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NON-PENETRATING INTRACANALICULAR PARTIAL TRABECULECTOMY VIA THE OSTIA OF SCHLEMM'S CANAL

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Abbreviations, notations and non-systemic units

- AG – Aktiengesellschaft (germ.),
- e.g. – example given, for example,
- DSCI – deep sclerectomy with collagen implant,
- Fig. – figure,
- IOP – intraocular pressure,
- MS – Microsoft,
- MTMT – maximal tolerated medical therapy,
- NPIT – non-penetrating intracanalicular partial trabeculectomy via the ostia of Schlemm's canal,
- NPDS – non-penetrating deep sclerectomy,
- NPGS – non-penetrating glaucoma surgery,
- POAG - primary open-angle glaucoma,
- SC – Schlemm's canal,
- SPSS – Statistical Analysis in Social Science, a computer program used for statistical analysis,
- TM – trabecular meshwork,
- YAG – Yttrium aluminium garnet laser.

Fundamental non SI units

Length

- **µm** – micrometer. 1 micrometer (micron) = 10^{-6} m
- **mm** – millimeter. 1 millimeter = 10^{-3} m

Others

- **mmHg** – millimetres of mercury – non-systemic pressure unit. 1mmHg = 133,22 Pa
- **µl/min** – flow rate. 1 µl/min=$1,67*10^{-10}$ m^3/s
- **µl/min/mmHg** – rate of the outflow facility. 1 µl/min/mmHg=$1,25*10^{-12}$ $m^3/s/Pa$

Contents

1 Introduction

Trabeculectomy is nowadays a routine procedure whenever incisional glaucoma surgery is indicated. It represents the gold standard with which all other procedures are compared [56, 83]. Trabeculectomy is associated with complications even if a stable IOP decrease and visual field maintenance can be achieved [10]. Complications include persistent hypotony, maculopathy, hyphema, increased cataract formation, bleb failure and late endophthalmitis.

Attempts to make the procedure safer have been made by employing different means to recreate the natural outflow path instead of fashioning a fistula with its inherent problems of too much or too little outflow. Trabeculotomy has been advocated with various success rates for that purpose [84]. Non-penetrating glaucoma surgery (NPGS) was introduced more than 20 years ago [25, 38, 86, 87] increasing in popularity over the last years. The relatively low rate of intraoperative as well as of postoperative complications represents the main advantage of this type of glaucoma surgery. NPGS has been proven to be a safer technique than other available types of glaucoma surgery including trabeculectomy [11, 47, 50, 66, 67]. The tissue sparing character of this surgical procedure allows for the quick recovery of eye functions as well as for establishing of a more natural persistent postoperative aqueous outflow without a marked filtering bleb even years after surgery [11].

The main claimed disadvantages of NPGS include a limited hypotensive effect [19, 43], which sometimes requires postoperative laser goniopuncture [49, 67], and the relative complexity of the NPGS technique for a surgeon with its long learning curve comparing to trabeculectomy[66].

The classic non-penentrating deep sclerectomy (NPDS) technique is improved. The new non-penetrating intracanalicular partial trabeculectomy via the ostia of Schlemm's canal

(NPIT), which I present here, is developed in order to overcome these two main disadvantages. The filtration zone is extended compared to the classic non-penetrating surgery. This is archived due to the additional removal of the inner wall of Schlemm's canal and the adjacent trabecular tissue, accessed through the ostia of Schlemm's canal (SC). The ostia are the cut ends of the canal as exposed through intraoperative dissection. Two surgical instruments were developed in order to standardize the surgical technique and to help a surgeon to improve the outcome.

2 Background

2.1 Anatomy of the drainage system

In the healthy eye flow of aqueous humor against resistance generates intraocular pressure (IOP) of approximately 15 mmHg, which is necessary for proper shape and optical properties of the eye globe [26]. The circulating aqueous humor nourishes the cornea and the lens. These structures must be transparent and therefore devoid of blood vessels. Additionally trabecular meshwork is nourished by the aqueous humor. The aqueous humor itself is transparent and colorless medium with a refractive index of 1,33. It constitutes an important component of the eye optical system between the cornea and the lens [53].

2.1.1 Formation of aqueous humor

Aqueous is derived from plasma within the capillary network of the ciliary processes by three mechanisms:

- Diffusion - lipid-soluble substances are transported through the lipid portions of the cell membrane proportional to a concentration gradient across the membrane.
- Ultrafiltration - water and water-soluble substances, limited by size and charge, flow through theoretical micropores in the cell membrane in response to an osmotic gradient or hydrostatic pressure; influenced by intraocular pressure, blood pressure in the ciliary capillaries, and plasma oncotic pressure.
- Active transport (secretion), accounting for the majority of aqueous production - water-soluble substances of larger size or greater charge are actively transported across the cell membrane, requiring the expenditure of energy; Na-K ATPase and glycolytic enzymes are present in nonpigmented epithelial cells.

Rate of aqueous humor formation: 2,0 – 3,0 µl/min. With the volume of the anterior chamber amounting to 250 µl and the volume of posterior chamber amounting to 60 µl, the turnover of the complete aqueous volume occurs in 1,5 - 2 hours. Aqueous humor formation decreases with sleep (suppression of ~20%), advancing age (decrease of 2% per decade), uveitis, retinal and ciliochoroidal detachment.

2.1.2 Aqueous humor outflow

Aqueous outflow occurs into several pathways (Fig. 1). The so-called conventional outflow pathway that conveys aqueous humor from within the anterior chamber outwards consists of trabecular meshwork, Schlemm's canal, collector channels, intrascleral venous plexus, aqueous veins, episcleral and conjunctival veins [1]. This outflow pathway accounts for 83-96% of the whole aqueous outflow. The uveoscleral outflow pathway first described by Bill [5, 6] is an accessory system which drains 5-15% of aqueous humor. This pathway allows free access from the anterior chamber to the supraciliary and suprachrooidal spaces via the collagen containing spaces between the ciliary-muscle-bundles. From there the fluid egresses the sclera and uveal vascular system. In addition there exists the transscleral outflow, which is a less known drainage route [2].

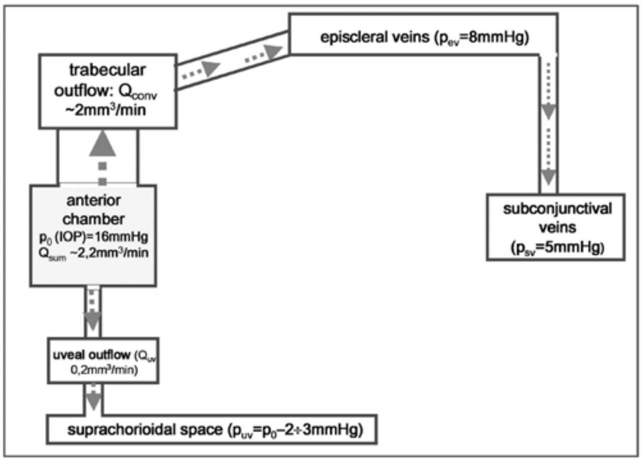

Fig. 1. Block-scheme of aqueous outflow in the non-operated human eye [37].

2.1.3 Conventional outflow system and trabecular meshwork

From the anterior chamber the aqueous is drained trough the trabecular meshwork, a sieve-like band of connective tissue about 750 μm in width [22]. The thickness of the trabecular meshwork in glaucomatous eyes ranges between 50-70 μm in the anterior region and between 100-130 μm for the posterior portion [18]. The trabecular meshwork consists of three main layers: the uveal meshwork, the corneoscleral meshwork and the juxtacanalicular meshwork also called endothelial or cribriform meshwork (Fig. 2).

Uveal meshwork - adjacent to the aqueous in the anterior chamber; formed of trabecular bands with irregular 25 - 75 µm openings extending from the iris root and ciliary body to Schwalbe's line [1, 55]. Each trabecular band or sheet in the uveal and corneoscleral meshwork is composed of a connective tissue core surrounded by elastic fibers, a glass membrane, and trabecular endothelium.

Corneoscleral meshwork - sheets of trabecular meshwork with elliptical openings ranging from 5 – 50 µm in diameter extending from the scleral spur to the anterior scleral sulcus [1, 55]. Juxtacanalicular connective tissue - outermost portion of trabecular meshwork composed of a connective tissue core lined on either side by endothelium. Outer endothelial layer is continuous with the inner wall of Schlemm's canal and may be the site accounting for the major resistance to aqueous outflow. A transcellular aqueous transport system consisting of pores and giant vacuoles may provide communication with Schlemm's canal.

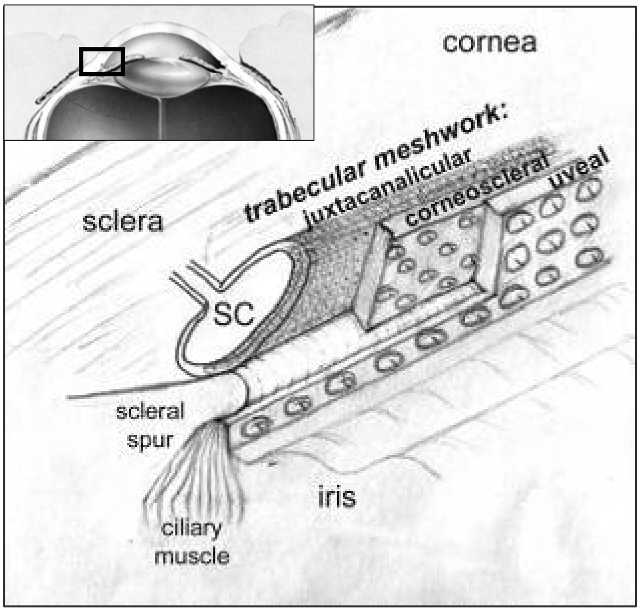

Fig. 2. Scheme of the anatomy of the anterior chamber angle.

Aqueous subsequently flows distally to Schlemm's canal (SC) - an endothelial-lined channel averaging 36-40 mm in length and 190-370 µm in diameter first described by Schlemm in 1830. The SC lumen is either elongated, oval, or triangular and sometimes is crossed by septa. Schlemm's canal has a vessel-like structure limited by a layer of endothelial cells with a bulging nucleus in the lumen. The inner wall of SC is characterised by the presence of giant vacuoles in the endothelial cells. These vacuoles contain aqueous humor and sometimes erythrocytes. In some cases vacuoles have apical openings that may connect trabecular meshwork with SC lumen, providing a transcellular channel [79]. It has been shown that the process of vacuole formation is pressure dependent [32, 78]: the number and the size of the vacuoles depend on IOP. There are many vacuoles at high IOP and few at low IOP [1]. The outer wall of SC consists of endothelial cells attached one to another by zonulae occludens laying on a basal lamina more dense than the one of the SC inner wall [23, 71]. SC is surrounded by a pericanalicular connective tissue.

From Schlemm's canal aqueous egresses into intrascleral collector channels - direct and indirect systems including aqueous veins of Ascher. The internal collector channels first described by Sondermann in 1933, are simple digitations of the SC inner wall without connection with the anterior chamber [1].

The external collector channels first described by Ascher in 1942, arise from the outer wall of SC and are limited by the same endothelium lining surrounded by a fine connective tissue in a complex system of 25-30 vessels running in two directions. The vessels (up to 8) that reach the episcleral plexus directly are called aqueous veins. Aqueous veins are thick and terminate in episcleral and conjunctival veins in a laminated junction called the laminated vein of Goldmann. The other outflow system consists of thinner vessels that drain indirectly into three staged venous plexuses: the deep and mid-scleral plexus, both constituting the intrascleral plexus, and the episcleral plexus (episcleral veins). The latter receives blood from the conjunctival veins of the perilimbal conjunctiva and drains into the cavernous sinus via the anterior ciliary and superior ophthalmic veins. Conjunctival veins drain to palpebral and angular veins and then into superior ophthalmic or facial veins [79].

2.1.4 Aqueous outflow resistance

The increased IOP in glaucoma is caused by an increase in aqueous outflow resistance within the drainage pathways, not by excess production of aqueous humor. The mechanism by which outflow resistance is generated in the normal eye and is increased in the glaucomatous eye is still not understood [31]. Aqueous humor passes from the anterior chamber through the outflow pathway as a bulk flow driven by a pressure gradient. This flow is neither affected by methabolic poisons [4] nor by temperature [80] and therefore the outflow system does not involve active transport [31]. There is consensus nowadays that the site of outflow resistance in the normal eye resides near or within the inner wall of Schlemm's canal. However there is no such consensus about the localisation of the increased outflow resistance in POAG. A valuable review on this topic by Johnson and Johnson [31] indicate that trabecular meshwork is the site of abnormally increased outflow resistance in POAG, though histological examinations of the trabecular meshwork does not show specific abnormalities or ultrastructural changes, that could account for the abnormal IOP elevation [44, 60].

2.2 Non penetrating glaucoma surgery

2.2.1 History of filtration glaucoma surgery

Surgical procedures to lower IOP were first developed in the middle of XIX century. The role of the filtering bleb in successful surgery for POAG was not initially recognized.

DeWecker introduced in 1869 an anterior sclerotomy, which was considered to be successful only if filtration continued postoperatively.

Elliot proposed limbal trepanation in 1909, a so-called full-thickness procedure which used to be the most popular glaucoma filtration surgery until 1940s. Later this surgery was rejected because the very thin conjunctival bleb predisposed to postoperative endophthalmitis.

Preziosi developed in 1924 thermal cautery of the scleral wound edges with entry into anterior chamber. Scheie modified this operation to thermal sclerostomy and posterior lip sclerectomy. Both these procedures rapidly became the most widely used operations.

However the following frequent complications were unavoidable: flat anterior chambers, choroidal detachments, postoperative cataract formation, bleb leaks and endopthalmitis.

In order to avoid those complications guarded filtration procedures were developed. In 1961 Sugar proposed trabeculectomy under a scleral flap (Fig. 3) [73]: a section of the trabecular meshwork and SC was removed with a punch forceps followed by a peripheral iridectomy and tight suturing of the scleral flap. All cases failed.

In 1968 Cairns reported first successful application of microsurgical techniques to perform a trabeculectomy under a scleral flap [9]. This procedure excised the length of SC, adjacent trabecular meshwork, the tip of the scleral spur as well as deep layers of the cornea. After iridectomy the scleral flap was hinged either posteriorly in the sclera or anteriorly at the limbus and sutured firmly. From 300 reported cases 6 showed a flat anterior chamber, in 5 cases moderate uveitis was present. In 80 from 300 cases reviewed by Cairns after 4 years follow up IOP was controlled in 97,8% cases, 30 % had no drainage bleb, but only 2,5% needed medical therapy. The incidence of endophthalmitis was significantly reduced with the introduction of trabeculectomy, although the surgery had high rates of failure in neovascular glaucoma, uveitis and in cases of previous surgery.

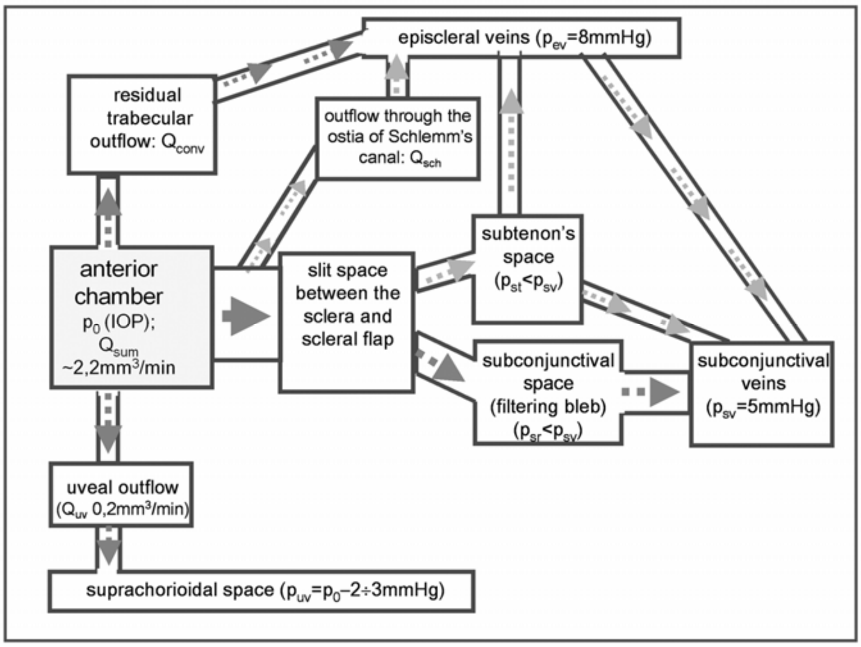

Fig. 3. Block-scheme of aqueous outflow after trabeculectomy [37] is commented further in the text.

Nevertheless trabeculectomy became the procedure of choice in glaucoma surgery for the past 40 years. Modification of this technique including laser suture lysis and releasable flap sutures allowed even finer control of postoperative filtration.

In 1969 Harms and Dannheim [14, 30] described trabeculotomy with a 60% rate for controlling IOP. This procedure was initially designed to increase outflow facility, not to be a filtering procedure. 12% of 300 cases developed a filtering bleb and in 8% of cases a big hyphema required anterior chamber washout.

Since trabeculectomy is the gold standard against which other procedures are compared the long-term follow up results of trabeculectomy are reviewed in the following table:

Table 1. Long-term results of trabeculectomy

Number of eyes	follow -up. yr	Criteria of successful surgery	Success	Citation
150	10 (1-20)	Final IOP<20 mmHg	90%; visual fields stable or improved in 41%	[83]
40	15	Init. successful trabeculectomy at 1 yr: IOP<21mmHg or a drop of at least 33% if IOP<21mmHg	success of IOP control: 83% at 1 year 73% at 10 years 42% at 15 years	[85]
78	1-9	Probability of single operation giving successful IOP control	48% at 3 years 40% at 5 years	[58]
700	3-12	IOP<21mmHg, through the study period, no evid. of progressive disk or VF deterioration, no VA drop no addit. Glaucoma surgery	44%	[33]
289	15	IOP≤21mmHg,	87% at 10 years 85% at 15 years 93% at 5 years	[54]
		Retaining VA greater than 20/400 and >5° radius of VA	60% at 15 years	
86 (mostly trabeculectomy)	10	Probability of blindness (resultant target IOP: 14 mmHg in getting blind and 15,4 mmHg in preserved VA)	46% at 10 years	[59]

2.2.2 History of non-penetrating filtration glaucoma surgery

In 1962 Krasnov introduced sinusotomy (externalisation of Schlemm's canal) following the assumption that the site of obstruction to outflow is situated intrasclerally beyond the outer wall of Schlemm's canal (Fig. 4A) [39, 40]. He supposed that if the the outer wall is opened leaving the inner wall intact, the IOP should be reduced. 340 cases were described by Krasnov with a follow up of 1-5 years and IOP normalization in 83% of cases. A sustained IOP reduction after sinusotomy was usually associated with visible subconjunctival filtration. Sinusotomy by Krasnov represents a safe non-penetrating filtering surgery with the trabecular meshwork and the inner wall of SC being left in place. Sinusotomy was definitely safer than full thickness procedures that were the standard filtering surgery at that time. However, sinusotomy never become popular, because it was a difficult operation, it needed a surgical microscope to find SC [51]. Additional surgical results were not convincing and were not confirmed by other researchers.

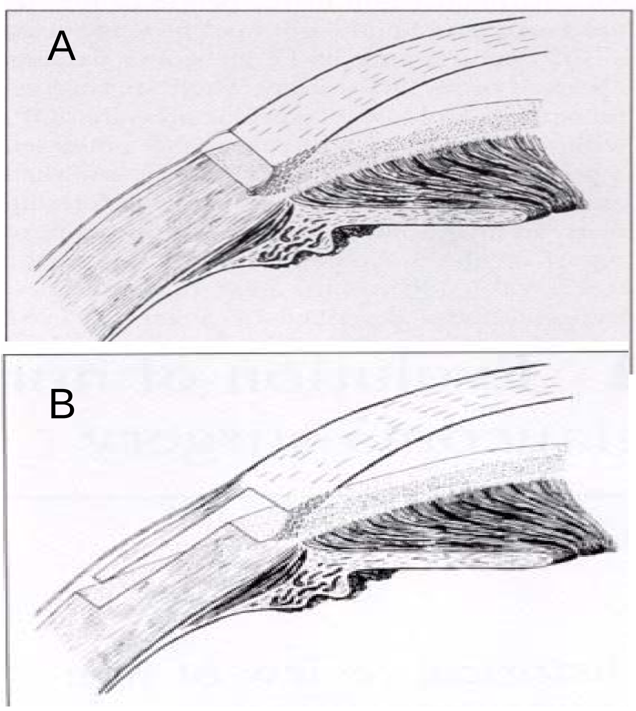

Fig. 4. Schematic representation of ***sinusotomy*** by Krasnov (**A**): SC is unroofed, no superficial flap covering the sclerostomy. SC inner wall is untouched. Schematic representation of ***trabeculectomy ab externo*** (**B**): sclerectomy unroofing SC is covered by superficial scleral flap. SC inner wall and juxtacanalicular TM are removed. Modified from [51]

Nevertheless several techniques of non-penetrating filtering surgery are based on sinusotomy. With recognition of juxtacanalicular meshwork and inner wall of SC being the site of major resistance to outflow [7] new procedures were designed to selectively remove tissue leaving a thin trabeculo-descemet membrane intact.

Already in 1959 Epstein reported for the first time filtration through deep layers of the sclera and the cornea adjacent to the trabecular meshwork after resection of pterygium [20]. Later he developed on this basis the technique of a perilimbal deep sclerectomy for the treatment of glaucoma.

Ab externo trabeculectomy was proposed by De Laage de Meux and Kantelip in 1976 [17] and later in 1984 by Zimmermann et al [86, 87], in 1991 by Arenas [3] and in 1993 by Tanihara et al. [74]. This technique is similar to sinusotomy except for the presence of a superficial scleral flap and the removal of the juxtacanalicular layer of TM and the inner wall of SC. (Fig. 4B). Valtot showed in an unpublished report (cited by [51]) that the tissues removed in trabeculectomy ab externo corresponded to the endothelium of SC and the juxtacanalicular TM. Roy examined a large series of excised fragments by transmission and electronic microscopy and confirmed these results by Valtot (unpublished work cited by [51]). The outflow facility of the remaining membrane after the trabeculectomy ab externo was studied by Rossier et al. [61] in enucleated human eyes. It increased from 0,21±0,6 to 2,03±1,43 µl/min/mmHg after the removal of 4 mm membrane consisting of the endothelium of SC and the juxtacanalicular TM.

Arenas reported a postoperative success rate of 88% of the trabeculectomy ab externo [3]. Other investigators who have used similar techniques reported statisfactorily controlled IOP in 85,8% to 90% of patients [74, 76]. Long term results have not yet been published except the work by Tanihara et al. [75], who reported “at least 1 year follow-up” of this surgery with 90% of well-controlled (IOP<21mmHg) and 81,7% of “overall success” (stabilisation of IOP, visual field and optic nerve status).

Another method to improve the aqueous outflow is to remove the corneal stroma behind the anterior trabeculum and Descemet’s membrane (Fig. 5). This surgical technique was first described by Fyodorov et al. [24, 25] and Kozlov et al. [38].

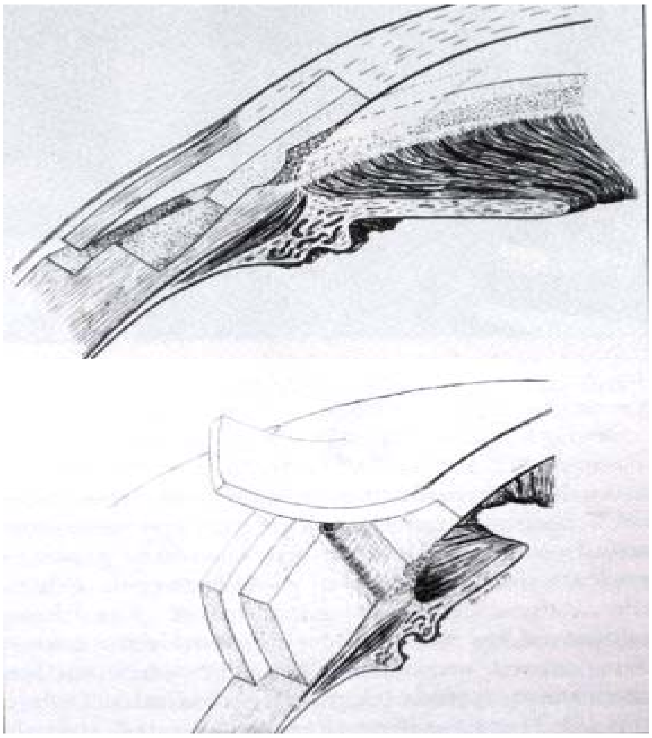

Fig. 5. Schematic representation of ***non-penetrating deep sclerectomy***. Deep corneosclerectomy is performed under superficial scleral flap. Corneal tissue is removed behind anterior TM and Descemet's membrane. Modified from [51]

The main outflow in this operation occurs at the level of the anterior TM and Descemet's membrane. In an ex-vivo model by Vaudaux et al. [81] the mean outflow facility increased from 0,19±0,03 to 24,5±12,6 μl/min/mmHg after deep sclerectomy. It was then ten times higher compared with the mentioned above results of the same experiment by Rossier et al. performed in trabeculectomy ab externo [61].

2.2.3 Surgical technique of NPDS

Standard NPDS technique in the description by Mermoud et al. [50, 51] consists of the following procedures:

The conjunctiva is opened either at the fornix or at the limbus. A 5x5 mm superficial scleral flap is made, which includes approximately one third (300 μm) of the scleral thickness. In order to reach Descemet's membrane in the dissection, the superficial scleral flap has to be cut 1-1,5 mm anteriorly into the clear cornea (Fig. 5). A second deep scleral flap measuring 4x4 mm is dissected leaving about 10% of the sclera over the choroids and the ciliary body. The horizontal dissection is started posteriorly moving anteriorly with a crescent blade. Near the limbus SC is thereby automatically unroofed.

The dissection is continued anteriorly with a blunt spatula or a sponge to find the natural cleavage plan between Descemet's membrane and the corneal stroma. The former is

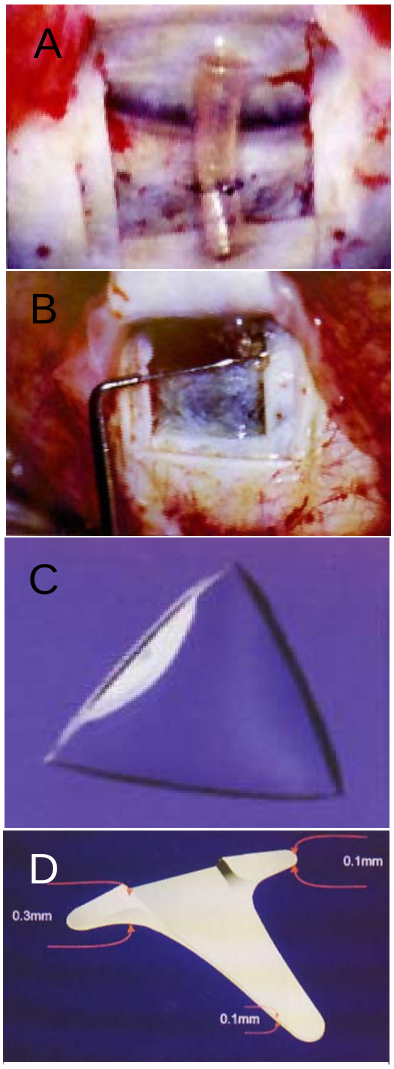

Fig. 6. Implants for non-penetrating glaucoma surgery: membrane. **A:** collagen implant Aquaflow; **B:** high viscosity hyaluronic acid implant used in viscocanalostomy. **C:** SK gel 3.5 implant. **D:** T-flux implant. From [62]

exposed for 1 mm and the second scleral flap is excised. At this stage the aqueous is seen percolating through the anterior trabeculum and Descemet's membrane. To keep the intrascleral space (scleral lake, Fig. 5, upper panel) an implant might be used. Kozlov et al. proposed a collagen implant which is resorbable within 6-9 months [38] (a later analogue: Aquaflow, Staar Surgical AG, Nidau, Switzerland, as shown in Fig. 6A). Stegmann et al. use high viscosity hyaluronic acid (Healon GV, Pharmacia, Upsalla, Sweden) [72] (Fig. 6B). Sourdille used reticulated hyaluronic acid [70] (SK gel implant, Corneal, Paris, France). Dahan introduced a non-absorbable Hema implant (T-flux, IOLtech, LaRochelle, France) [13, 12] (Fig. 6C,D).

2.2.4 **Modifications of the classic NPDS technique**

In 1984 March et al. reported successful experimental use of YAG laser to produce a corneoscleral perforation in human cadaver eyes [45]. Later on this approach has been applied by surgeons in NPDS [34, 82].

In 1989 Hara et al. proposed Nd:YAG goniopuncture as an adjunctive to non-penetrating glaucoma surgery [29]. This approach has been extensively used long-term after deep sclerectomy in order to improve long-term results of this procedure [38, 49, 64]. Goniopuncture is performed shortly after NPDS if there is insufficient percolation of aqueous humor at the trabeculo-Descemet's membrane, probably due to the lack of surgical dissection

[65]. Some glaucoma surgeons nowadays consider NPDS as a two-stage procedure with a second stage represented by Nd:YAG goniopuncture, which converts the whole procedure into trabeculotomy ab interno [29]

In 1990 Traverso et al. reported the first application of an eximer laser in NPGS [77].

In the early 1990s Stegmann introduced viscocanalostomy [72]. This technique represents trabeculectomie ab externo with presumable extension of the aqueous filtration to a part of SC adjacent to the surgically created intrascleral space. Those parts of SC are expanded with viscoelastic substance (Healon GV, Pharmacia, Upsalla, Sweden) through its ostia during the operation. Viscocanalostomy aims to restore the natural outflow pathway by allowing the aqueous to leave the eye through SC and collector channels.

In 2005 Stegmann proposed a modification of the NPGS named canaloplasty [28, 27]. A suture is introduced inside SC along its whole length using a special catheter. By pulling the suture intraoperatively the inner wall of SC becomes more permeable in its whole length thus providing IOP lowering and increased aqueous outflow through the natural outflow pathways.

2.2.5 Long term results and outflow mechanisms of NPDS

Table 2. Long-term results of NPDS

N of eyes	follow -up. yr	Criteria of successful surgery	Success	IOP preop, mmHg	IOP after yrs of the follow-up	Complications	Ref
22 EXG	4,04 ±1,02	Complete succ.: IOP ≤18mmHg without medic.	54,5%	29,9±8,1	13,2±3,2	7 eyes cataract progression, 4 eyes, 5FU injection	[48]
		Qualified succ.: IOP≤18mmHg, with or without medic.	90,9%				
14 (Erb. YAG-laser DS)	4,02 ±0,56	Complete succ.: IOP ≤21mmHg + IOPreduct ≥ 20% without medic.	50,5%	37,7±10,5	17,6±8,7	Single case of anterior-chamber penetration, requiring iridectomy	[35]
		IOP ≤21mmHg + IOPreduct ≥ 20% with or without medic.	78,6%				

258	4,53 ±1,42	Complete succ.: IOP ≤21mmHg + without medic.	66,5%	24,5±5,9	15,8± 3,8	Perop. micro-perforations in 27 eyes, shallow AC in 2 eyes, hyphema in 2 eyes, cataract in 5 eyes, dellen in 1 eye	[41]
		Qualified succ.: IOP ≤21mmHg with medical or new surg. treatment	80,3%				
105	10,00 (8,45 ±3,50)	Complete succ.: IOP ≤21mmHg without medic.	47,7%	26,8±7,7	12,2±4,7	One major complication; 25 eyes, 5FU injection, needling in 5 eyes therefrom	[8]
		Qualified succ.: IOP≤21mmHg, with or without medic.	89,0%				
105	8,00	Complete succ.: IOP ≤21mmHg without medic.	57%	26,8±7,7	12,0±3,0 (at 6,5 years)	26 patients: progression of preexist. senile cataract. 25 eyes, 5FU injection, because of encysted blebs.	[68]
		Qualified succ.: IOP≤21mmHg, with or without medic.	91%				

EXG = exfoliative glaucoma, AC= anterior chamber, FU= Fluorocil, DS=deep sclerectomy

On the basis of a 10-year follow-up deep sclerectomy with collagen implant demonstrated its efficacy in controlling IOP with few postoperative complications. Combining with postoperative goniopuncture NPDS (DSCI) has a similar long-term hypotensive effect as trabeculectomy.

Postoperative aqueous outflow after trabeculectomy and the classic variant of NPDS by Kozlov [38] follows three main pathways (dark grey arrows in Fig. 3, Fig. 7):

- through the surgically created fistula or filtration membrane into the subconjunctival venous plexus;
- into the uveal tract;
- through the residual trabecular meshwork using the conventional drainage outflow pathway via the trabecular meshwork into the episcleral veins.

Possible additional outflow paths through the ostia of Schlemm’s canal [27] and an outflow into the episcleral veins through subtenon’s space, that are present in other glaucoma filtration surgeries [8, 19, 20, 27, 29] are demonstrated in Fig. 3, Fig. 7 (light grey arrows). Clinical and experimental issues on mechanisms of filtration after non-penetrating glaucoma surgery were reviewed by Mermoud & Ravinet [52] and by Nguyen & Shaarawy [57].

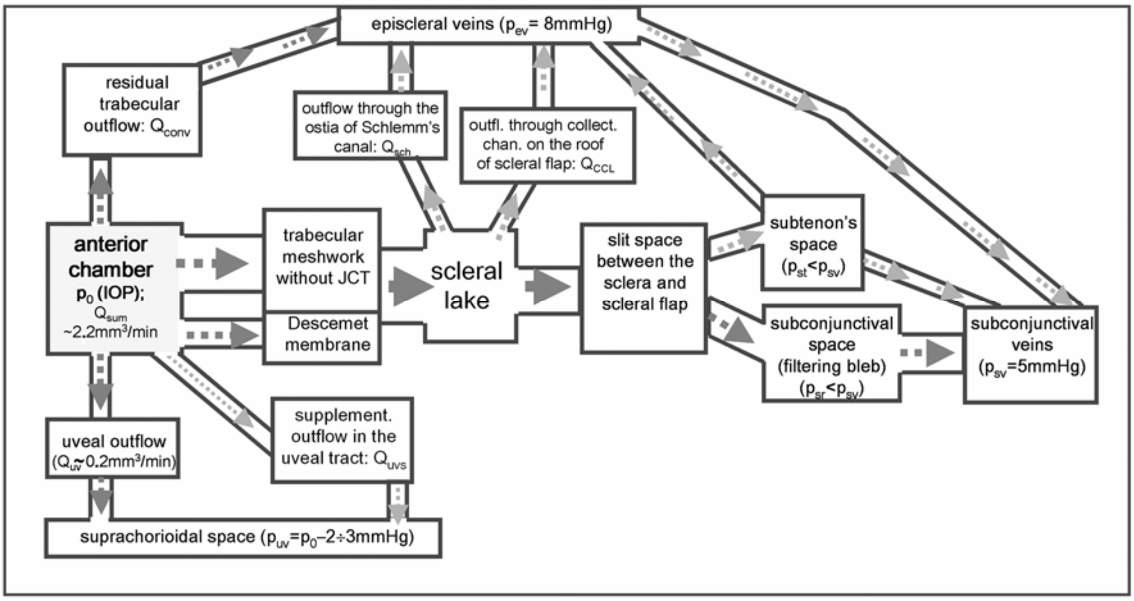

Fig. 7. Block-scheme of the aqueous outflow after classic non-penetrating deep sclerectomy [37].

2.2.6 Comparison of non-penetrating vs. penetrating glaucoma surgery

Table 3. Comparison of non-penetrating vs. penetrating glaucoma filtration surgery.

	Non-penetrating glaucoma filtration surgery	Penetrating glaucoma filtration surgery
1	Aqueous humor filtration from the anterior chamber through a semi permeable membrane	Aqueous humor drainage from the anterior chamber through a fistula
2	Gradual IOP decrease during the operation	Abrupt IOP decrease during the operation
3	**Uncommon** intra- und postoperative complications are: hypotony shallow anterior chamber hyphema choroidal detachment cystic filtering bleb postoperative cataract formation	**Common** intra- und postoperative complications are: hypotony shallow anterior chamber hyphema choroidal detachment cystic filtering bleb postoperative cataract formation
4	**Common** postoperative complication: Tamponade of the filtration zone by the iris root	**Rare** postoperative complication: Tamponade of the filtration zone by the iris root
5	**Persistent** hypotensive effect (10 years and more)	**Persistent** hypotensive effect (10 years and more)

6	**More sophisticated** surgical technique, flat learning curve.	**Less sophisticated** surgical technique, steeper learning curve.
7	Cytostatics or intrascleral implants in order to overcome wound modulation	Cytostatics in order to overcome wound modulation
8	Possibility of YAG-laser goniopuncture in the postoperative period in order to improve the hypotensive effect	Laser fine-tuning is possible only for suture adjustment

From the weight of evidence, which is currently available, the following conclusion can be drawn: Non-penetrating glaucoma surgery is certainly safer than trabeculectomy with lesser rates of intra- and postoperative complications. It offers similar IOP control to trabeculectomy with slightly higher postoperative IOP values. The use of implants and postoperative laser goniopuncture offers better IOP control for longer durations thus enhancing success rate.

2.2.7 **Purpose**

The present work aimed to develop a modified NPGS technique named non-penetrating intracanalicular partial trabeculectomy via the ostia of Schlemm's canal (NPIT), which keeps the advantages of NPGS and overcomes its two main disadvantages which are inadequate hypotensive effect, and the relative complexity of the surgical technique compared to trabeculectomy. The results of this new modified surgical technique are observed in a pilot study with long-term postoperative follow up and are compared with same surgeons' long term results of the classic NPDS.

3 Material and Methods

The study was designed as a prospective pilot study to reveal the hypotensive effect of the new non-penetrating intracanalicular partial trabeculectomy via the ostia of Schlemm's canal, developed and performed by the author [16] and to compare this effect with a classic version of NPDS **(classic NPDS)** which was performed by the author earlier.

Patients

In 33 eyes of 28 patients with open angle glaucoma (IOP: 32,7±10,9 mmHg; range 21,0 – 54,0 mmHg; age: 72,7±9,8 years, range 55,0 - 91,0 years) **classic NPDS** with the excision of a deep scleral flap including the outer wall of Schlemm's canal was performed.

In 21 eyes of 17 patients with open angle glaucoma (IOP: 32,4 ± 4,7 mmHg [mean ± standard deviation], range 22,0 – 43,0 mmHg; age: 69,2 ± 4,4 years, range 61,0 - 76,0 years) non-penetrating intracanalicular partial trabeculectomy via the ostia of Schlemm's canal (**NPIT**) was carried out.

Goldmann applanation tonometry was used for IOP measurements. Tonometry data were corrected using pachimetry data and the Dresden correction table [36]. IOP of all the glaucoma patients were measured repatedly before the decision for surgery. A single preoperative IOP value was used as baseline value. This served for the decision making for the surgical treatment. The following criteria had to be met for the glaucoma surgery: IOP > 22 mmHg with optimized medical therapy; decrease in visual field parameters in the last 1 year.

In all patients postoperative IOP was measured 1 day after surgery, 1 month, 1 year and 2 years after surgery. 17 of 28 patients in the classic NPDS group and 13 of 17 patients in the NPIT group were controlled more frequently: once every three months in the first year after the first month following the surgery and once every 6 months a year thereafter. All 33+21 eyes of 28+ 17 subjects were evaluated during the follow-up.

Informed consent was obtained from all the subjects. The study followed the guidelines for clinical investigations required by the Ethics Committee of Medical Faculty at Munich University of Technology. All procedures adhered to the tenets of the Declaration of Helsinki.

Short description of the technique: non-penetrating deep sclerectomy (classic NPDS).

The less permeable layers of the trabecular meshwork namely the inner wall of SC, the juxtacanalicular and the corneoscleral trabecular meshwork (Fig. 2) are removed with an atraumatic trabecular spatula developed by the author (Geuder AG, Heidelberg, Germany; G-16240) at the site of the deroofed area of SC (Fig. 8). This provides the a semi-permeable filtration membrane, which consists of the uveal layer of the trabecular meshwork as well as of the exposed part of Descemet's membrane. When finishing the surgery a collagen drainage device (STAAR Surgical Company, Monrovia, CA, USA) is implanted at the site of filtration.

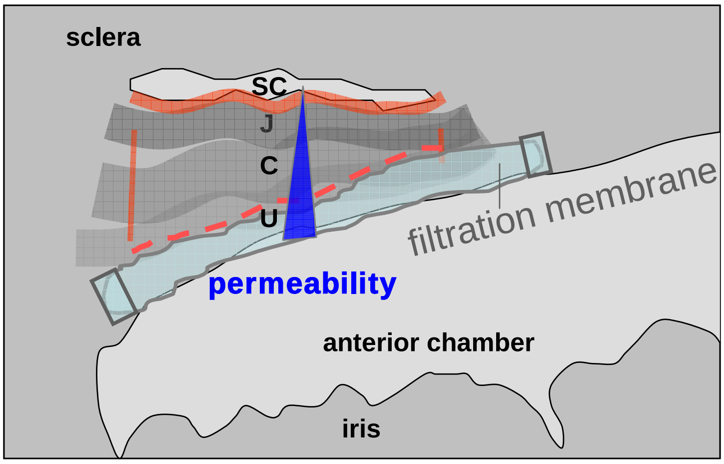

Fig. 8. Anatomical scheme of the classic NPGS procedure: a section across the scleral lake. Since the permeability of the trabecular meshwork decreases towards Schlemm's canal, all less impermeable layers of the trabecular meshwork need to be removed (area bounded with the red line) from outside. The filtration membrane is extended towards Descemet's membrane. SC – Schlemm's canal; J – juxtacanalicular, C – corneoscleral, U – uveoscleral layers of trabecular meshwork. A continuous red line adjacent to SC represents the inner wall of SC.

Short description of the technique: non-penetrating intracanalicular partial trabeculectomy via the ostia of Schlemm's canal (NPIT).

The less permeable layers of the trabecular meshwork: the inner wall of SC, the juxtacanalicular and the corneoscleral trabecular meshwork (Fig. 8) are removed with an atraumatic trabecular spatula developed by authors at the site of the open area of SC.

Through both ostia of SC the cannula-harpoon developed by the author (Geuder AG, Heidelberg, Germany, G-S02199) is introduced between the less permeable layers of the trabecula meshwork (presumably corneoscleral and juxtacanalicular meshwork and the inner wall of SC) and well-permeable uveal trabecular layer. The layers are separated with this maneuver. The superficial less permeable trabecular layers are removed via SC through its ostia during the retraction of the cannula. Thus the post-operative filtration zone becomes extended using the natural outflow pathways as SC, providing sufficient postoperative aqueous outflow. Neither penetration into the anterior chamber (as in trabeculectomy) nor exposing a substantial part of Descemet's membrane (as in the classic non-penetrating deep sclerectomy) is performed (Fig. 5). After the extended filtration membrane is thus created the last step of the surgery is performed in the classic way with implantation of collagen drainage device at the site of filtration.

3.1 Detailed surgical technique

The initial part of the surgery follows the classic technique of non-penetrating deep sclerectomy (NPDS) described by Kozlov [38] which is modified and standardized as follows.

A fornix based conjunctival flap is prepared from limbus. A superficial scleral flap ~ 4 x 4 mm is separated deeply into the corneal stroma, approximately 1,5 mm in corneal tissue.

Its thickness reaches about 1/3 of the sclera which is approximately 270-300 µm (Fig. 9). The flap is elevated parallel to the surfaces of the sclera and the cornea.

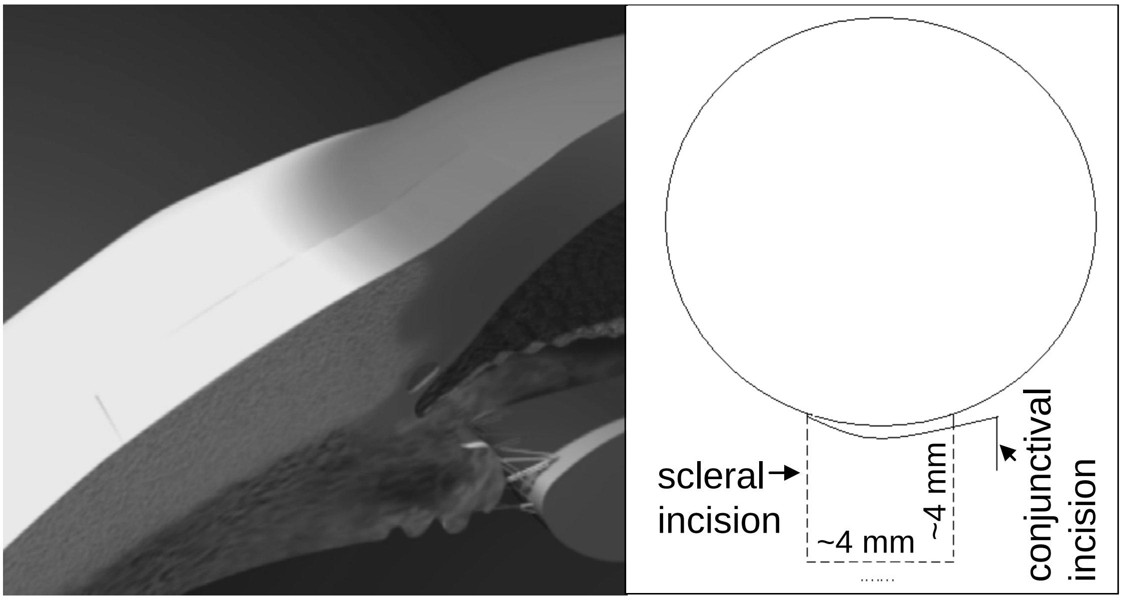

Fig. 9. Beginning of the surgery. Dissection of the conjunctiva and preparation of fornix-based conjunctival flap, followed by the dissection of the outer corneo-scleral flap of 4 mm x 4 mm in dimension.

For easier handling during the following separation of the deep flap in the region of Schlemm's canal and Descemet's membrane, as well as for the final excision of the flap, the flap is designed as a pentagon with two parallel sides. The deep flap is fashioned with a

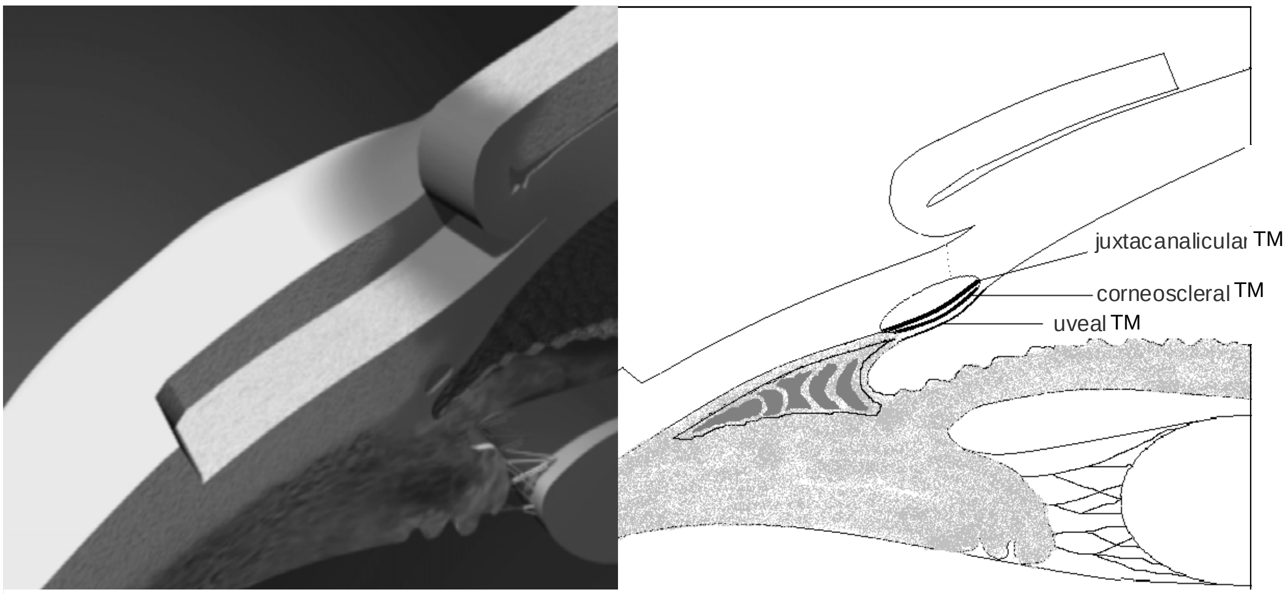

Fig. 10. Dissection of the scleral flap of 1/3 of scleral thickness (270-300 µm) 1 mm through the limbus towards the cornea. TM - trabecular meshwork.

thickness of 2/3 of the sclera (Fig. 10) so that during separation of the flap towards the cornea the lumen of Schlemm's canal is entered automatically.

The deep scleral flap is separated in deep sclera very close to the ciliary body which can be observed by a change in scleral color. In order to provide a correct orientation in the scleral layers, the sclera is perforated at the apex of the deep scleral flap up to the ciliary body. This orientational local sclerotomy in one place is small and does not represent a cyclodialysis, because there is no contact of the instrument to the ciliary body.

Next, preparation is performed moving away from the apex "flying at zero altitude" with only a thin semi-transparent scleral layers left under the knife (Fig. 11). Thereby an opening to Schlemm's canal is created.

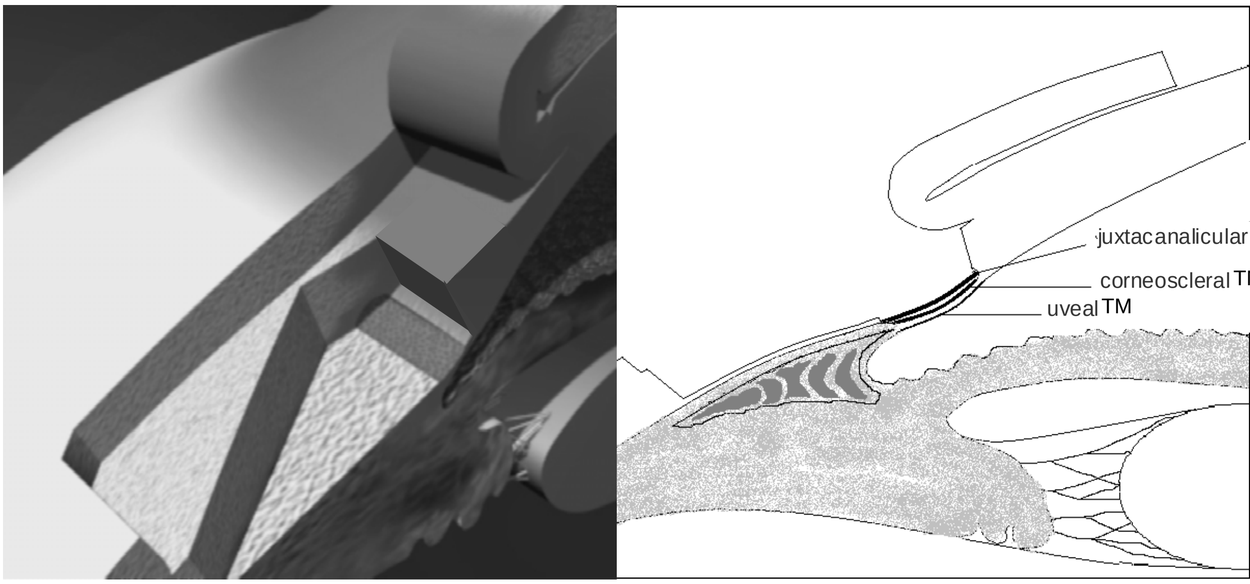

Fig. 11. Excision of a deep triangular scleral flap including the outer wall of Schlemm's canal in NPIT.
TM - trabecular meshwork.

Fig. 11 shows the preparation field in **NPIT**. In the classic NPGS a relatively large part of Descemet's membrane is exposed to filtration. In order to obtain sufficient filtration rates postoperatively, in the **classic NPDS** the deep scleral flap is fashioned two SC widths central from SC into corneal tissue.

If the lumen of Schlemm's canal has been entered at once and the deep flap has been separated well into the cornea, the trabecular tissue becomes visible and a thin film on the surface of the inner wall of Schlemm's canal can be easily removed with a microsponge. This film represents the less permeable trabecular layers (corneoscleral TM, juxtacanalicular TM and the inner wall of SC), while the more permeable layer (uveal TM) remains intact (Fig. 8). In other versions of NPDS this stage is usually performed with a forceps only. When grasping the superficial film perforation is not unusual.

In NPIT technique the superficial less permeable trabecular layers are separated with an atraumatic trabecular spatula (Fig. 12) in order to prevent microperforation of the uveal trabecular layer and Descemet's membrane. This spatula is inserted along the tangent to the surface of Descemet's membrane between the trabecular layers. Then the superficial layers are separated from the less permeable layers with a motion from below upwards (Fig. 12, right panel). Finally, the dissected layers are removed with a forceps. Any acute contact of the instrumentation to the remaining trabecular layer and Descemet's membrane is avoided. The deep scleral layer is then excised.

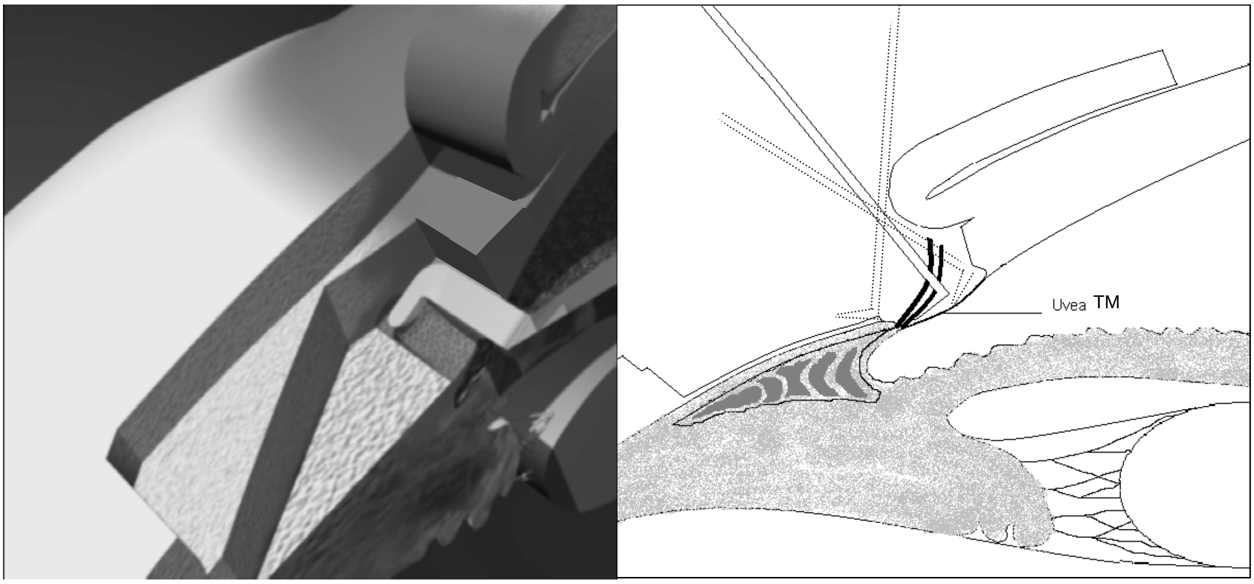

Fig. 12. Removal of less permeable (corneoscleral TM, juxtacanalicular TM and the inner wall of SC) trabecular layers with the atraumatic trabecular spatula by Dashevsky in the site of the scleral flap. Initial and and final positions of the spatula are shown with dashed lines. TM - trabecular meshwork.

In classic NPDS the formation of the filtration membrane is usually finished at this step. An absorbable collagen implant (STAAR Surgical Company, Monrovia, CA, USA) is inserted into the scleral lake in order to create a postoperative intrascleral space, preventing its scarring. Neither Mitomycin C nor other chemical agents are needed additionally. The scleral lake is closed with the superficial scleral flap. The latter is sutured in its two distal corners. Then the conjunctival incision is closed with two separate sutures at the limbus and an additional paralimbal suture.

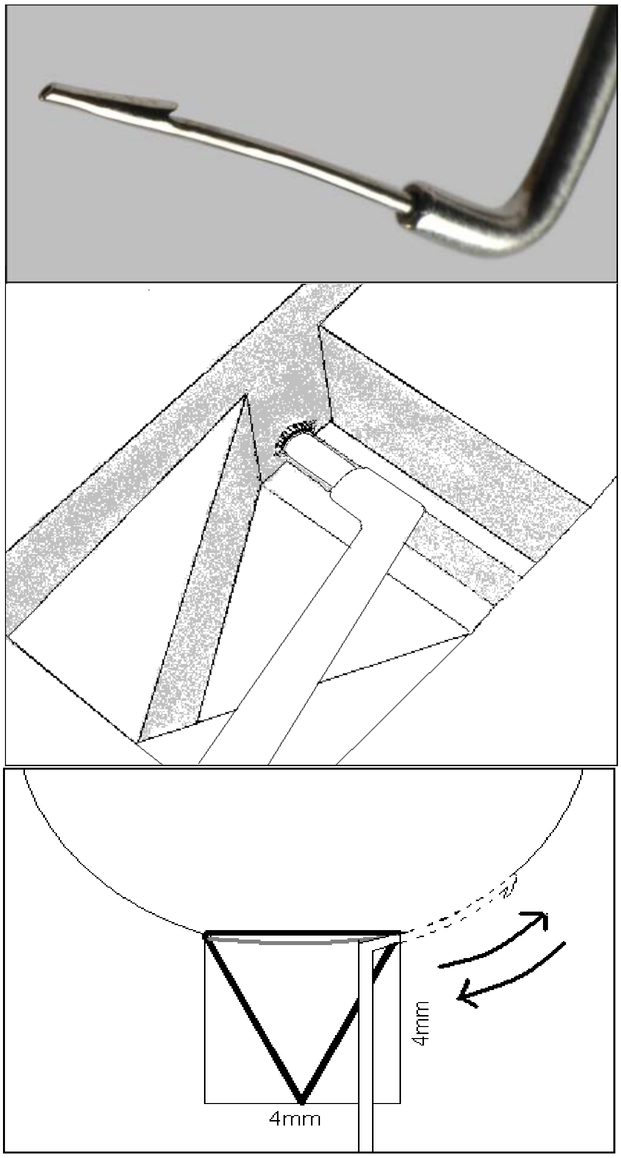

Fig. 13. Introduction of the cannula-harpoon by Dashevsky through the ostia of Schlemm's canal.

In the novel NPIT technique an additional stage is added before the insertion of the collagen implant in order to improve the postoperative case of filtration. At this stage of the surgery a cannula-harpoon is introduced alternately through both ostia of Schlemm's canal between the less permeable (corneoscleral TM, juxtacanalicular TM and the inner wall of SC) trabecular layers above and the well-permeable (uveal TM) trabecular layer below (Fig. 13) to a depth of 3,5-4 mm. It is not difficult to distinguish those layers in the visible ostia.

The harpoon-cannula represents a modification of the classical cannula for the viscocanalostomy procedure which provides the delivery of viscoelastic through the SC ostia (Fig. 13, top panel). There is a hook attached on the tip of the cannula, which looks like a crochet hook. The narrow end of the hook provides its easy insertion between trabecular layers and its movement inside Schlemm's canal through SC ostium away from the scleral lake, whereas the distant part of the hook allows its backwards manoeuvre with the dissection (a kind of husking) of less permeable trabecular layers inside Schlemm's canal and their subsequent extraction trough SC ostium (Fig. 14).

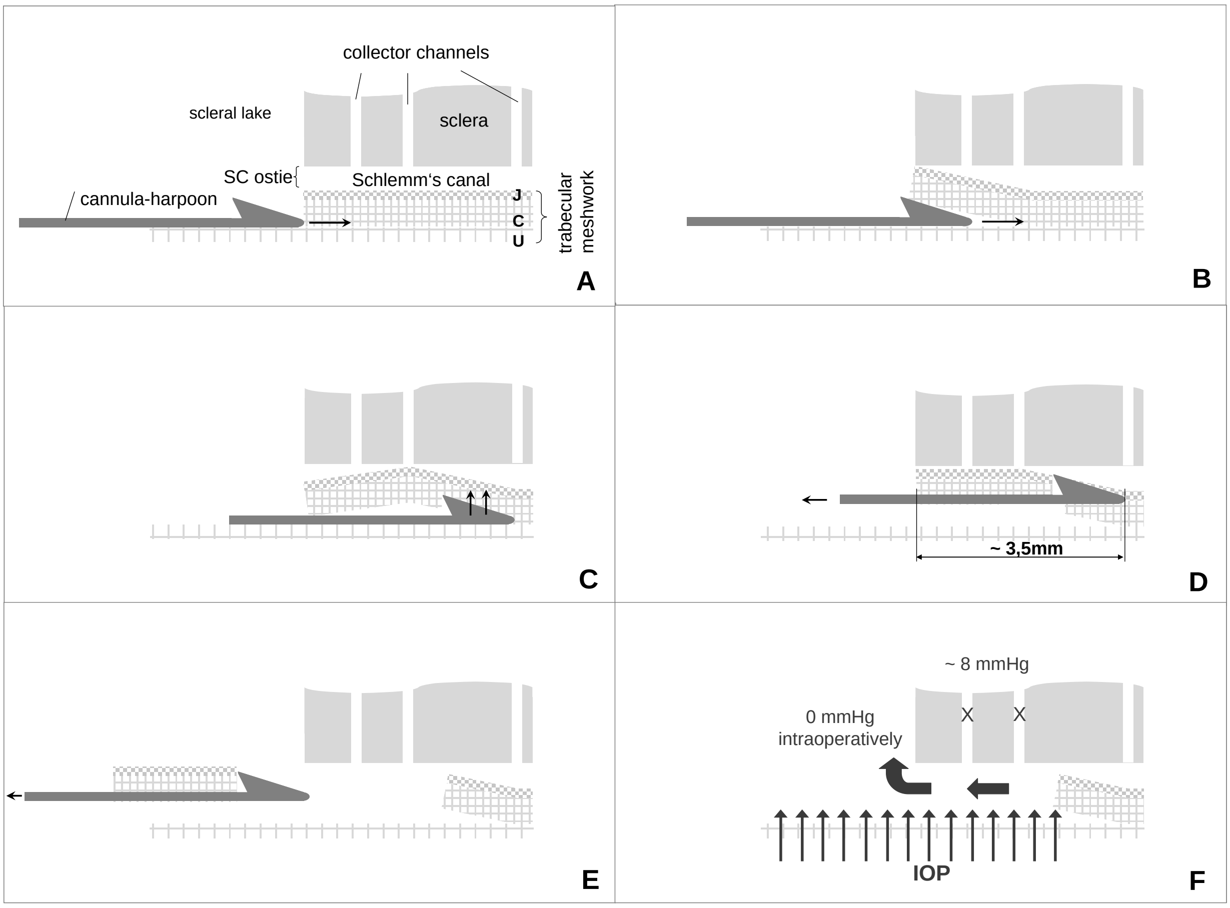

Fig. 14. Schematic drawing of intraoperative application of the cannula-harpoon. It is introduced with injected viscoelastic alternately in each ostium of SC between less permeable (corneoscleral TM, juxtacanalicular TM and the inner wall of SC) trabecular layers above and the well-permeable (uveal TM) trabecular layers below (A). In such a way a permeable trabecular layer is separated from two other less permeable layers within SC. Through SC ostium the cannula is moved up (C) and then backwards (D) inside SC. Due to its' harpoon orientation two superficial less penetrated trabecular layers within the ostie are removed (E). Aqueous filtration trough the extended area of the permeable membrane is provided into the scleral lake (F). SC – Schlemm's canal; J – juxtacanalicular, C – corneoscleral, U – uveoscleral layers of the trabecular meshwork.

In the beginning the cannula is simply sliding within the opening on the surface of the already prepared more permeable trabecula towards an ostium. Thereby it exits SC through its ostium remaining on the surface of more permeable trabecular layer and separating it from cuts of less permeable layers (Fig. 14). In distinction to viscocanalostomy viscoelastic is injected through the cannula-harpoon during its introduction through the SC ostium ***between trabecular layers*** in the present procedure. In such a way a permeable trabecular layer is separated from other less permeable layers within Schlemm's canal. Being inside SC the cannula-harpoon is moved up and then backwards. Due to its harpoon orientation the superficial less penetrated trabecular layers within SC are removed (Fig. 14), which is not the case in viscocanalostomy. Thus the postoperative filtration zone becomes extended into Schlemm's canal through its ostia.

As the extended filtration membrane is created the last step of the surgery is performed in the classical way. An absorbable collagen implant (STAAR Surgical Company, Monrovia, CA, USA) is inserted into the scleral lake in order to create a postoperative intrascleral space, preventing its scarring. Neither Mitomycin C nor other chemical agents are needed additionally. The scleral lake is closed with the superficial scleral flap. The latter is sutured in its' two distal corners. Then the conjunctival incision is closed with two separate sutures at the limbus and an additional paralimbal suture.

3.2 Data evaluation and statistical methods

A table with corresponding macros in MS Excel 2000 was created for data analysis. The normal distribution of measurement data was proved with Kolmogoroff-Smirnoff Test. The parametric Student-Test for two dependent samples (glaucoma patients before and after the treatment) and Bonferroni Post-Hoc test for multiple comparisons (glaucoma patients before, 1 month and 2 years after the treatment) were used in order to assess statistical differences of the evaluated characteristics. Since in some patients (5 subjects in the classic NPDS group and 4 patients in the NPIT group) the surgery was performed in two eyes, single-eye IOP observations for each subject were averaged and then analyses for one-eye designs were performed on the averages. Because of the small number of subjects all the tests were applied on the level of significance of $p = 0,05$ for each evaluated parameter. Statistical evaluation was performed with MS Excel 2000 for Windows and SPSS 11.0.

4 Results

Classic NPDS

Postoperative IOP of 16,6 ± 4,4 mmHg after two years of follow up (ranged 7,0 – 25,0 mmHg) was measured in the evaluated group of glaucoma patients. IOP reduction of 14,0±9,0 mmHg (ranged 0,0 – 25,0 mmHg) due to the surgery at this time was significant (p<0,001; t-test). In 10 cases (30%) surgically arceived hypotensive effect was relative (with medications); in 22 cases (67%) it was absolute. Short-term postoperative IOP 1 month after the surgery amounted to 15,3 ± 6,9 mmHg.

In 6 cases (18%) surgery was combined with phacoemulsification. In 2 cases (6%) micro-perforations of the filtration membrane could not be avoided. In one case (3%) this lead to the absence of a hypotensive effect after two years. In this case a tamponade of the perforation occured by the iris root. Consequently formation of goniosynechias at the site of filtration occurred. In 4 cases (12%) a goniopuncture with Nd:YAG (Neodynium:Yttrium Aluminium Garnet) laser was carried out at the site of filtration 2 to 7 months postoperatively, in order to reinforce the hypotensive effect of the surgery.

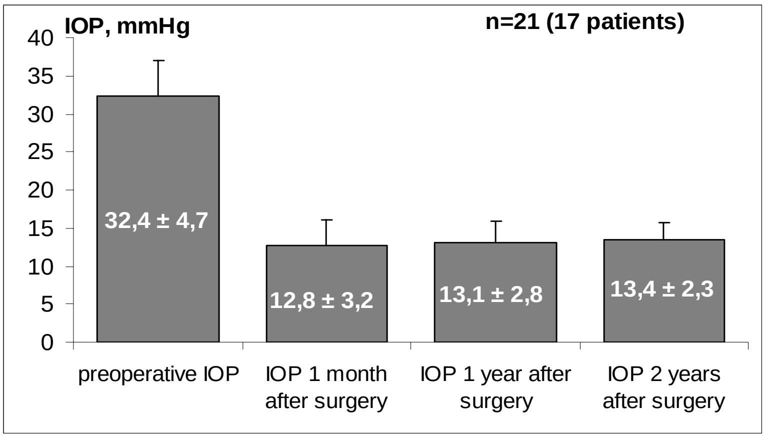

Fig. 15. IOP lowering during the follow up of NPIT: n=21 (17 patients).

In 2 cases (6%) a formation of a cystic filtering bleb was seen 1 to 3 months postoperatively. In both cases a revision of filtering blebs was carried out with Mitomycin C. No other complications, which are usual for glaucoma surgery, such as hypotony, choroidal detachment, hyphema, shallow anterior chamber, inflammation in the anterior chamber were observed.

NPIT

As a result of the surgery the filtration zone is extended improving the natural outflow pathways towards SC without the disturbing principles of non-penetrating surgery.

Short-term postoperative IOP 1 month after the surgery amounted to 12,8 ± 3,2 mmHg (ranged 8,0 – 16,0 mmHg) and was significant lower than the preoperative IOP (p<0,001; t-test with Bonferroni correction, Fig. 15). Postoperative IOP of 13,4 ± 2,3 mmHg (ranged 9,0 – 18,0 mmHg) at two years of follow-up was measured in the evaluated group of glaucoma patients (Fig. 15). IOP reduction of 18,0±7,0 mmHg (ranged 9,0 – 31,0 mmHg) due to the surgery was significant (p<0,001; t-test with Bonferroni correction). In all 21 eyes the hypotensive effect was absolute (without medications).

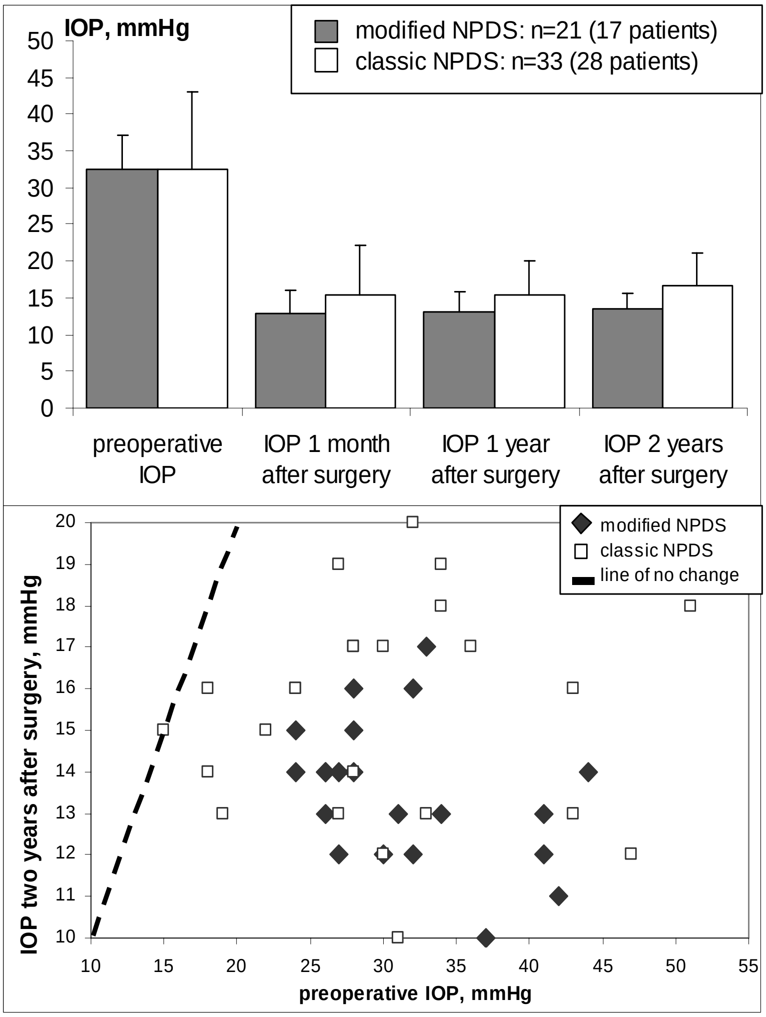

Fig. 16. Comparison of the results of the modified NPDS, called NPIT (n=21, 17 patients) with the results of classic NPDS technique (n = 33, 28 patients) [15]. **Upper panel:** Comparison of IOP lowering after two years of follow up. At one month, one year and two years after the surgery the difference in IOP between both groups was statistically significant (p<0,01). **Bottom panel:** Diagram IOP pre- and two years after the surgery.

In 7 (33%) cases during the surgery a hyphema appeared, which dissolved uneventful in all the cases at 2 - 3 days postoperatively. No other complications, which are usual for glaucoma surgery, like hypotony, choroidal detachment, formation of the cystic filtering bleb, shallow anterior chamber, inflammation in the anterior chamber etc. were observed.

In order to show the advantage of the proposed new glaucoma surgery two years follow-up results of the **classic NPDS** and the **NPIT** surgeries were compared (Fig. 16). One month and one year after the surgery the difference in IOP between surgical versions was statistically significant ($p<0,05$). Two years after surgery the difference between the two techniques was highly significant: 13,4±2,3 mmHg after NPIT vs. 16,6±4,4 mmHg after classic NPDS ($p<0,01$)(Fig. 16, upper panel). The scatter-plot diagram of pre- and postoperative IOP demonstrated the better outcome of the novel surgery technique (Fig. 16, bottom panel).

5 Discussion

In order to improve the main disadvantages of classic non-penetrating deep sclerectomy by Kozlov and to reduce the main disadvantages, namely: an insufficient hypotensive effect and the relative complexity of the surgery technique, the author developed this novel non-penetrating surgery technique in a stepwise fashion.

At first a classic atraumatic standardised NPDS was developed, which is called **classic NPDS** in this Thesis. This first step introduced an atraumatic spatula to remove the non-permeable layers of the trabecula meshwork inside the scleral. The introduction of the atraumatic spatula leads to a standardisation of the NPGS technique and improves the learning curve of this surgical procedure thus making it safer. The postoperative hypotensive effect of this type of surgery is comparable with the effect of classic NPDS performed by an experienced surgeon.

Consequently a modified procedure called non-penetrating intracanalicular partial trabeculectomy via the ostia of Schlemm's canal was developed on the basis of the **classic NPDS**. At this second step a harpoon-cannula to remove non-permeable layers of the trabecula meshwork through the ostium of Schlemm's canal was introduced. The introduction of the harpoon-cannula allows to extend the filtration membrane and improve the hypotensive effect of this non-penetrating surgery. The well-established hypotensive effect of NPIT is persistent over at least two-years of follow up and is comparable to the effect after trabeculectomy with much lower intra- and postoperative complication rates.

In this Thesis the postoperative results with both techniques are presented and compared to each other.

5.1 Classic NPDS with atraumatic spatula

The preparation of the internal wall of Schlemm's canal and Descemet's membrane with removal of juxtacanalicular and corneoscleral trabecular layers as well as the absence of macro-and microperforations in the so-called filtering membrane are crucial for a successful application of this technique, since both of these layers cause the main resistance to the aqueous outflow from the anterior chamber into Schlemm's canal [7, 21, 63]. That is why special attention should be paid to the technique of superficial and deep scleral flap fashioning and to the removal of juxtacanalicular and corneoscleral trabecular layers.

The presence of micro- and macro perforations at the site of the filtration membrane represents an intraoperative complication. The aqueous flows into the perforation directly, and the homogeneous filtration through the whole membrane is disturbed. This leads to postoperative complications and consequently, to the uncontrolled postoperative IOP. On the other hand, trying to avoid such perforations the surgeon can inadvertently tend to remove less tissue leaving a too thick less permeable membrane.

The use of the spatula proposed by the author allows a surgeon to avoid perforations and to fashion a thin well-permeable membrane faster and more safely. Application of the spatula assures controlled removal of less permeable portions of the trabecula in the operation zone providing sufficient postoperative aqueous outflow and a persistent hypotensive effect at 2 years of follow up in the present study. The introduction of the spatula allows the standardisation and the simplification of the NPDS technique, which makes it much easier to learn for a beginner. The results of the present study demonstrate a pronounced and sustained effect of the classic atraumatic NPDS technique with the spatula and show that this surgery can be successfully applied in patients with uncontrolled on maximal tolerated medical therapy (MTMT) open angle glaucoma.

On the base of his experience the author recommends postoperative IOP control at least once every 3 months of the first year. The possibility of non-invasive postoperative “fine-tuning“ of the IOP represents one of the NPDS advantages. If IOP rises later postoperatively the permeability of the filtering membrane can be increased using YAG-laser goniopuncture at the site of the dissected filtering membrane. This “tuning” should be performed timely before scarring of the scleral lake and the filtration membrane occurs. It was performed in some cases during follow-up after the reported classic NPDS procedure.

5.2 NPIT

The reported results demonstrate a pronounced and sustained effect of the new improved non penetrating glaucoma surgery (NPIT) and show that this surgery can be successfully applied in patients with MTMT open angle glaucoma as a valuable sparing alternative to medical therapy and other types of glaucoma surgery including laser surgery.

For the reported two year follow-up period a sufficient hypotensive effect was maintained in all eyes without any medications. Additionally the usual postoperative “fine-tuning“ of the IOP in NPDS using YAG-laser goniopuncture at the site of the dissected filtering membrane [49] has not been necessary in any of eyes that underwent NPIT. However the author cannot exclude that it might be necessary occasionally.

In order to show the advantage of the new glaucoma surgery two years follow-up results of NPIT and the classic NPDS surgeries are compared (Fig. 16). The technique of NPIT is made efficient by using the cannula-harpoon instrument. Since both surgeries were performed by one surgeon, surgical skills did not play a role in the comparison. A hypotensive effect of NPIT technique is well comparable to this of trabeculectomy after two years follow-up, while the hypotensive effect of the classic NPDS technique is rather insufficient and less pronounced compared to trabeculectomy.

The removal of less permeable layers of the trabecular meshwork represents the necessary condition for the NPDS surgery, since these layers cause the main resistance to the aqueous outflow from the anterior chamber into Schlemm's canal [21, 46]. The extension of the filtration membrane into SC through its ostia in the proposed NPIT technique amounts to approximately 175% of the initial membrane inside the scleral lake: in NPIT 3,5 mm left and right into SC are added to approximally 4 mm of the membrane inside the scleral lake:

$$(3{,}5mm+3{,}5mm+4mm) \cdot 100\%/ 4mm = 175\%.$$

Considering the filtration rate of the dissected Descemet's membrane to be less than the filtration rate of the dissected trabecula inside the scleral lake [38], one would need to involve a relatively large part of Descemet's membrane in the classic NPGS, going to more than two Schlemm's canal widths central to the cornea from the scleral lake, in order to gain similar filtration rates.

The author assumes that the postoperative outflow inside SC occurs both into collector channels and through the SC ostia into the scleral lake. Even if the scleral lake is scarred postoperatively, the outflow through the extended filtration membrane inside SC into collector channels would remain thus providing a major part of the aqueous outflow.

The filtering bleb after NPIT is diffuse and flat short-term postoperatively. It almost disappears in most cases long-term postoperatively. Formation of a filtering bleb is not the aim of the surgeon in NPIT any more, hence we did not see any postoperative cystic blebs in the present study. After NPIT a major part of aqueous outflows not through the intrascleral lake over the supperficial scleral flap under the conjunctiva but through the natural outflow pathways including SC and collector channels into intrascleral venous system. We assume, that flat, almost invisible postoperative flap represents a sign of successful postoperative filtration through the natural outflow pathways. However, we cannot exclude a certain incidence of postoperative cystic blebs after NPIT as a usual complication of filtration glaucoma surgery. After a classic NPDS this incidence is reported by Mermoud as 15% [51] and is apparently lower after NPIT. Hence more cases of NPIT need to be reported in order to reveal it.

No cytostatic drugs like Mitomycin C or 5 Fluorouracil were used intraoperatively in order to prevent postoperative scarring in either technique. For this purpose the STARR sponge has been chosen as a part of the procedure. Comparing the reported results of **NPIT** surgery with the **classic NPDS** technique, where the same sponge was used to prevent scarring [15], the author did not observe any microcysts or cystic blebs one and two years postoperatively in **NPIT**. However, in the **classic NPDS** a formation of a cystic filtering bleb was seen in 2 cases and a postoperative revision of filtering blebs was carried out with Mitomycin C.

An attempt to increase the postoperative aqueous filtration through the ostia of Schlemm's canal has been first made by viscocanalostomy as described by Stegmann [72] and later on in his modern glaucoma surgery named canaloplasty [42, 69]. To the opinion of the author not enough attention is paid to the dissection of the filtering membrane in viscocanalostomy both inside the scleral lake and in the parts of SC adjacent to its ostia. In viscocanalostomy Schlemm's canal is opened and dilated using viscoelastic injected into its ostia with the goal to increase the permeability of the trabecula inside SC. According to Johnson and Johnson [31] the dilation of SC with viscoelastic substance causes most probably a microrupturing of the canal and converts the procedure into a trabeculotomy in SC adjacent to the ostia. Such a microrupture is avoided in NPIT.

The procedure of canaloplasty causes a mechanical stretching of the whole trabecular tissue along the canal. This might lead to an unnatural remodelling of this tissue, with possible scarring of the whole trabecular tissue and diminishing success of any re-operation. In the proposed NPIT only approximately 29% of SC is involved. This might allow for a possible re-operation in the future at the resting part of the canal.

$$(4\text{mm}+2 \cdot 3{,}5\text{mm})/(\pi \cdot 12\text{mm}) \cdot 100\% = 29\%.$$

Here the length of the postoperative filtration membrane in NPIT as estimated above is divided by the whole SC length calculated with a limbus diameter of 12 mm.

Only one type of intra- and postoperastive complication was observed in NPIT namely hyphema. This might be either due to the unavoidable damage of the outer SC wall during backwards cannula-harpoon motion. Another explanation of this findingh could be the changed pressure relationship in the operated eye with some blood from collector channels (pressure ~8-10 mmHg) entering SC after its opening and further progression into the scleral lake (pressure ~0 mmHg). Already at the stage of removal of less permeable trabecular layers inside the scleral lake intraoperative hypotony might occur. After the removal of less permeable trabecular layers inside SC through its ostia, the pressure inside SC can be higher than the decreased IOP. Hence, blood from collector channels might penetrate through the residual more permeable trabecular layers inside SC into the anterior chamber, causing hyphema. This may occur at the initial postoperative time, as a steady state pressure distribution has not yet been established. In the classic NPDS version all trabecular layers inside the SC are intact and blood from collector channels flows directly intraoperatively to the scleral lake with a pressure of ~0 mmHg, which is less than the IOP. Therefore blood remains in the scleral lake intraoperatively. Consequently hyphema does not normally represent a postoperative complication after classic NPDS.

Lately a tendency has been observed, that most eye surgeries are performed on an outpatient basis. This requests high quality surgery technique, minimal operative trauma, as well as reduction of intra- and postoperative complications. The conversion towards outpatient operations has already happened in cataract surgery and is now observed in vitreo-retinal surgery. Moreover, outpatient surgery is already a standard for trabeculectomy in many places. To the opinion of the author refined surgical technique without any perforation of the filtering membrane allows to perform NPIT as an outpatient procedure.

5.3 Limitations of the study

Some limitations to the study need to be mentioned. The relatively small number of patients included in the study does not allow for generalized conclusions for a large population. Moreover, a multicenter approach and additional inclusion of two control groups including glaucoma patients undergoing classic trabeculectomy and glaucoma patients undergoing classic NPDS would allow better conclusions on the safety and long-term effexts of the surgery.

Doubtless the presented stepwise modifications of the common NPDS technique by Kozlov need further follow-up evaluation in 3, 5 and 10 years to control the persistence of the hypotensive effect of the surgery.

6 Conclusions

1. The reported results demonstrate a pronounced and sustained effect of the new improved non-penetrating glaucoma surgery: non-penetrating intracanalicular partial trabeculectomy via the ostia of Schlemm's canal (NPIT) and show that this surgery can be successfully applied in patients with therapy resistant open angle glaucoma as a valuable drug sparing and almost complicationsless alternative to medical therapy and other types of glaucoma surgery including laser surgery.
2. The novel NPIT technique possesses advantages of both trabeculectomy (well established hypotensive effect during the follow up) and classic NPDS by Kozlov (low rates of intra- and postoperative complications) without the main disatvantages of both techniques.
3. The refined surgical technique of the novel NPIT without any perforation of the filtering membrane allows performing this surgery as an outpatient procedure.
4. Two new instruments were introduced for the proposed novel surgery technique. The use of the **atraumatic spatula** developed by the author assures well-controlled removal of less permeable layers of the trabecula in the surgical zone providing sufficient postoperative aqueous outflow and a well persistent hypotensive effect after two years of the follow up in the present study and improves the learning curve of NPDS. The introduction of the **harpoon-cannula** allows to extend the filtration membrane and improve the hypotensive effect of NPDS making the hypotensive effect of NPIT persistent, sufficient and almost complicationsless during at least two-years of follow up.

7 Abstract

Purpose: In order to distinguish a more pronounced and sustained hypotensive effect of non-penetrating glaucoma surgery, a novel surgical procedure is proposed, which provides enlargement of the filtration membrane area with maximal maintenance of natural aqueous outflow pathways.

Methods: In 21 eyes of 17 patients (IOP: 32,4 ± 4,7 mmHg; age: 69,2 ± 4,4 years) the following non-penetrating surgery was performed. After the excision of the outer wall of Schlemm's canal (SC) outer layers of the trabecular meshwork were removed with a trabecular spatula (Geuder Inc., G-16240) at the site of the open area of SC. A cannula-harpoon (Geuder Inc., G-S02199) was introduced through both SC ostia between the less permeable and well-permeable trabecular layers and separating them. Due to the harpoon configuration of the cannula the superficial less permeable trabecular layers were removed within SC adjacent to its ostia during the retracting movement of the cannula. Thus the filtration zone becomes extended using the outflow pathways into SC. The new procedure named non-penetrating intracanalicular partial trabeculectomy via the ostia of Schlemm's canal, was compared with the classic non-penetrating glaucoma surgery performed earlier by the author in 33 eyes of 28 patients.

Results: A postoperative IOP of 13,4 ± 2,3 mmHg after two years of follow-up was measured. In all 21 eyes the hypotensive effect was absolute (without medications). In 7 (33%) cases a hyphema appeared during surgery, which dissolved in all cases within 2-3 days postoperatively.

Conclusions: The results of the study demonstrate a pronounced and sustained effect of the novel surgery technique and show that this surgery can be applied successfully in patients with therapy resistant open angle glaucoma.

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9 List of illustrations

other less permeable layers within SC. Through SC ostium the cannula is moved up (C) and then backwards (D) inside SC. Due to its' harpoon orientation two superficial less penetrated trabecular layers within the ostie are removed (E). Aqueous filtration trough the extended area of the permeable membrane is provided into the scleral lake (F). SC – Schlemm's canal; J – juxtacanalicular, C – corneoscleral, U – uveoscleral layers of the trabecular meshwork.

Fig. 15. IOP lowering during the follow up of NPIT: n=21 (17 patients).

Fig. 16. Comparison of the results of the modified NPDS, called NPIT (n=21, 17 patients) with the results of classic NPDS technique (n = 33, 28 patients) [15]. Upper panel: Comparison of IOP lowering after two years of follow up. At one month, one year and two years after the surgery the difference in IOP between both groups was statistically significant ($p<0,01$). Bottom panel: Diagram IOP pre- and two years after the surgery.

10 List of tables

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Instrumenten für Augenchirurgie

- Trabekelspatel für nicht-perforierende tiefe Sklerektomie nach Dashevsky (G-16240). Fa. Geuder. Heidelberg
- Harpoon-Kanule für nicht-perforierende tiefe Sklerektomie nach Dashevsky (G-S02199). Fa. Geuder. Heidelberg

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