 months: r = -0.26, p = 0.11). Furthermore, there was no evidence of a correlation between the preoperative MD value on SAP and the postoperative RNFL loss (6 months: r = -0.18, p = 0.27; 12 months: r = -0.16, p = 0.32; 24 months: r = -0.99, p = 0.22).

# Surgical Success Rates

Overall, the IOP-lowering effect of the trabeculotomy procedures performed can be described as good (see scatter plot in  $\triangleright$  Fig. 2). Among all of the eyes examined at 24 months after TE, the rate of complete success falling within category C (> 20% IOP reduction compared to initial pressure, no use of antiglaucoma medication, IOP < 15 mmHg) was 68%, and 40% for complete success in category D (> 20% IOP reduction compared to initial pressure, no use of antiglaucoma medication, IOP < 12 mmHg). The exact success rates are set out in  $\triangleright$  Table 3.

## Changes in RNFL over Time

Prior to TE, the mean global peripapillary RNFL thickness for the study population was  $67.8 \pm 2.9 \,\mu$ m. After the operation, this dropped to  $64.7 \pm 2.9 \,\mu$ m at 6 months, then remained virtually unchanged at the 12 and 24-month timepoints. The difference between the preoperative mean global RNFL thickness and values measured at 6, 12, and 24 months after the operation was statistically significant in all cases (6 months: p<0.01; 12 months:

p < 0.01; 24 month: p < 0.01; see ► **Table 2**). Individual changes in RNFL in all 40 operated eyes over a period of 24 months are presented in ► **Fig. 3**. The Garway-Heath sector analysis shows a significant decrease in RNFL thickness during the postoperative follow-up period in the nasal superior sector (p < 0.01 at 12 and 24 months), the temporal superior sector (12 months: p < 0.1; 24 months), the temporal superior sector (p < 0.01 at 12 and 24 month), and the nasal sector (12 months: p < 0.01; 24 months) , and the nasal sector (12 months: p = 0.01; 24 months: p < 0.01). The reduction in RNFL in the temporal sector was clearly smaller than the reduction in other sectors; the difference compared to the initial preoperative value was not statistically significant (12 months: p = 0.36; 24 months: p = 0.55). The difference in RNFL loss in the temporal sector compared to all five other sectors was not statistically significant (**> Fig. 4**).

Within the total study population, a mean RNFL loss of  $-3.5 \pm 1.3 \,\mu$ m was observed at 6 months after TE. We also considered the results according to the rate of surgical success achieved (at 24 months after TE). In each of the four subgroups in which complete surgical success was achieved, the mean RNFL loss was almost identical: a mean RNFL loss of  $-5.1 \pm 10.2 \,\mu$ m was observed in the category A–D subgroup (IOP <21 mmHg), and a mean value of  $-5.1 \pm 10.4 \,\mu$ m was observed in the category B–D subgroup (IOP <18 mmHg). In addition, the RNFL fell by  $-5.4 \pm 10.4 \,\mu$ m in the category C–D subgroup (IOP <15 mmHg), and by  $-3.75 \pm 10.4 \,\mu$ m in the category D subgroup (IOP <12 mmHg). A comparison between the four groups did not show any statistically significant difference; this is why no further individual comparisons between the groups have been reported (ANOVA: p = 0.63).

# Discussion

The results from this study, in particular the analysis of the postoperative OCT examinations, show that in the medium-term follow-up period after TE, there can be further insidious progression ► **Table 2** Postoperative changes in mean IOP, mean number of IOPlowering medications, mean visual acuity, mean deviation in static automatic perimetry, and mean global RNFL thickness during the first 24 months after TE (n = 40).

		TE	Comparison with baseline (Wilcoxon test) p-value
IOP (mmHg)	Baseline	25.0 ± 0.9	n/a
	6 months	14.1 ± 0.8	< 0.01
	12 months	14.0 ± 0.7	< 0.01
	24 months	13.9 ± 0.6	< 0.01
Anti- glaucoma drugs (n)	Baseline	3.3 ± 0.2	n/a
	6 months	$0.4 \pm 0.9$	< 0.01
	12 months	0.6 ± 0.2	< 0.01
	24 months	0.5 ± 0.2	< 0.01
Visual acuity (logMAR)	Baseline	$0.14 \pm 0.03$	n/a
	6 months	0.16 ± 0.03	0.19
	12 months	0.17 ± 0.03	0.17
	24 months	0.23 ± 0.08	0.24
MD (dB)	Baseline	8.5 ± 0.8	n/a
	6 months	7.9 ± 0.8	0.16
	12 months	$8.0 \pm 0.8$	0.45
	24 months	8.1 ± 0.8	0.53
Global	Baseline	67.8 ± 2.9	n/a
RNFL thickness (µm)	6 months	64.7 ± 2.9	< 0.01
	12 months	63.7 ± 2.9	< 0.01
	24 months	63.4 ± 2.9	< 0.01

TE: trabeculectomy; IOP: intraocular pressure; n: number; MD: mean deviation; dB: decibels, n/a: not applicable, RNFL: retinal nerve fiber layer,  $\mu$ m: micrometer

of glaucoma with a loss of nerve fiber tissue; however, this was not observed to have any relevance in terms of function. While this progression could be seen in the results from OCT examinations of the peripapillary RNFL, it was not reflected in the perimetry results.

TE has long been the gold standard for surgical treatment of glaucoma; this is due to it being a relatively simple technique, requiring no more than the average level of infrastructure, which can be utilized broadly to treat different glaucoma entities.

The efficacy of TE in achieving adequate reduction in IOP and in the number of required medications has been unequivocally demonstrated through a large number of studies, some multicentric in design, with long follow-up observation periods [16–18]. A large-scale, retrospective, multicentric study in Great Britain investigated 428 POAG patients who underwent TE. In the first 24 months after TE there was a significant reduction in IOP, from 23.0 ± 5.5 mmHg to 12.4 ± 4.0 mmHg, and in the number of anti-



▶ Fig. 2 Scatter plot comparing baseline IOP to IOP at 24 months after TE (n = 40).

**Table 3** Rates of complete or limited success at 24 months after trabeculectomy (n = 40).

Success rate	Complete (without addi- tional IOP- lowering medi- cations)	Limited (Antiglaucoma medication allowed if < pre- operative)
A (IOP < 21 mmHg)	70%	83%
B (IOP < 18 mmHg)	70%	80%
C (IOP < 15 mmHg)	68%	70%
D (IOP < 12 mmHg)	40%	40%

IOP: intraocular pressure

glaucoma medications applied, from  $2.5 \pm 0.9$  to  $0.1 \pm 0.4$ . Our results also showed a significant reduction in IOP (from  $25.0 \pm 0.9$  mmHg to  $13.9 \pm 0.6$  at 24 months after TE) and in the number of required eye drop treatments (from  $3.2 \pm 0.2$  to  $0.5 \pm 0.2$  at 24 months after TE).

Lowering IOP remains one of the main goals of glaucoma treatment, as IOP is a factor that can be influenced to positively affect the progression of the disease. Data published to date, which come in part from multicentric studies with large cohorts, have demonstrated this with the help of functional tests such as perimetry [19, 20]. It has even been observed in individual cases that a pronounced reduction in IOP can lead to improved visual field parameters [21].

Moreover, various studies have already demonstrated that a reduction in IOP can slow down but not completely prevent the progression of visual field defects. Junoy Montolio et al. investigated preoperative and postoperative SAP results in a cohort of 100 eyes treated with TE (n = 39) or with a Baerveldt glaucoma implant (n = 61). The study was able to show that at 1.5 years after the glaucoma operation, progression of visual field defects was slower compared to progression in patients who declined an operation [22]. Folgar et al. also demonstrated an insidious but clearly decelerated progression in visual field defects after filtration surgery in 206 eyes (MD increase of  $-0.86 \pm 0.8$  dB/year without surgery vs. MD increase of  $-0.49 \pm 0.9$  dB/year after surgery; p < 0.01) [23]. Our results also showed a slight decrease in MD of 0.4 dB during an observation period of two years following TE; however, there was no evidence of a statistically significant difference compared to the values at the time of the operation.

New developments in the field of retinal imaging have made it possible to visualize and measure the nerve fiber layer which represents the axons of the retinal ganglion cells in the region of the optic disc and the macula. To date, differing results for RNFL changes after surgery or drug-induced IOP-lowering have been published in the literature. This may be due to the heterogeneous nature of the patient cohorts, differing glaucoma entities, or the use of different surgical methods. Individual working groups have described a significant loss of RNFL at 12 months after TE [12, 13]. In a study of 60 patients over a period of 12 months following TE or Ahmed valve implantation, Kim et al. observed a significant loss of RNFL which correlated to higher initial preoperative IOP values (> 37 mmHg); however, this did not result in an increase in visual field defects [12]. Another study of 100 eyes demonstrated a significant mean decrease in global RNFL of  $-4.2 \pm 0.3 \,\mu$ m/year in the first year after TE [13]. This is comparable to our results, which show a mean decrease in RNFL of  $-4.7 \pm 1.5 \,\mu$ m/year at 12 months after TE. Conversely, other groups did not find any measurable difference in RNFL thickness at 6 to 12 months after IOP-lowering surgery [14, 24, 25].

Our data indicate that loss of global RNFL thickness slows down starting at 6 months after TE, and that no further loss was observed in the examinations performed at 12 and 24 months after the operation. It is possible that RNFL thickness measured by OCT



▶ Fig. 3 Presentation of individual changes in RNFL over a period of 24 months after TE (n = 40).

does not immediately reflect postoperative changes in IOP. A factor here may be cell dysfunction due to oxidative stress caused by high preoperative IOP, leading to death of the retinal ganglion cells through triggering of apoptosis. This is reflected in the further decrease in postoperative RNFL thickness within the first 6 months after TE; however, the exact timing of the RNFL loss cannot be defined. It is likely that a postoperative reduction in IOP is not able to stop a cell death cascade that has already been triggered; this is why the global RNFL initially continues to decrease after TE, but then remains almost constant from 6 months after the operation. For this reason, it seems that results from RNFL measurements only become significant for treatment decisions after the first year following surgery. Despite this, the floor effect





should also be taken into account when assessing RNFL thickness [26, 27]. This refers to the fact that once the measured global RNFL thickness reaches a value of < 50  $\mu$ m, it is no longer possible to determine a further decrease with any certainty. In our patient cohort, seven patients (17.5%) had a global RNFL thickness < 50  $\mu$ m at the start of the follow-up period. If the data from these eyes are excluded from the analyses, the results still show a mean loss of global RNFL thickness of  $-3.8 \pm 12.1 \,\mu$ m over a period of 24 months after TE. In addition, the Garway-Heath sector analysis showed a significant postoperative decrease in RNFL thickness in all sectors except for the temporal sector.

In our study we included a homogenous group of 40 POAG patients, who underwent regular follow-up examinations over a period of 2 years after TE. With the exception of cataract operations, all eyes were surgically naive at the time of TE. Cataract operations performed via corneal access were the only exceptions to this, because in order to achieve the most successful outcome after TE, the conjunctiva should ideally not have been altered by previous surgery at the time of TE. We would also like to emphasize the long follow-up period of 2 years, as well as the use of spectral domain OCT when enabled objective and reproducible examination results. In the context of our study, it appears that RNFL values do not stabilize until 6 months after TE. The significance of our results is limited by the monocentric, retrospective study design and the high variability of "subjective" visual field testing. In addition, the assessment of RNFL based on OCT can be limited by artefacts, suboptimal examination conditions, software errors, or myopia. However, in our study we endeavored to ensure that the OCT scans were free of artifacts to the extent possible through visual checks performed by the examiner and by averaging the scans. Also, we did not record possible systemic diseases that may have been present in our study population; this means we cannot exclude their influence on RNFL values. In particular, we did not collect any data relating to diabetes mellitus or neurodegenerative disease which can lead to RNFL thinning.

In order to better assess the course of persisting RNFL loss during the first postoperative year, it would be desirable to perform a study with as large a cohort as possible and with more frequent OCT examinations.

## **CONCLUSION BOX**

- For many years now, IOP and perimetry have been important components in the assessment of glaucoma progression. In recent years, however, we have seen the development of supplementary imaging techniques, such as optical coherence tomography (OCT), which make it possible to better visualize and quantify the thickness of the peripapillary retinal nerve fiber layer (RNFL).
- The goal of this study was to observe RNFL thickness using OCT for a period of 24 months following TE.
- Despite a successful reduction in IOP and in the number of antiglaucoma medications applied, the mean global RNFL thickness decreased during the first 6 months after surgery.

 Only after this period did the mean RNFL appear to stabilize, and then remained virtually constant up to 24 months after TE. For this reason, it seems that results from RNFL measurements only become significant for treatment decisions after the first year following surgery.

# Conflict of Interest

Focke Ziemssen has received fees from Biogen, Abbvie/Allergan, Alimera, Bayer Healthcare, Roche/Genentech, Acelyrin, Clearside, Kodiak, Sandoz, Apellis, Boehringer Ingelheim, Oxurion, Novartis, NovoNordisk, MSD Sharp & Dohme, Sanofi and Stada. There are no relevant potential conflicts in connection with the study.

#### References

- Flaxman SR, Bourne RRA, Resnikoff S et al. Global causes of blindness and distance vision impairment 1990–2020: a systematic review and meta-analysis. Lancet Glob Health 2017; 12: e1221–e1234
- [2] Leske MC, Connell AM, Wu SY et al. Risk factors for open-angle glaucoma. The Barbados Eye Study. Arch Ophthalmol 1995; 113: 918–924
- [3] Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. JAMA 2014; 311: 1901–1911
- [4] Quigley HA. Ganglion cell death in glaucoma: pathology recapitulates ontogeny. Aust N Z J Ophthalmol 1995; 23: 85–91
- [5] Heijl A, Leske MC, Bengtsson B et al. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. Arch Ophthalmol 2002; 120: 1268–1279
- [6] Leske MC, Heijl A, Hussein M et al. Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial. Arch Ophthalmol 2003; 121: 48–56
- [7] Razeghinejad MR, Spaeth GL. A history of the surgical management of glaucoma. Optom Vis Sci 2011; 88: E39–E47
- [8] Mahmoudinezhad G, Moghimi S, Nishida T et al. Association Between Rate of Ganglion Cell Complex Thinning and Rate of Central Visual Field Loss. JAMA Ophthalmol 2023; 141: 33–39
- [9] Zhang X, Dastiridou A, Francis BA et al. Advanced Imaging for Glaucoma Study Group. Comparison of Glaucoma Progression Detection by Optical Coherence Tomography and Visual Field. Am J Ophthalmol 2017; 184: 63–74
- [10] Jeoung JW, Choi YJ, Park KH et al. Macular ganglion cell imaging study: glaucoma diagnostic accuracy of spectral-domain optical coherence tomography. Invest Ophthalmol Vis Sci 2013; 54: 4422–4429
- [11] Hood DC. Improving our understanding, and detection, of glaucomatous damage: An approach based upon optical coherence tomography (OCT). Prog Retin Eye Res 2017; 57: 46–75
- [12] Kim WJ, Kim KN, Sung JY et al. Relationship between preoperative high intraocular pressure and retinal nerve fibre layer thinning after glaucoma surgery. Sci Rep 2019; 9: 13901
- [13] Chua J, Kadziauskiene A, Wong D et al. One year structural and functional glaucoma progression after trabeculectomy. Sci Rep 2020; 10: 2808
- [14] Waisbourd M, Ahmed OM, Molineaux J et al. Reversible structural and functional changes after intraocular pressure reduction in patients with glaucoma. Graefes Arch Clin Exp Ophthalmol 2016; 254: 1159–1166
- [15] Theilig T, Rehak M, Busch C et al. Comparing the efficacy of trabeculectomy and XEN gel microstent implantation for the treatment of primary open-angle glaucoma: a retrospective monocentric comparative cohort study. Sci Rep 2020; 10: 19337

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- [16] Fontana H, Nouri-Mahdavi K, Caprioli J. Trabeculectomy with mitomycin C in pseudophakic patients with open-angle glaucoma: outcomes and risk factors for failure. Am J Ophthalmol 2006; 141: 652–659
- [17] Kirwan JF, Lockwood AJ, Shah P et al. Trabeculectomy in the 21st century: a multicenter analysis. Ophthalmology 2013; 120: 2532–2539
- [18] Edmunds B, Thompson JR, Salmon JF et al. The National Survey of Trabeculectomy. II. Variations in operative technique and outcome. Eye (Lond) 2001; 15: 441–448
- [19] [Anonymous]. The Advanced Glaucoma Intervention Study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration. The AGIS Investigators. Am J Ophthalmol 2000; 130: 429– 440
- [20] Leske MC, Heijl A, Hyman L et al. Factors for progression and glaucoma treatment: the Early Manifest Glaucoma Trial. Curr Opin Ophthalmol 2004; 15: 102–106
- [21] Unterlauft JD. [Secondary Neuroprotection in Glaucoma by Reduction of Intraocular Pressure]. Klin Monbl Augenheilkd 2019; 237: 150–157

- [22] Junoy Montolio FG, Muskens R, Jansonius NM. Influence of glaucoma surgery on visual function: a clinical cohort study and meta-analysis. Acta Ophthalmol 2019; 97: 193–199
- [23] Folgar FA, De Moraes CG, Teng CC et al. Effect of successful and partly successful filtering surgery on the velocity of glaucomatous visual field progression. J Glaucoma 2012; 21: 615–618
- [24] Sanchez FG, Sanders DS, Moon JJ et al. Effect of Trabeculectomy on OCT Measurements of the Optic Nerve Head Neuroretinal Rim Tissue. Ophthalmol Glaucoma 2020; 3: 32–39
- [25] Gietzelt C, von Goscinski C, Lemke J et al. Dynamics of structural reversal in Bruch's membrane opening-based morphometrics after glaucoma drainage device surgery. Graefes Arch Clin Exp Ophthalmol 2020; 258: 1227–1236
- [26] Mwanza JC, Budenz DL, Warren JL et al. Retinal nerve fibre layer thickness floor and corresponding functional loss in glaucoma. Br J Ophthalmol 2015; 99: 732–737
- [27] Mwanza JC, Kim HY, Budenz DL et al. Residual and Dynamic Range of Retinal Nerve Fiber Layer Thickness in Glaucoma: Comparison of Three OCT Platforms. Invest Ophthalmol Vis Sci 2015; 56: 6344–6351