From deep sclerectomy to canaloplasty
Is it possible to re-establish the natural outflow in patients with chronic open-angle glaucoma

Ph.D. Thesis

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1. Abbreviations

IOL	intraocular lens
IOP	intraocular pressure
LED	light emitting diode
NDYAG	Neodyme-Yttrium-Aluminium-Granat
OCT	optical coherence tomography
OCTAASS	optical coherence tomography assisted anterior segment surgery
OVD	ophthalmic viscosurgical device
PAS	peripheral anterior synechiae
UBM	ultrasound biomicroscope

2. Introduction

Glaucoma is an optic neuropathy in which the optic nerve is damaged with typical loss of nerve fibers and increasing cupping of the optic disc, leading to progressive, irreversible loss of vision. It is often, but not always, associated with increased pressure of the fluid in the eye. The nerve damage involves loss of retinal ganglion cells in a characteristic pattern.
There are many different sub-types of glaucoma but they can all be considered a type of optic neuropathy. Raised intraocular pressure (IOP) is a significant risk factor for developing glaucoma. Untreated glaucoma leads to permanent damage of the optic nerve and resultant visual field loss, which can progress to blindness.
Glaucoma has been nicknamed the "sneak robber of sight" because the loss of vision normally occurs gradually over a long period of time and is often only recognized when the disease is quite advanced. Once lost, this damaged visual field cannot be recovered.
Worldwide, glaucoma is the second leading cause of blindness and affects aproximatelly 66 million people in the world. In some countries, e.g. United States of America were approximately 100000 people are totally blind and approximatelly 300000 are blind in one eye from glaucoma, it is the leading cause of blindness. Glaucoma affects 1 in 200 people aged fifty and younger, and 1 in 10 over the age of eighty. **1-4**
Glaucoma can be divided roughly into two main categories, "open angle" and "closed angle" glaucoma. Open-angle Glaucoma accounts for 90% of glaucoma cases in the United States and Europe. It is painless and does not have acute attacks. The only signs are gradually progressive visual field loss and optic nerve changes (increased cup-to-disc ratio on funduscopic exam). Closed-angle Glaucoma accounts for <10% of glaucoma cases in the United States and Europe, but as much as half of glaucoma cases in other nations (particularly Asian countries). About 10% of patients with closed angles present with acute angle closure crises characterized by sudden ocular pain, seeing halos around lights, red eye, very high intraocular pressure (>30 mmHg), nausea and vomiting, sudden decreased vision, and a fixed, mid-dilated pupil. Acute angle closure is an ophthalmologic emergency.
The major risk factor for most glaucomas and focus of treatment is increased intraocular pressure. Intraocular pressure is a function of production of liquid aqueous humor by the ciliary processes of the eye and its drainage through the trabecular meshwork. Aqueous humor flows from the ciliary processes into the posterior chamber, bounded posteriorly by the

lens and the zonules of Zinn and anteriorly by the iris. The aqueous humor then flows through the pupil of the iris into the anterior chamber, bounded posteriorly by the iris and anteriorly by the cornea. From here the trabecular meshwork drains aqueous humor via Schlemm's canal into scleral plexuses and general blood circulation. In open angle glaucoma there is reduced flow through the trabecular meshwork and/or the Schlemm´s canal; in angle closure glaucoma, the iris is pushed forward against the trabecular meshwork, blocking fluid from escaping.

The inconsistent relationship of glaucomatous optic neuropathy with ocular hypertension has provoked hypotheses and studies on anatomic structure, eye development, nerve compression trauma, optic nerve blood flow, excitatory neurotransmitter, trophic factor, retinal ganglion cell/axon degeneration, glial support cell, immune, and aging mechanisms of neuron loss. But lowering intraocular pressure is the only proven means to slow or halt disease progression in studies of those at high risk of developing glaucoma (Ocular Hyertension Treatment Study OHTS) **5**, those with early to moderate glaucoma (Collaborative Initial Glaucoma Treatment Study and early Manifest Glaucoma Trial EMGT) **6-8** and those with more advanced glaucoma (Collaborative Initial Normal-Tension Glaucoma Study **9,10** and Advanced Glaucoma Intervention Study AGIS) **11**. Across all randomized, controlled trials, lowering IOP by at least 18% (mean) from baseline resulted in at least a 40% reduction in rates of worsening of glaucoma over 5 years. These studies confirm that a pathophysiological basis for glaucoma is elevated intraocular pressure.

If the condition is detected early enough it is possible to arrest the development or slow the progression by medical and surgical means.

There is some evidence that prmary surgical treatment is superior to primary medical treatment in pateints with open-angle glaucoma. **12**

First successful antiglaucomatous surgery was performed by german ophthalmologist Albrecht von Graefe in 1852. This was a peripheral iridectomy, which is only successful in acute closed angle glaucoma. In the following one hundred years various surgical techniques addressed the problem of open angle glaucoma. Since early 1970s trabeculectomy described by Sugar, Cairns and later Fronimopoulos became the standard of care in open-angle glaucoma surgery. **13-15** This widely used procedure involves a surgically formed pathway for aqueous humor between the anterior chamber and the subconjuntival space to lower intraocular pressure in the treatment of glaucoma. The main goal is the formation of a conjunctival filtering bleb. This is a relatively unphysiological approach and scleral as well as conjunctival scarring led to introduction of antimetabolites as an adjunctive for filtering bleb-

depending glaucoma surgeries. Numerous intraoperative and postoperative complications have been cited. **16-20** These include hypotony, maculopathy, blebitis/endophthlamitis, hyphema, suprachoroidal hemorrhage or effusions, encapsulation of the bleb with resultant IOP elevation, loss of visual acuity, and increased risk for cataract formation. In addition, intensive postoperative care, including bleb massage, laser suturolysis, release of releasable sutures, needling, or 5-fluorouracil injections, may be needed to achieve primary success. Recently several authors reported relatively high failure rates of trabeculectomy after long term follow-up.

All this led surgeons to search for a more physiological and bleb independent surgical approach in IOP lowering glaucoma surgery. Surgical treatment of the natural aqueous outflow system, including Schlemm´s canal, to restore normal function and IOP control without penetration of the intraocular space has long been the interest in the study of open-angle glaucoma as an alternative to penetrating and bleb-depending methods. **21,22**

In 1964 Krasnov published his first report on sinusotomy. This operation consisted of removing a lamellar band of the sclera, opening the Schlemm´s canal over 120 degrees from 10 to 2 o´clock. The inner wall of Schlemm´s canal was untouched and then the conjunctiva was closed. Krasnov believed that the aqueous outflow resistance in the majority of patients with primary open-angle glaucoma was situated at the level of the scleral drainage veins and not in the trabeculum. **23,24** In the same year Walker published a paper about surgery of the Schlemm´s canal. **25** Other authors also reported on nonpenetrating filtering surgery, leaving in place the trabeculum and the inner wall of Schlemm´s canal. **26-29** Sinusotomy was relatively safer then full-thickness surgery with almost no postoperative complications. But this procedure never became populare, possibly because it was a difficult operation. It needed a surgical microscope at a time when this was not readily available. Moreover the surgical results were not convincing. **30-35**

However, several techniques of nonpenetrating filtering glaucoma surgery based on Krasnov´s sinusotomy have been described. Nonpenetrating trabeculectomy was proposed by Zimmermann in 1984 **36** and Arenas **37** first published the term ab-externo trabeculectomy in 1991. Fyodorov stressed on removing the corneal stroma behind the anterior trabeculum and Descemt´s membrane and termed this deep sclerectomy. **38** Stegmann et al. described a variant of nonpenetrating glaucoma surgery and termed it viscocanalostomy to emphasize the

importance of injecting high-viscosity sodium hyaluronate (Healon GV) into the Schlemm´s canal and the surgically created ostia as well as into the sclerectomy site under the superficial scleral flap. **39**

Further development of non-penetrating approaches included the use of implants at the surgical site in the late 1990s and early 2000s **40-42**. These implants were either absorbable (e.g. SK Gel, AquaFlow, HealaFlow) or non-absorbable (e.g. T-Flux). Most surgeons preferred to close the scleral flap loose to induce subconjunctival fitration in contrast to a watertight closure in viscocanalostomy, which could be named the first bleb independent non-penetrating glaucoma surgery. Although these non-penetrating surgical procedures for glaucoma effectively reduced IOP and lowered the incidence of postoperative complications compared with penetrating procedures such as trabeculectomy, comparative clinical studies indicated that IOP decreases more significantly with trabeculectomy, especially when used in conjunction with antimetabolites **43-49**.

Cannulation of Schlemm´s canal with a silk suture was described in 1960 for partial trabeculotomy **50**. A modified technique using a 6x0 polypropylene suture was later used for 360° trabeculotomy for treatment of congenital glaucoma **51**.

All previous non-penetrating glaucoma surgeries were able to reach two to three clock hours of Schlemm´s canal while a procedure treating the entire canal should be theoretically more effective. We reported on a technique using the 6x0 polypropylene suture for catheterization of the entire Schlemm´s canal and while withdrawning the suture a 10x0 polypropylene suture is installed in the canal and finally knotted under tension **52**. This is a very difficult and time consuming technique with a relatively high risk of mispassage of the 6x0 polypropylene suture into the anterior chamber or suprachoroidal space. Recent advances in technology have allowed surgeons to use a flexible microcatheter to access the entire length of Schlemm´s canal more atraumatically. This technique is called canaloplasty and seems to be the logical evolution to viscocanalostomy. **53,54**

3. Aims of the investigation

Based on previous studies, we hypothesized that in patients with open-angle glaucoma

- deep sclerectomy with different implants may be used to prevent collaps of the scleral lake and to lower the intraocular pressure

- a cause for failure in nonpenetrating glaucoma surgery could be goniosynechia

- canaloplasty effectively lower the intraocular pressure

- canaloplasty could be successfully performed without the use of an expensive commercially available catheter

-an intraoperative visualisation of the anterior chamber angle and the Schlemm´s canal is possible with a newly developed non-contact system

- viscocanalostomy and canaloplasty could be truly bleb-independent incisional glaucoma surgeries by re-establishing the natural outflow

and

- to develop surgical device / instrument for simplification and cost-cutting in canaloplasty

In order to answer the hypotheses above, data of our patients undergoing incisional nonpenetrating glaucoma surgery were analized.

The aim of this study were:

- to perform nonpenetrating glaucoma surgery with two different implants in open-angle glaucoma and analyzing postoperative outcomes

- to develop a new surgical technique for glaucomatous eyes with increased outflow resistance due to peripheral anterior synechiae and analyzing postoperative outcomes

- to perform iTrack-assisted canalolasty and analyzing the postoperative intraocular pressure lowering effect

- to develop a surgical technique and instrumentation for canaloplasty with placing a 360° tensioning suture into the Schlemm´s canal

- to develop an intraoperative non-contact system for visualisation of the anterior chamber angle and the Schlemm´s canal during canaloplasty

- to directly demonstrate the way of aqueous outflow after incisional glaucoma surgery and to boost the concept of bleb-independent incisional glaucoma surgery

4. Methods

4.1. Principle surgical techniques

The conjunctiva may be opened either at the fornix or at the limbus. A 5x5 mm rectangular or parabolic shaped scleral flap is created including one-third of the scleral thickness (about 300µm, depending on the total scleral thickness in the particular case). To be able to reach the Descemet´s membrane later during the dissection of the deeper scleral flap, the superficial scleral flap has to be prepared 1-1.5mm anteriorly into the perilimbal clear cornea. The initial incision is made with a no.11 stainless steel blade (or 15° slit knife for paracentisis) or a diamond knife. The flap dissection is made with a ruby blade or a bevel-up crescent knife (e.g. 1mm ultrasharp minidisc knife, Grieshaber Alcon, USA). Next deep sclerokeratectomy is performed by making a slightly smaller second flap then the superficial one, leaving a step of sclera at the sides allowing for a tighter closure of the superficial flap in case of an intraoperative perforation of the trabeculo-Descemet´s-membrane or intendet watertight closure for viscocanalostomy / canaloplasty. Then the deep scleral flap is dissected towards the cornea using ruby knife or crescent stainless steel knife. This dissection has to be made down to a depth very close to the choroids / ciliary body and carefully carried anteriorly keeping the level of dissection as constant as possible. In case of opening of the suprachoroidal space dissection is continued just a few scleral fibers above. The change of the direction of the scleral fibers to a limbusparallel bundle indicates the scleral spur. Just behind this the Schlemm´s canal is opened and unroofed. Care is taken to dissect the ostia of Schlemm´s canal clearly, because it is believed that this reduces the risk of collapse and scarring of these surgical ostia. A paracentisis / side port incision, which should be performed latest now is used to reduce intraocular pressure to very low level. This manoeuvre reduces the risk of perforation of the trabeculo-Descemet´s-membrane. The dissection was carried forward to expose a small segment of the Descemet´s membrane, creating a trabeculo-descemetic window of about 1-1.5mm. The corneal stroma can be blunt separated from the Descemet´s membrane e.g. with a sponge while the edges of the deep scleral flap are cut towards the cornea with the knife. In some cases the adhesion of Descemet´s membrane to the stroma is more tight. In these cases a blunt spatula or the mini crescent knife could be used with sweeping like limbusparallel motion to release these adhesions. This part of the surgery

is quite challenging because there is a high risk of perforation of the anterior chamber. The deep sclerocorneal flap is then removed by cutting in the clear corneal part with a delicate small and very sharp scissor (e.g. Vannas or Galand scissor). At this stage of the procedure, there should be percolation of aqueous through the remaining membrane evident. This can be checked also by applicating flourescein to the surgical area (socalled Rentsch-Seidel test). The amount of percolation is checked while drying the surgical area with a sponge. To increase the outflow facility the inner wall of the Schlemm´s canal is peeled partially including the endothelium and the juxtacanalicular trabecular meshwork. A specially designed forceps or an ordinary capsulorhexis forceps could be used. Occasional the inner wall of the Schlemm´s canal is fibrosed and an initial radial cut is necessary to be able to start the peeling. During the next step of the surgery ophthalmic viscosurgical device (OVD) is injected in the surgical ostia of Schlemm´s canal. To keep the intrascleral space (scleral lake) created patent, an implant or OVD may be used. The superficial scleral flap is then repositioned and sutured with 10x0 nylon or absorbable sutures. The superficial scleral flap is sutured as watertight as possible for forcing internal filtration into the Schlemm´s canal and then into the collector channels.

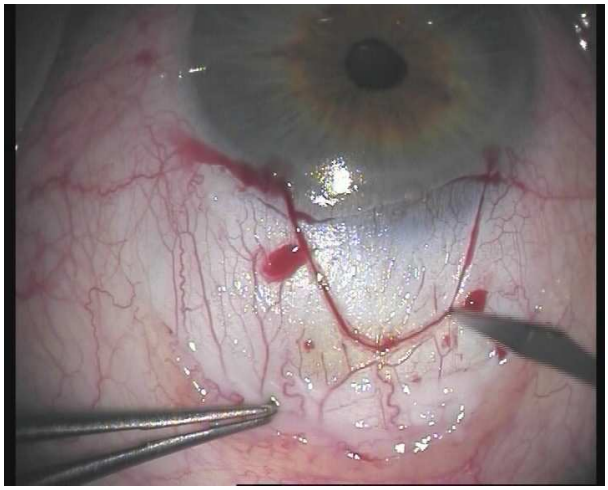

Fig.1 superficial scleral flap, note no diathermy of episcleral vessels is performed

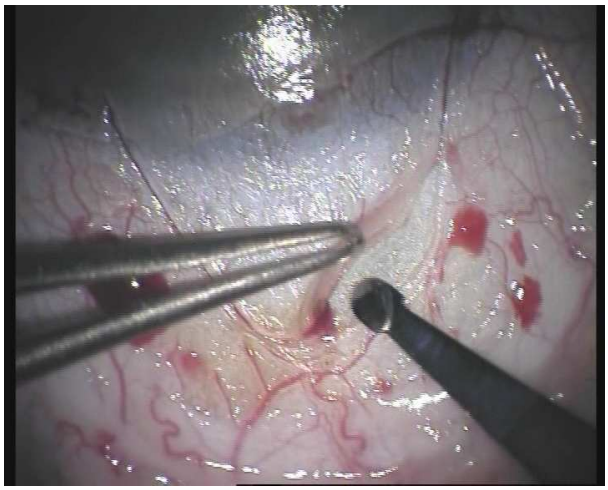

Fig. 2 preparation of the superficial scleral flap with a mini crescent knife

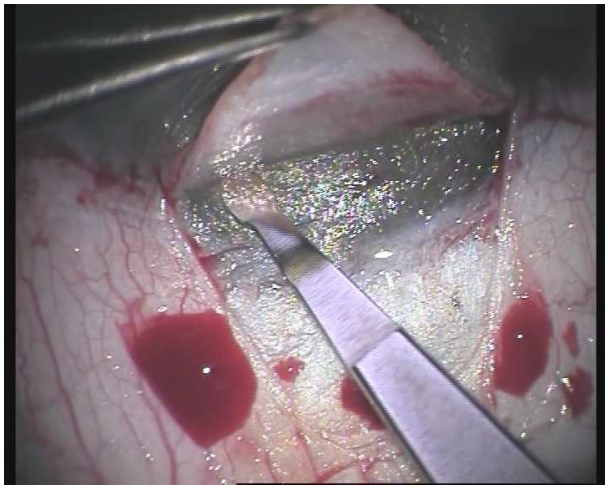

Fig. 3 dissecting the superficial scleral flap into the clear cornea

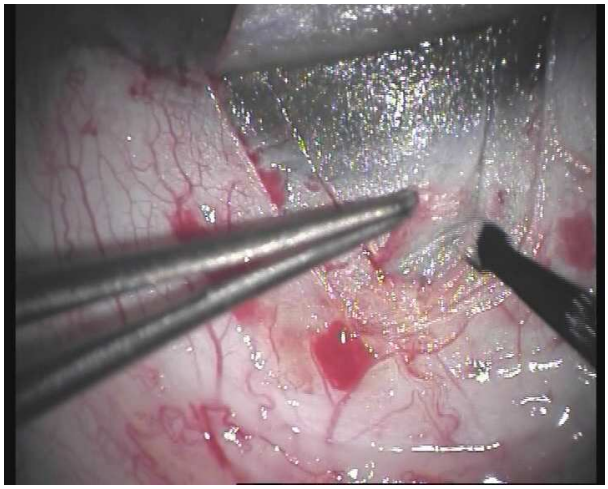

Fig. 4 preparation of the deeper scleral flap using a mini crescent knife, note the smaller size of the deeper scleral flap

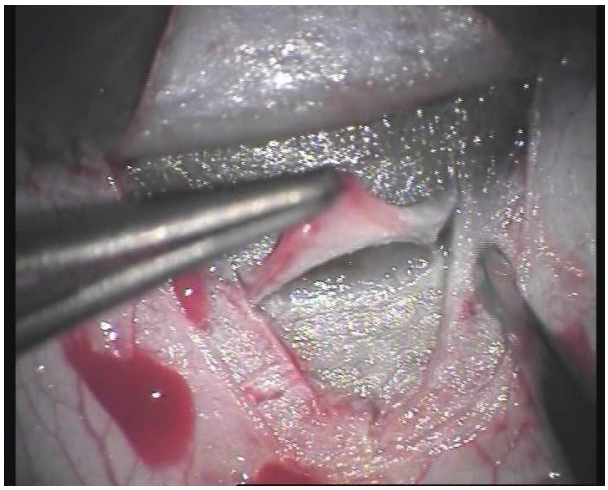

Fig. 5 opening of the Schlemm´s canal, note the colour difference in the scleral bed indicating the right depth of preparation

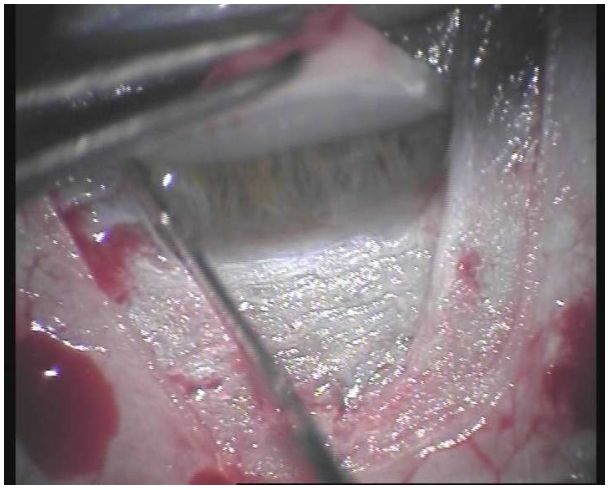

Fig. 6 enlarging the descemetic window for optimal exposition of the trabeculo-Descemetic membrane, note the percolation of aqueous humor without perforation of the membrane, iris is visible through the intact membrane

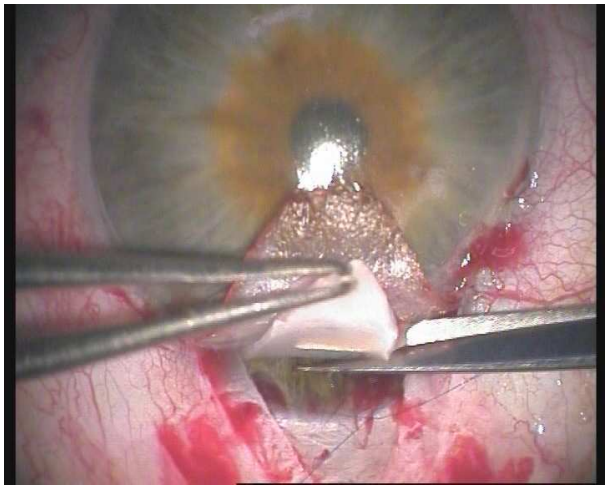

Fig .7 deep sclerectomy - dissection of the deeper scleral flap with Vannas scissors

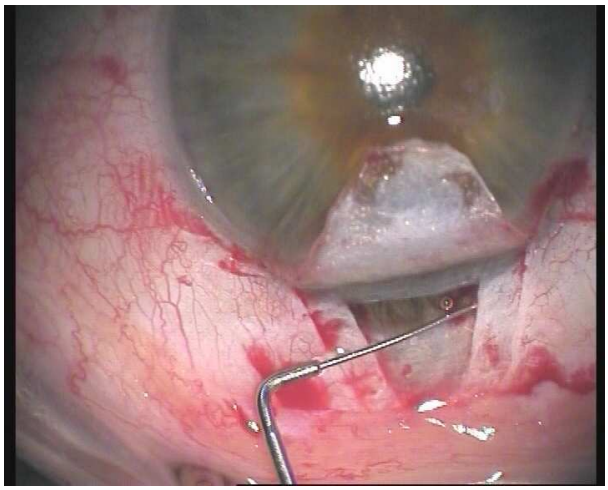

Fig. 8 viscocanalostomy with injection of OVD into the ostia of Schlemm´s canal with a special canula

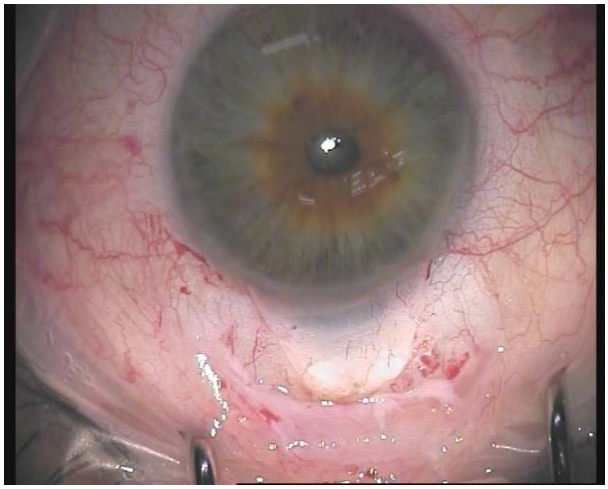

Fig. 9 watertight closure of the superficial scleral flap with 5-7 interrupted sutures (10x0 absorbable suture)

4.2. Deep sclerectomy with implants

To avoid secondary collapse of the scleral lake due to adhesion of the superficial scleral flap or contact of descemetic window, a space-maintainer implant is placed in the surgically created scleral bed. In deep sclerectomy we have used over the past decade SK-Gel (Corneal, France) and T-Flux (Carl Zeiss Surgical GmbH, Germany, fomer produced by Ioltech, France).

SK-Gel, has been used in deep sclerectomy to maintan the scleral lake is a reticulated hyaluronic acid implant of 500µm thickness. It was available in two sizes 3.5 x 3mm and 4.5 x 3mm. While the first one was designed for watertight closure the second was partially left outside the superficial scleral flap to increase the subconjunctival filtration. To provide

watertight closure we have used the smaller model. Fig. 10 The material is biocompatible and absorbable over a long period of several months, occasionally years. The advantage of this implant is that it occupies a large volume in the filtration area without swelling while allowing for a sufficient circulation of the aqueous humor and does not require suture fixation.

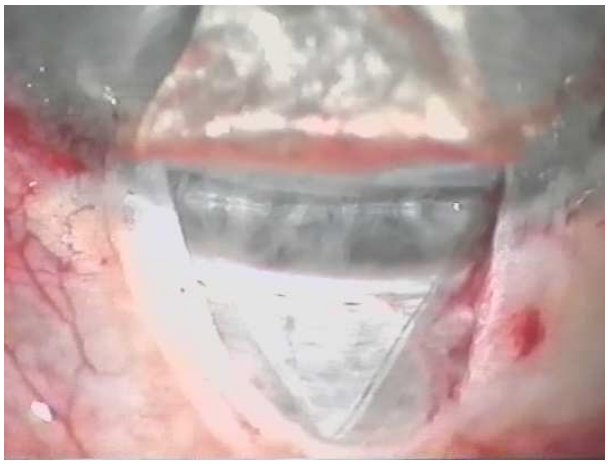

Fig. 10 SK-Gel in deep sclerectomy placed in the scleral bed

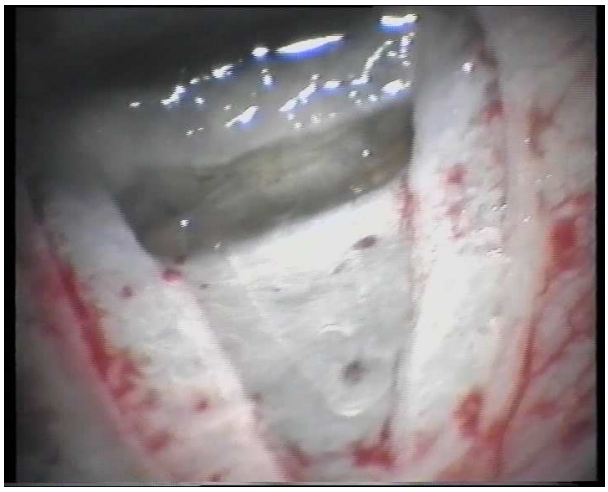

Fig. 11 T-Flux positioned in scleral bed, note both arms are implanted in the surgical ostia of Schlemm´s canal

A hydrophilic acrylic implant (T-Flux implant, IOL Tech Laboratories, France, now Carl Zeiss Surgical GmbH, Germany) which is non-absorbable, has been used to maintain the scleral lake and to prevent collapse of the surgical ostia of Schlemm´s canal. It is a T-shaped implant with a 4mm arm length, 2.75mm body height, and 0.1 - 0.3mm thickness. Each arm is inserted into the surgical ostia of Schlemm´s canal and the design is supposed to facilitate drainage into the Schlemm´s canal. Fig. 11 The implant was either secured with a 10x0 nylon

suture in the foot´s hole or the shape of the deep sclerectomy is adapted to the implant design to stabilize it in the scleral bed. A second hole in the anterior part of the T-Flux implant is designed to facilitate a goniopuncture (NdYAG laser descemetotomy) to the descemetic window to increase outflow postoperatively.

Initially an interindividual retrospective analysis was carried out to compare the outcome of both implants. For this retrospective study a decided approval of an IRB/Ethics Committee was not required. The study was in compliance with the Declaration of Helsinki. All patients had open-angle glaucoma and were treated with deep sclerectomy as intraocular pressure lowering approach. Indications for surgery were insufficient medical control of intraocular pressure, drug intolerance and compliance problems. Patients with failed previous glaucoma surgery were not excluded. If indicated, cataract surgery with implantation of an intraocular lens was performed simultaneously. Written informed consent was obtained from all patients for deep sclerectomy and, if planned, for phacoemulsification in one session.
For the study we analyzed four groups. First group included 13 patients with deep sclerectomy and implantation of SK-Gel. Second group included 5 patients with combined phacoemulsification, intraocular lens implantation and deep sclerectomy with SK-Gel. In the third group in 31 patinets deep sclerectomy with implantation of T-Flux was performed. And finally the fourth group phacoemulsification, intraocular lens implantation and deep sclerectomy with T-Flux was performed in 23 patients.
All patients were at least controlled on the preoperative day, postoperative day and 12 months postoperatively. Some patients had additional visits at 6 weeks and at 6 months postoperative. If the intraocular pressure at any postoperative visite was higher then the individual target pressure and medical treatment and/or NdYAG laser goniopuncture were ineffective a second antiglaucomatous surgery was performed. These patients were consiered as a drop-out and not included in the study.
Following parameters were recorded: intraocular pressure with Goldmann tonometry at each visit, amount of anitglaucomaous drugs, number of postoperative interventions, preoperative best corrected visual acuity, standard automated static white-on-white 30-2 visual field test with Humphrey-perimeter, cup-disc-ratio with Heidelberg Retina Tomograph.
The SSPS10.0 was used to compare the pre- and postoperative IOP measurements. As a post-hoc test the Turkey-HSD-test was used for unpaired samples. A p-value of less than 0.05 was considered statistically significant.

A second study with intraindividual comparison of both implants in combined phacoemulsification and nonpenetrating glaucoma surgery was performed.
For this retrospective study a decided approval of an IRB/Ethics Committee was not required. The study was in compliance with the Declaration of Helsinki. From January 2000 to December 2006, 321 eyes of 189 patients were treated with deep sclerectomy and simultaneous phacoemulsification in the Augenzentrum (eye centre) Recklinghausen, Germany. Out of this number, a total of 17 patients with 34 eyes were identified who had received the absorbable device SK-GEL 3.5 (Corneal Laboratories, Paris, France) in one eye and the nonabsorbable T-Flux device (IOLTECH Laboratories, La Rochelle, France) in the contralateral eye. The first of these 17 patients had his first eye operated in April 2002, the last patient his second eye in April 2006, so that postoperative IOP was followed for a maximum of 4 years and a minimum of 6 months. Assuming that both SK-GEL and T-Flux should decrease IOP to the same extent and that both have the same safety profile, the surgeon had no preference for any of the devices to be implanted. Indication for surgery was medically uncontrolled primary open-angle glaucoma defined by an intraocular pressure (IOP) higher than 21 mm Hg under maximal therapy; or progression of visual field defects in standard automated perimetry or progression of the optic nerve excavation with or without elevated IOP, intolerance to antiglaucomatous drops, low patient compliance, as well as a clinically relevant senile cataract. Additional criteria to include a patient in the analysis were bilateral combined surgery with a postoperative follow-up of at least 6 months and no previously performed glaucoma surgery. In case of small, microscopic perforations of the trabeculo-Descemet's membrane during surgery, the eye was nevertheless included, as long as the intervention was completed as a deep sclerectomy. Written informed consent was obtained from all patients for both phacoemulsification and deep sclerectomy in one session. Prior to consenting all patients were informed that a device would be implanted, that several kinds of implants exist, and that the type chosen depended on the surgeon's decision. Before surgery, all patients underwent the following examinations: best corrected visual acuity, full slit-lamp examination, fundus examination, gonioscopy, IOP with Goldmann applanation tonometer and standard automated static white-on-white 30° perimetry (Octopus 101, Peridata software, program G2, Haag-Streit, Switzerland). All combined operations were performed by one surgeon (G.S.). Normally both operations were carried out within 3 months, only in one patient the interval was longer than one year due to general health problems. Deep sclerectomy was made in the superior quadrant. A fornix-based conjunctival flap was created

and the sclera exposed. A one-third scleral thickness limbus-based scleral flap of approximately 5 x 4 mm in size was marked using a 15° slit knife. The flap was dissected up to 1 mm into perilimbal clear cornea using a bevel-up crescent knife (1-mm ultrasharp knife, Grieshaber, Alcon). This was followed by nasal and temporal paracenteses and a clear corneal phacoemulsification in the same site through a 2.8 mm incision under the superficial scleral flap. A foldable acrylic intraocular lens was placed in the capsular bag. After IOL placement, glaucoma surgery was continued: A triangular smaller flap of deep sclera was dissected, leaving only a thin layer of scleral fibers over the choroid. The base of the flap was extended up to 1 mm into clear cornea and down to the Descemet's membrane, unroofing Schlemm's canal. The deep flap was excised with scissors, carefully avoiding tears in the Descemet. The inner wall of the Schlemm canal and the juxtacanalicular trabecular meshwork was peeled off with Utrata forceps. After establishing that aqueous humour percolates through the trabecular-Descemet's membrane, either the SK-GEL or the T-Flux implant was placed into the scleral bed without a suture. Both arms of the T-Flux device were carefully inserted into the openings of Schlemm's canal. Both the superficial scleral flap and the conjunctiva were repositioned and tightly closed with 4-5 single absorbable sutures (10x0 Biosorb, Alcon). Postoperatively, all patients received topical corticosteroids (prednisolone acetate 1%) for at least 6 weeks. Postoperative visits were performed at one day, one week, one month, 3 months, 6 months, and depending on the date of surgery, for up to 4 years at least once a year. During these visits the following data were collected: IOP, best corrected visual acuity, existence of a filtration bleb, complications, and need for additional antiglaucoma therapy. Standard automated perimetry was carried out every 6 months. Follow-up was partly done by referring ophthalmologists outside the eye centre. At the end of the individual observation period, glaucoma surgery was considered a complete success when IOP was 21 mm Hg or less without antiglaucoma medication and a qualified success when IOP was 21 mm Hg or less with or without antiglaucoma treatment. The operation was considered a failure when IOP was higher than 21 mmHg, or when further glaucoma surgery was needed or when deterioration of the visual function was detected. However, small interventions like needle revision or laser goniopunctures would not have been judged as failures.

Unpaired sample two-tailed Student's t-test was used to compare the pre- and postoperative IOP measurements. A p-value of less than 0.05 was considered statistically significant.

4.3. Nonpenetrating glaucoma surgery with goniosynechiolysis ab-interno

The presence of peripheral anterior synechiae (PAS or goniosynechiae) usually prevents sufficient aqueous humor outflow, possibly leading to surgical failure. To prevent the need to convert to penetrating glaucoma surgery a release of this goniosynechiae is necessary.
We therefore developed a surgical technique for selective treatment of peripheral anterior synechiae during nonpenetrating glaucoma surgery. After recognizing the reduced outflow and the appearance of peripheral anterior synechiae the anterior chamber is filled by air through a paracentesis, followed by introduction of a fine iris spatula to the anterior chamber towards the surgery area. This is done under full visual control through the previously prepared Descemet´s window. Air injection is useful for stabilization of the anterior chamber. Then, the peripheral goniosynechiae are gently released by swinging the spatula under direct visibility. Air movement towards the irido-corneal angle, which now opens, provides successful gonisynechiolysis ab interno. In our experience this maneuver is usually followed by clear improvement of aqueous humor outflow through the trabecular meshwork.
The surgery may be completed either by injection of an ocular viscosurgical device (OVD) and/or through the introduction of an implant into the sclerectomy site.

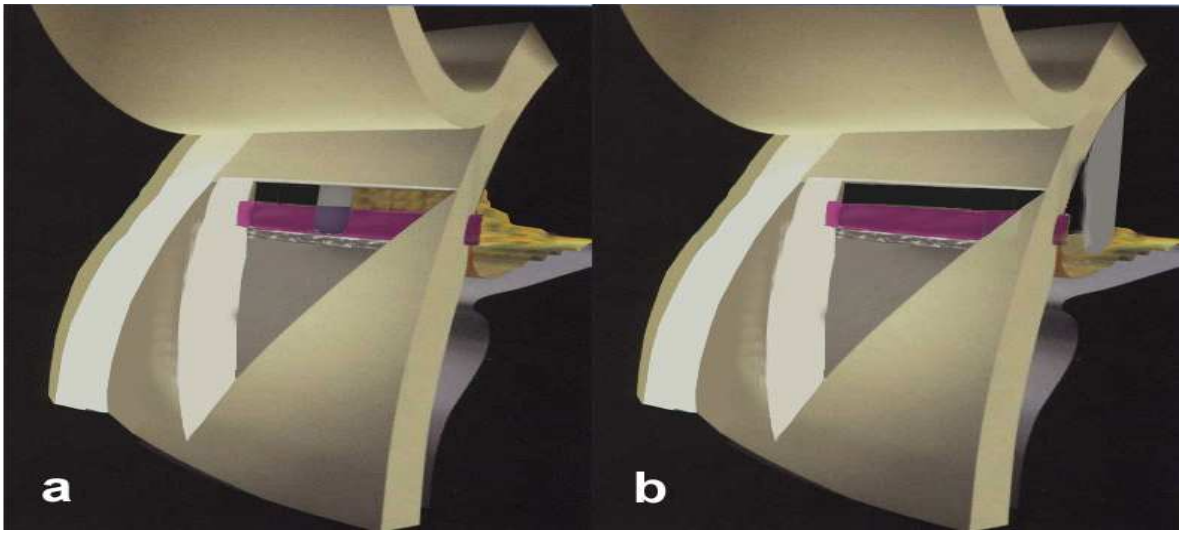

Fig. 12 illustration of the operative field in presence (a) and after treatment of peripheral anterior synechiae (b)

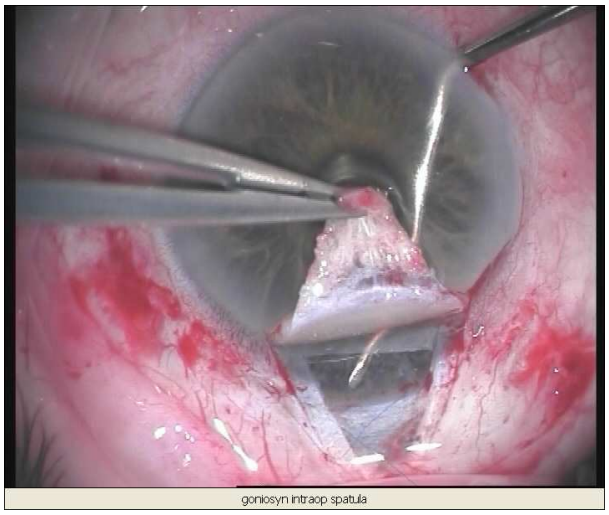

Fig. 13 Goniosynechiolysis ab interno using a spatula introduced through a paracentesis. Full visual control is given through the peripheral Descemet´s window

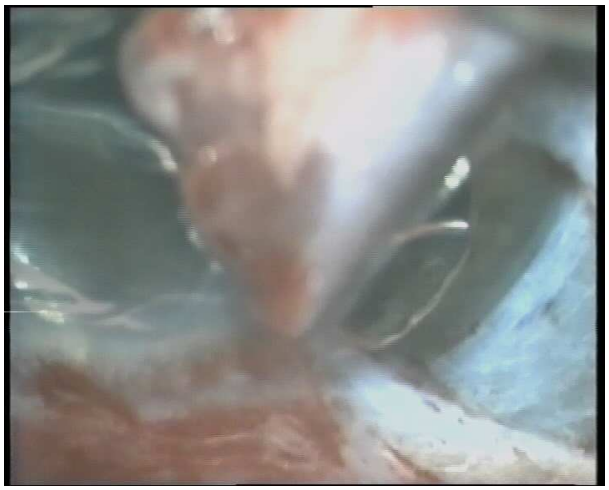

Fig. 14 Note the air bubble advancing into the angle after releasing the peripheral goniosynechia

We retrospectively reviewed medical records of patients who had been subject to nonpenetrating glaucoma surgery at our department between January 2000 and December 2006. 20 eyes of 16 patients (8 female, 8 male, mean age 70.0 y, range, 59 – 82) were identified who had been scheduled for a combined surgery with non-penetrating glaucoma surgery, namely deep sclerectomy with goniosynechiolysis ab interno, introduction of an adjuvant implant (SK-Gel, T-Flux or Healon GV), phacoemulsification and posterior chamber intraocular lens (IOL) implantation. In all cases the indication for the surgery was primary open angle glaucoma with peripheral anterior synechia (PAS, goniosynechia) at the superior part of the irido-corneal angle and cataract. In none of the eyes the target pressure could be achieved by conservative medical therapy because of insufficient efficacy or drug intolerance. The cataract was clinically relevant in all eyes and surgical removal was considered useful. A

minimum follow-up of 12 months was necessary to qualify for inclusion to this study. Following data were collected and analyzed: age, gender, pre- and postoperative intraocular pressure (IOP), pre- and postoperative glaucoma medication, type of glaucoma implant and complications during and after the surgery.

All data was collected and stored by the same person, using Microsoft Excel. The statistical analysis was performed with the program Bias for Windows (version 8.6.0, Frankfurt, Germany). Beside descriptive statistical analysis the paired T-test was applied for comparison of preoperative IOP vs. 12 months after the surgery. The significance level was set at 0.05.

4.4. iTrack assisted canaloplasty

Recently a new procedure called canaloplasty was introduced. **53** This procedure is intended to overcome some of the problems of the previous procedures with deep sclerectomy. The idea of implanting a fine tensioning suture into the Schlemm´s canal to enlarge the entire 360° of Schlemm´s canal should theoretically widen the intertrabecular spaces, preventing collaps of the canal, the surgical ostia and the descemetic window and herniation of the inner wall into the ostia of collector channels.

From March 2008 a microcatheter (iTrack, iScience, USA) for a canaloplasty became commercially available. This device has a 200µm diameter shaft with an atraumatic distal tip approximately 250µm in diameter. The device incorporate an optical fiber to provide an illuminated beacon tip to assist in surgical guidance. The illuminated tip was seen transsclerally during catheterization of Schlemm´s canal to identify the location of the distal tip of the microcatheter. The microcatheter has a lumen of about 70µm with a proximal Luer lock connector through which an OVD (i.e. Healon GV) or dye (i.e. trypan blue, indocyanin green, fluorescein) could be delivered. A tying forceps was used to manipulate the microcatheter and place the tip into the surgically created ostia of Schlemm´s canal. The microcatheter is advanced 12 clock hours within the canal while the surgeon observes the location of the beacon tip through the sclera. After the catheterization of the entire canal length with the microcatheter and with the distal tip exposed at the surgical site, a 10x0 polypropylene suture is tied to the distal tip and the microcatheter withdrawn, pulling the suture into the canal. The suture is cut from the microcatheter and then tied in a loop, encircling the inner wall of the canal using a slip knot or a looked four throw knot. To reduce risk of rupture of descemetic membrane and to facilitate a more effective tensioning of the 10x0 polypropylene suture the IOP was previously lowered through a paracentesis. The superficial scleral flap is repositioned and tightly closed with five to seven single absorbable sutures (e.g. 10x0 Biosorb, Alcon, USA). Now OVD is gently injected under the scleral flap to reduce the risk of bleeding into the sclerectomy site and to prevent scarring in this area. Anterior chamber is refilled with balanced salt solution to normal or slightly elevated IOP and conjunctiva is repositioned and fixed with two to four single absorbable sutures.

If additional injection of OVD into the entire canal is necessary is unclear while we could prove with catheterless canaloplatsy, that the procedure did work without the use of iTrack catheter and circumferential injection of OVD.

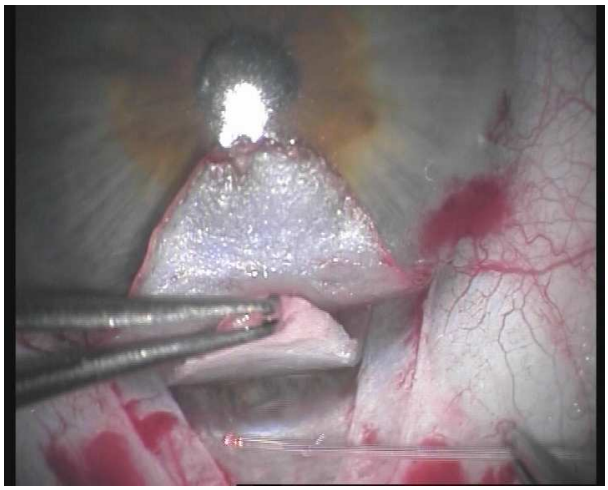

Fig. 15 iTrack microcatheter before insertion into the Schlemm´s canal

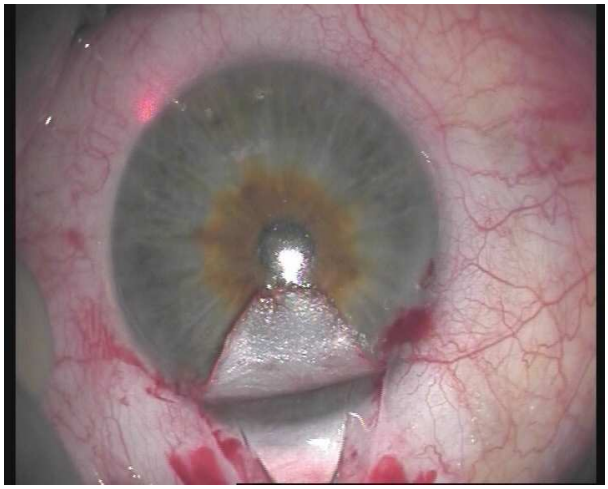

Fig. 16 red spot indicating the position of the iTrack microcatheter at 5 o´clock position in the Schlemm´s canal

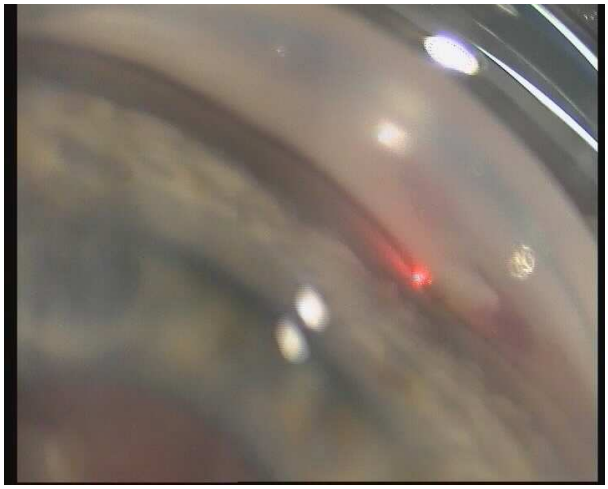

Fig. 17 intraoperative gonioscopic few with illumintated tip of the iTrack microcatheter (red dot) in the Schlemm´s canal, note the heavily pigmented trabecular meshwork in this eye

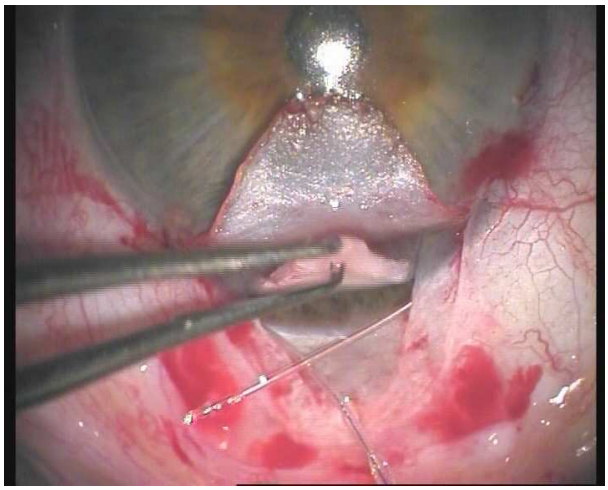

Fig. 18 after complete 360° cannulation of the schlemm´s canal

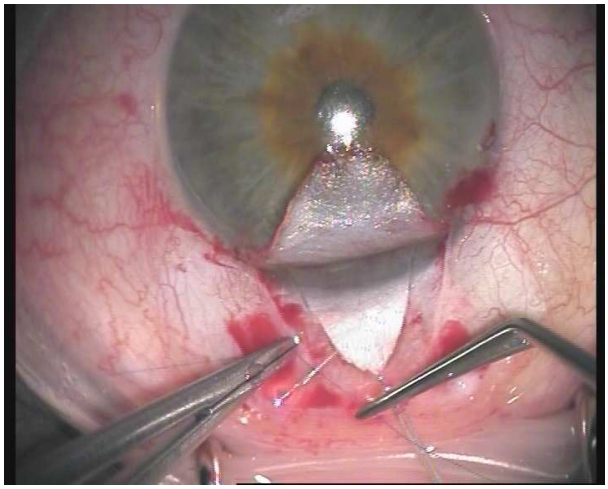

Fig. 19 10x0 Prolene tensioning suture is fixed to the microcatheter

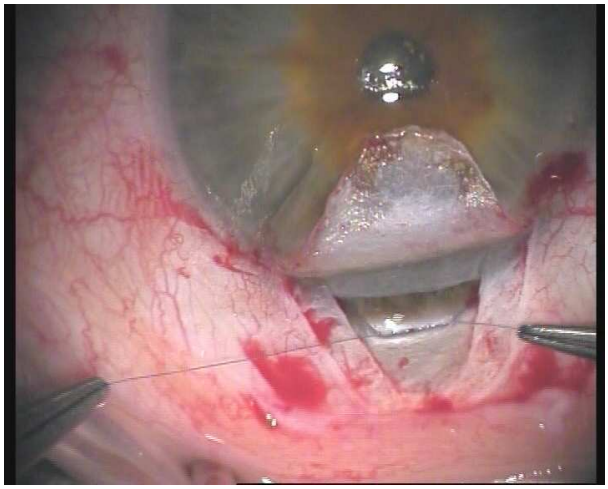

Fig. 20 after withdrawning of the microcatheter the suture is cut off and knotted under tension to pull the inner wall of Schlemm´s canal and the descemetic window towards the anterior chamber to prevent failure of the surgery due to collaps of these structures

To evaluate the effect of this procedure pre- and postoperative intraocular pressure and antiglaucomatous medical therapy in 73 consecutive eyes with open-angle glaucoma (including primary open-angle glaucoma, pseudoexfoliation syndrome and pigment dispersion) were analyzed with a minimum follow-up of 12 months. Eyes with previous glaucoma surgery or combined other procedures, like phacoemulsification with implantation of an intraocular lens, were excluded from this study. Only eyes with completed 360° cannulation of the Schlemm´s canal and placed tensioning suture were included. Even if the cannulation was completed eyes with obviuous intraoperative defect of the Descemet´s membrane with iris prolaps (macro perforation) were excluded.
For this retrospective study a decided approval of an IRB/Ethics Committee was not required. The study was in compliance with the Declaration of Helsinki. Indications for surgery were insufficient medical control of intraocular pressure, drug intolerance and compliance problems. Written informed consent was obtained from all patients for deep sclerectomy and canaloplasty.

4.5. Catheterless canaloplasty

If an iTrack assisted canaloplasty would reduce the intraocular pressure by using a commercially available, but very expensive catheter, is it possible to bypass the entire Schlemm´s canal with a self made catheter? Would this be also an effective pressure lowering procedure?

The cannulation of the Schlemm´s canal was described as early as 1960 by Smith and later mainly used for various techniques of trabeculotomy.

We have used a 6x0 polypropylane suture with self made blunt tip for the procedure. After deep sclerectomy as previously described, the ostia of schlemm´s canal are enlarged by injecting viscosurgical device (OVD) and the 6x0 polypropylene suture is introduced into the Schlemm´s canal. The suture is careful advanced 12 clock hours within the canal while the surgeon observes the resistance, possible iris movements etc. to anticipate possible misdirection. In case of increased resistance or perforation of the tip the polypropylene suture is introduced in the opposite direction. After the catheterization of the entire canal length with the polypropylene suture and with the distal tip exposed at the surgical site, a 10x0 polypropylene suture is tied to the distal tip and the 6x0 polypropylene suture withdrawn, pulling the 10x0 polypropylene suture into the canal. The 10x0 suture is cut from the 6x0 polypropylene suture and then tied in a loop, encircling the inner wall of the canal using a slip knot or a locked four throw knot. To reduce the risk of rupture of descemetic membrane and to facilitate a more effective tensioning of the 10x0 polypropylene suture the IOP was previously lowered through a paracentesis.

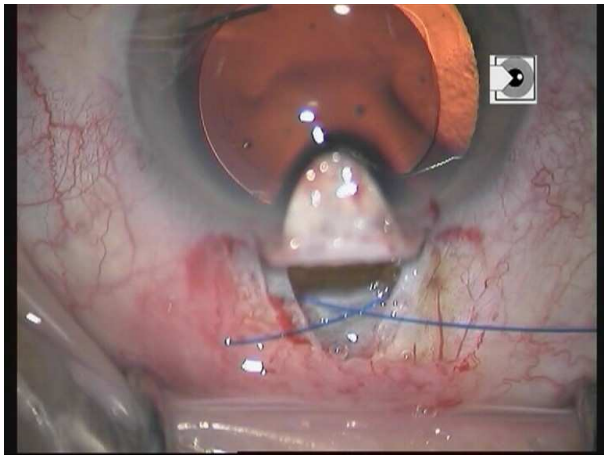

Fig. 21 after successful 360° cannulation of entire Schlemm´s canal with 6x0 polypropylane suture

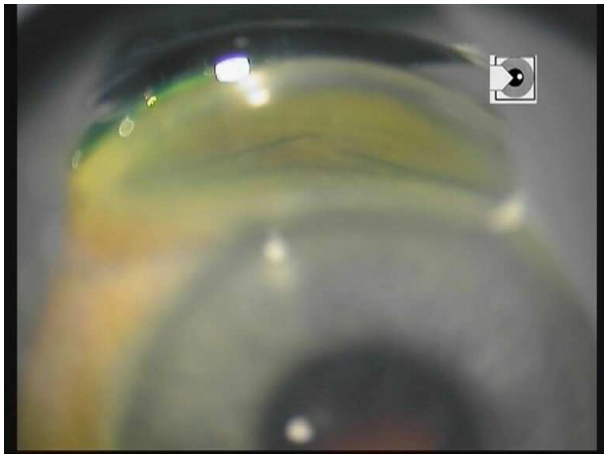

Fig. 22 intraoperative gonioscopic view with 6x0 polypropylane suture after 360° cannulation of the entire Schlemm´s canal

In the previously described manner then the superficial scleral flap is repositioned and tightly closed with five to seven single absorbable sutures (e.g. 10x0 Biosorb, Alcon, USA). Now OVD is gently injected under the scleral flap to reduce the risk of bleeding into the sclerectomy site and to prevent scarring in this area. The anterior chamber is refilled with balanced salt solution to normal or slightly elevated IOP and conjunctiva is repositioned and fixed with at least four single absorbable sutures.

4.6. Intraoperative optical coherence tomography

Intraoperative visualization with ultrasound biomicroscopy is an option, but to use this technique under sterile conditions is quite difficult and needs at least the surgeon´s one hand and the divece placed on the eye is relatively large. This makes simultaneous ophthalmic surgery impossible.

Recently an anterior segment optical coherence tomograph was introduced (Visante, Carl Zeiss Meditech, Germany). To evaluate the use of an intraoperative online anterior segment optical coherence tomography (OCT) imaging system for modern glaucoma surgery we used a specially designed microscope mounted anterior segment optical coherence tomography device (modified Visante, Carl Zeiss Meditech, Germany). This device uses 1300µm wavelength and should be therefore suitable for anterior segment visualization including superficial intrascleral structures like Schlemm´s canal.

Initial tests with a Visante OCT were performed in patients after deep sclerectomy to visualize the scleral lake and intrascleral implants. Schlemm´s canal could not be shown in this setting.

Then the modified microscope mounted technology was used for different ophthalmic surgeries but especially for glaucoma surgery to visualize the anterior chamber angle and, if possible, the canal of Schlemm.

Fig. 23 intraoperative setting with the OCTAASS system during a canaloplasty procedure, simultaneously recording surgical video and video of optical coherence tomography, note surgeons hands are free for bimanual manipulations

4.7. Flow test after incisional glaucoma surgery

There is still controversy about the mechanism of aqueous humor outflow / resorption in intraocular pressure lowering glaucoma surgery. Many studies have been conducted to prove postoperative outflow pathway after glaucoma surgery using high resolution ultrasound or optical coherence tomography. But all these techniques could only interpret indirect postoperative findings like bleb formation, suprachoroidal space formation etc. The flow of aqueous humor could not be proven in this way. We therefore looked for a way to visualize the aqueous humor. Different dyes are used in ophthalmic surgery but only trypan blue is approved for intarcameral use during cataract surgery.

Trypan blue is a vital stain used to selectively colour dead tissues or cells blue. It is a diazo dye. Live cells or tissues with intact cell membranes are not coloured. Since cells are very selective in the compounds that pass through the membrane, in a viable cell trypan blue is not absorbed; however, it traverses the membrane in a dead cell. Trypan blue is derived from toluidine, that is, any of several isomeric bases, $C_{14}H_{16}N_2$, derived from toluene. Trypan blue is so-called because it can kill trypanosomes, the parasites that cause sleeping sickness. Trypan blue is also known as tryptane blue, diamine blue and Niagara blue.

We have used trypan blue filling of the anterior chamber prior to intended cataract surgery in eyes after incisional glaucoma surgery. After creating a side port incision the anterior chamber was filled with trypan blue and then the intraocular pressure was increased by pressing on the eye. Then for about 60 seconds the anterior segment was observed to check for appearance of the dye. All cases were recorded and afterwards analyzed. After creating a clear corneal tunnel the dye was evacuated while filling the anterior chamber with ophthalmic viscosurgical device. Standard phacoemulsification and implantation of an intraocular lens was performed. Between December 2008 and December 2009 twelve eyes with previous incisional glaucoma surgery have been tested in this way.

4.8. Development of new surgical device / instrument for canaloplasty procedure

After intensive experience with different nonpenetrating glaucoma surgery procedures and canaloplasty some changes in the used instruments and devices became obvious to the author.

First after comparision of the results of catheterless canalolasty and iTrack assisted canaloplasty with circumferential injection of OVD no difference in results in regards to intraocular pressure lowering effect of the procedure was noted. But injection of OVD into the small lumen of the Schlemm´s canal could potentially cause rupture of the wall of Schlemm´s canal leading to detachment of Descemet´s membrane.
On the other hand the illuminated tip of the iTrack catheter is an important improvement to the procedure and increases the safety of the 360° cannulation of the Schlemm´s canal.

Finally the high costs of the commercially available iTrack catheter prevents the widespread use. Also the necessity of an external additional light source (iLumin) connected to the unsterile distal end of the iTrack catheter was found a drawback of the procedure.

A well-known international company (DORC Internation, The Netherlands), experienced in the development of ophthalmic microsurgical devices and instruments, was contacted and asked to develop a new simplified catheter for canaloplasty and for improved instrumentation. Co-work was started in spring 2009 with first development of a lumenfree catheter with reduced diameter connected to a standard light source for vitreoretinal surgery. Since this type of light source was found to be not available in all ophthalmic surgery centers performing glaucoma surgery, as a next step a device with an integrated sterile light source was developed.

For iTrack assisted canaloplasty most surgeons use a standard tying forceps for manipulation of the catheter. This may be ineffective and difficult especially during complicated manipulation during the catheterization. The grasping surface and instability of the forceps during manipulation of the relatively thick catheter was found to be insufficient. The company was asked to produce a prototype of a special designed forceps and this was tested and improved.

5. Results

5.1. SK-Gel versus T-Flux in nonpenetrating glaucoma surgery

5.1.1. Interindividual comparision of SK-Gel versus T-Flux in nonpepetrating glaucoma surgery

Out of the 72 patients included in this study 65 could be followed after 12 months. In the only SK-Gel group 10 patients and in the phaco+SK-Gel group 5 patients could be controlled after 12 months. In the only T-Flux group 28 patients from initially 31 and in the phaco+T-Flux group 22 patients from initially 23 could be controlled at the 12 months visit. All patients not included at 12 months were excluded because of a second incisional glaucoma surgery during the follow-up period.
The mean preoperative intraocular pressure was 18.4±5.5mmHg and after 12 months 13.1±3.8mmHg. At no point a significant difference between the subgroups was recognized.

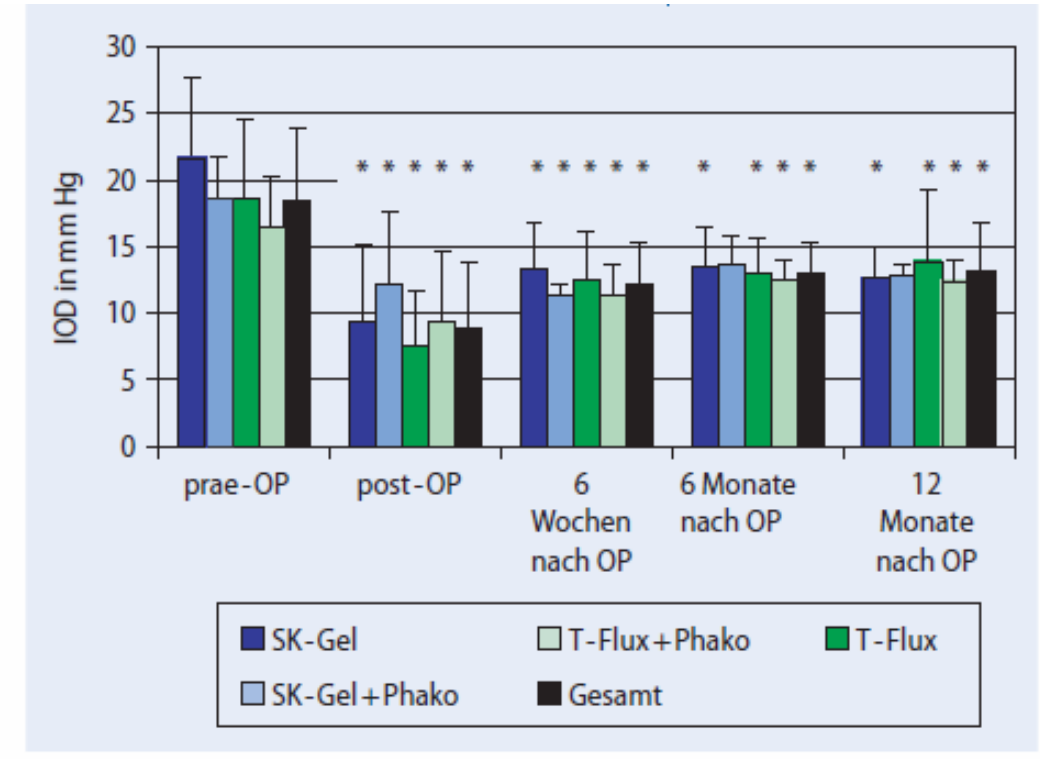

Fig.24 intraocular pressure preoperative, day 1, after 6 weeks, 6 months and at final visit 12 months postoperative in all subgroups and overall

Medical antiglaucomatous therapy was significant reduced from preoperative 2.3±1.3 (n=72) to postoperative 0.2±0.6 (n=65) after 12 months.

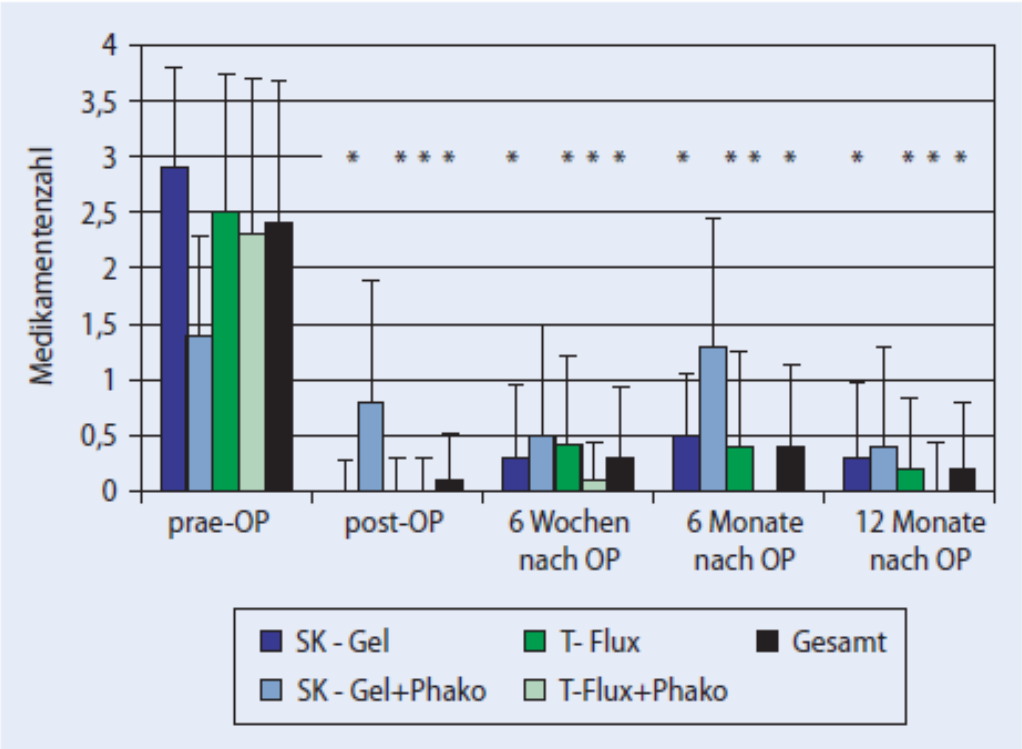

Fig. 25 medical antiglaucomatous therapy preoperative, day 1, after 6 weeks, 6 months and at final visit 12 months postoperative in all subgroups and overall

	Prä OP	Post OP	6 Wochen post OP	6 Monate post OP	12 Monate post OP
SK-Gel	2,8±0,9 (n=13)	0,0±0,3[a] (n=13)	0,3±0,6[a] (n=11)	0,5±0,5[a] (n=6)	0,3±0,7[a] (n=10)
SK-Gel+Phako	1,4±0,9 (n=5)	0,8±1,1 (n=5)	0,5±1,0 (n=4)	1,3±1,1 (n=3)	0,4±0,9 (n=5)
T-Flux	2,5±1,2 (n=31)	0,0±0,3[a] (n=31)	0,4±0,8[a] (n=22)	0,4±0,8[a] (n=14)	0,2±0,6[a] (n=28)
T-Flux+Phako	1,9±1,4 (n=23)	0,0±0,3[a] (n=23)	0,1±0,3[a] (n=19)	0,0±0,0[a] (n=12)	0,0±0,4[a] (n=22)
Gesamt	2,3±1,3 (n=72)	0,1±0,4[a] (n=72)	0,3±0,7[a] (n=56)	0,4±0,7[a] (n=35)	0,2±0,6[a] (n=65)

Fig.26 mean medical antiglaucomatous therapy preoperative, day 1, after 6 weeks, 6 months and at final visit 12 months postoperative in all subgroups and overall

a = significant reduction

Complications were minor and included one eye with postoperative positive Seidel test (SK-Gel group) and one eye with cataract formation requiring surgery at 6 months after the deep sclerectomy with T-Flux. Transient ocular hypotension with intraocular pressure below 7mmHg were found in 28 eyes (39%). In only one eye a revison with resuturing of the scleral flap was necessary.

	Direkt post OP	6 Wochen post OP	6 Monate post OP	12 Monate post OP
Gesamt	n=72	n=71	n=67	n=65
– Druck senkende OP	1	4	2	4
– Goniopuncture	0	6	3	14
SK-Gel	n=13	n=13	n=11	n=10
– Druck senkende OP	0	2	1	1
– Goniopuncture	0	1	0	2
SK-Gel+Phako	n=5	n=5	n=5	n=5
– Druck senkende OP	0	0	0	0
– Goniopuncture	0	0	0	2
T-Flux	n=31	n=31	n=29	n=28
– Druck senkende OP	0	2	1	2
– Goniopuncture	0	5	2	6
T-Flux+Phako	n=23	n=22	n=22	n=22
– Druck senkende OP	1	0	0	1
– Goniopuncture	0	0	1	4

Fig.27 descriptive statistics of number of postoperative interventions, including ND-YAG goniopuncture and second antiglaucomatous surgery

5.1.2. Intraindividual comparision of SK-Gel versus T-Flux in nonpenetrating glaucoma surgery

Of the 17 patients eligible for case analysis under the above mentioned criteria, 3 were male and 14 female with a mean age of 77.1 +6.8 years (± standard deviation). The overall mean follow-up period was 26.5 +16.4 months in the SKGEL group and 27.2 +16.0 months in the T-Flux group, with a range from 6 to 48 months in both groups. The mean preoperative IOP was 20.6 +7.3 in the SKGEL group and 19.9 +7.2 mm Hg in the T-Flux group and hence considered comparable ($p > 0.05$).
In both groups the surgical intervention led to a clinically relevant result: In the SKGEL group the mean preoperative IOP decreased to a mean final IOP of 14.8 +5.3 mm Hg (-5.8 mm Hg or -28.1%), and in the T-Flux group to 14.7 +3.3 mm Hg (-5.2 mm Hg or -26.1%). The difference between both groups is statistically not significant ($p > 0.05$). IOP results over the full observation period in both groups are displayed in Figure 28.

Time	SKGEL		T-Flux	
	n	IOP ± SD (mm Hg)	n	IOP ± SD (mm Hg)
Preop.	17	20.6 ± 7.3	17	19.9 ± 7.2
D 1	16	12.8 ± 8.3	17	9.2 ± 6.2
M 1	17	13.9 ± 4.2	17	12.8 ± 4.3
M 3	17	12.4 ± 4.4	17	12.7 ± 3.1
M 6	17	12.4 ± 3.3	17	12.2 ± 2.9
M 12	14	14.6 ± 5.0	14	14.4 ± 3.3
M 24	10	14.4 ± 5.7	11	15.6 ± 2.8
M 36	8	14.8 ± 5.0	8	14.9 ± 3.8
M 48	4	12.3 ± 3.8	4	12.8 ± 2.9

Fig. 28 preoperative and postoperative intraocular pressure in SK-Gel group versus T-Flux group

Four eyes in each group were followed up for up to four years, three eyes in both groups for at least 6 months. After implantation of T-Flux or SKGEL the curves of IOP measurements in both groups were similar in the long-term (Fig. 29).

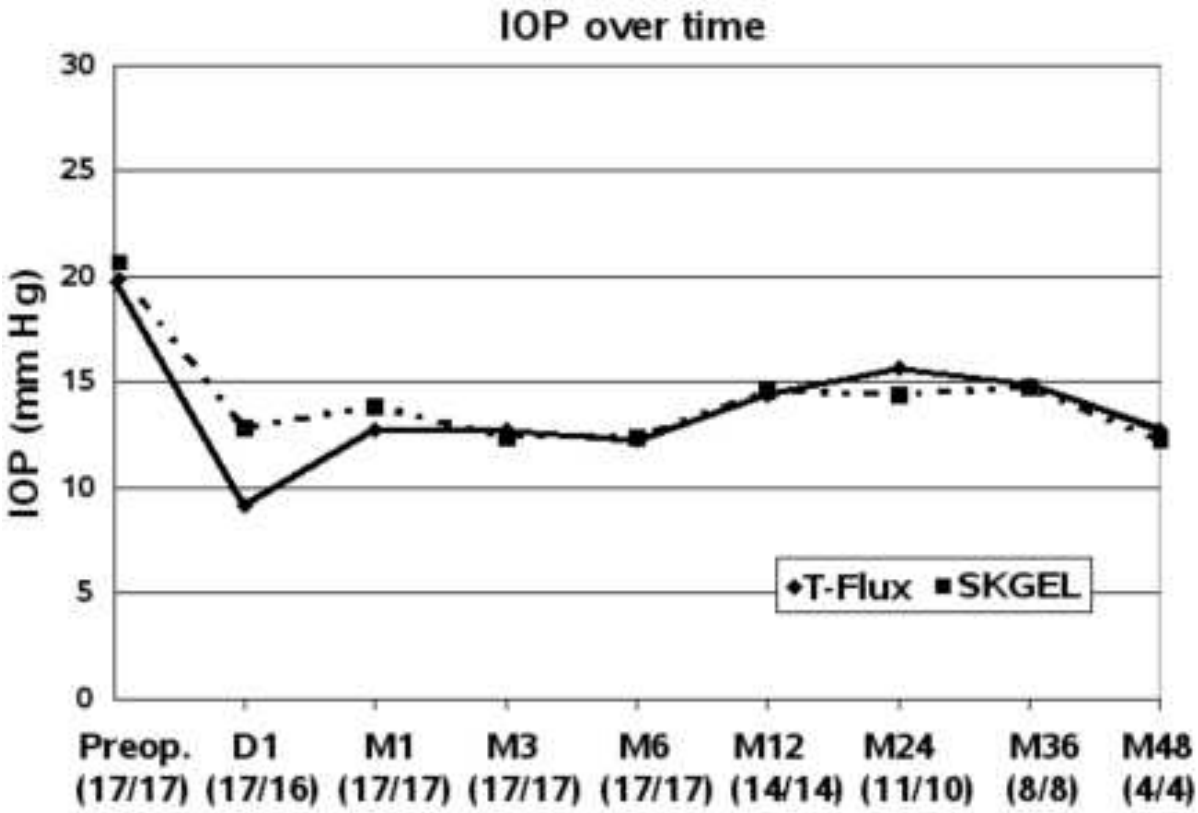

Fig. 29 intraocular pressure over postoperative period after deep sclerectomy with SK-Gel versus T-Flux

The mean number of antiglaucoma medications before surgery was 2.0 +0.8 substances in both groups, with a minimum of one substance and a maximum of 4 substances. With both implants the need for antiglaucoma treatment decreased after surgery to 0.3 +0.7 medications at the final visit. In other terms, only 3 eyes per group required a permanent treatment after surgery, with a maximum of 2 substances. 2 eyes, one in each group, needed a transitory therapy with betablocker drops for a short time, and no further therapy was necessary in these eyes afterwards.

At the end of the observation period a qualified success (IOP < 21 mm Hg with or without treatment) was found in all 17 eyes with the T-Flux device (100%), and in 16 eyes with a SKGEL implant (94.1%). Complete success (IOP < 21 mm Hg without treatment) was achieved in 14 T-Flux eyes (82.4%) and in 13 SKGEL eyes (76.5%). One eye in the SKGEL

group has to be considered a failure, as cyclokryocoagulation was inevitable 6 months postoperatively due to a strong increase in IOP which was refractory to any medical therapy. Complications during glaucoma surgery were: microperforation of the trabeculo-Descemet's membrane in 2 eyes in the T-Flux and in one eye in the SKGEL group. However, in all cases the deep sclerectomy with implantation of a device could be completed as planned. Apart from the usual non-serious intraocular inflammatory signs, in the early postoperative phase a massive hyphema was observed in one eye with a T-Flux implant, possibly due to a hypertensive crisis the patient suffered. The bleeding stopped spontaneously and was managed by anterior chamber irrigation. In the other group one eye with SKGEL had longstanding corneal erosion with corneal edema which might have been caused by the cataract operation. However, cataract surgery was done in all 34 eyes without any intraoperative complication. In all patients a foldable acrylic posterior chamber IOL was implanted. In the observation period no other severe complications related to the IOL occurred. There was no indication that visual acuity was worse in the eyes of these patients than in those who had a simple phacoemulsification without a combined deep sclerectomy in our centre. In some eyes an opacified posterior capsule was treated uneventfully by Nd: YAG laser capsulotomy. Visual field results did not reveal clinically relevant deteriorations apart from some fluctuation of scotomas, i.e. no increase in scotomas were detected in follow-up visual field tests. In one eye which was implanted with an SKGEL device and that had well-controlled IOP without antiglaucomatous therapy, a sharp increase in IOP was noted after approximately 6 months. The rise in IOP was due to neovascular glaucoma secondary to a central vein occlusion. Despite full medical treatment, the IOP remained uncontrolled with values over 30 mm Hg, and a decision was made to perform a cyclokryocoagulation, after which the IOP remained at low values throughout the following 4 years of observation without any treatment. This was the only case where surgical intervention was necessary after glaucoma surgery. No laser goniopuncture, no needling or other procedures, e.g. antimetabolite injections, were required. Most eyes had no filtering bleb, and only a few had a flat or diffuse filtering bleb.

5.2. Deep sclerectomy with goniosynechioysis ab interno

All surgeries were performed by the same experienced glaucoma surgeon. With the presented surgical technique, a selective treatment of peripheral anterior synechiae was possible during nonpenetrating glaucoma surgery by direct visual control through a trabeculo-Descemet's window in 19 of 20 eyes (95%). In one case the surgery was converted to phaco-trabeculectomy with iridectomy because of intraoperative rupture of the Descemet's window. All other cases were operated on uneventfully. To avoid secondary collapse of the superficial flap, SK-Gel was implanted in 10 eyes (50%), T-Flux in 6 eyes (30%) and Healon GV (AMO, Ettlingen, Germany) in 3 further eyes (15%). Further glaucoma surgery was not necessary in any case during the follow-up period.

The mean preoperative IOP was 20.3 ±5.2 mmHg (median 20, range 12 – 30) on 2.4 ±1.0 medication (median 2, range 0 – 5). The course of intraocular pressure was as follows day 1: mean 11.7 ±6.1 mmHg (median 11, range 2 – 21); week 1: mean 13.2 ±6.7 mmHg (median 13.5, range 2 – 24); month 1: mean 12.7 ±3.5 mmHg (median 12, range 6 – 21); month 3: mean 14.2 ±4.2 mmHg (median 14, range 6 – 21). One year postoperatively the mean IOP was 15.3 ±3.3 mmHg (median 16, range 10 – 20) on 0.6 ±1.0 medication (compared to preoperative IOP: p=0.004).

A postoperative IOP of ≤21mmHg was achieved in 17/19 eyes (89.5%) 3 months, and in 12/19 eyes (63.2%) 12 months postoperatively without medication. In the remaining 10.5% (month 3) and 36.8% (month 12) an addition of a mean of 0.3 and 0.6 medication respectively achieved an IOP ≤21mmHg or the target pressure.

One year after the surgery the mean IOP lowering was 5.0 ±6.4 mmHg (median 4, range: -18 to +8). The mean number of medication was lowered from 2.4 (median 2) before the surgery to 0.63 (median 0) one year postoperatively.

5.3. iTrack assited Canaloplasty

Out of more the 200 successfully performed iTrack assisted canaloplasties since March 2008 seventythree eyes were eligible for case analysis under the above mentioned criteria. The mean preoperative intraocular pressure was 23.8±5.6 mmHg. At the 12 months visit the mean intraocular pressure was 13.8±2.4 mmHg. Antiglaucomatous medication preoperative was 2.2±1.0 drugs and dropped to 0.23±1.0 drugs at 12 months. Additional ND-YAG laser goiniopuncture had to be performed in 4 eyes. In 32 eyes postoperative hyphema of more then 1mm was noted. In the remaining 41 eyes at least some erythrozytes or a minimal hyphema was noted. None of the cases required an anterior chamber lavage. In 19 eyes a circumscribed peripheral descemetic detachment was noted, sometimes with blood in this cavity. In none of these cases this complication caused a reduced best corrected visual acuity in the postoperative period. Absorbtion of the OVD and/or blood could take up to several months. Two eyes had transient choroidal detachment. Non of these eyes developled a maculopathy. Overall no serious complication was noted. No eye required additional glaucoma surgery during the first 12 months postoperative period.

All eyes had a postoperative intraocular pressure of less then 20mmHg at 12 months follow-up visit. But seven eyes had a postoperative intraocular pressure of 19mmHg at that time. Seven eyes required postoperative medication. Of these eyes four had an intraocular pressure of 19mmHg and three eyes were 18mmHg or less.

Qualified success rate after 12 months with regards to a postoperative target pressure of 18mmHg was 90.4%. Complete success rate was 86.3%.

5.4. Catheterless Canaloplasty

Since September 2006 we have performed 156 deep sclerectomies with 6x0 polypropylene assisted canaloplasty with successful placing 10x0 tensioning suture. Preparation of a blunt tipped slightly curved 6x0 polypropylene suture was possible. After initial success with relatively easy passage of the suture, encqouraging us to continue and improve the technique, most cases did require several attemps to pass the suture 360°. If the suture could not pass in one direction a second attempt was made in the opposite direction. In case of sudden stop, indicating a mispassage into a large collector channel or a fibrosed Schlemm´s canal, the 6x0 polypropylane suture was left in place and a second 6x0 polypropylene suture was advanced into the canal. In same cases additional maneuvers like benting the tip of the suture like with iTrack assisted canaloplasty was necessary.

In 15 eyes a misdirection of the suture with perforation into the anterior chamber or the suprachoroidal space was noted. But in all of these eyes finally the 360° cannulation could be completed and a 10x0 polypropylene suture placed.

In another 26 eyes the cannulation of the Schlemm´s canal could not be completed. In these cases SK-Gel was implanted in the sclerectomy site. Finally in 3 eyes macro perforation with conversion to penetrating glaucoma surgery with peripheral iridectomy occurred. In these eyes no implant could be placed under the superficial scleral flap.

In two eyes with aphakia and open angle glaucoma secondary to pseudoexfoliation syndrome we have used catheterless canaloplasty in combination with implantation of a posterior chamber intraocular lens with intrascleral haptic fixation. **54** This technique we have developed for eyes with insufficient or no capsular support. Because this technique does not require anterior chamber angle haptic fixation or iris fixation it is especially usefull in glaucomatous eyes.

5.5. Intraopertive optical coherence tomography

With permission of the local ethics committee we have performed optical coherence tomography in more then 80 ophthalmic surgeries, including nonpenetrating glaucoma surgery. In all cases we have initially looked for Schlemm´s canal. In none of the cases the canal was clearly visible preoperatively. In all 8 cases of canaloplasty with intraoperative use of optical coherence tomography the Schlemm´s canal was clearly visible during the cannulation with iTrack catheter. In these cases we have used the iTack catheter to inject ophthalmic viscosurgical device to enlarge the lumen of the Schlemm´s canal. This was clearly visible, but in 3 eyes the lumen of the canal did enlarge less dramatically due to microperforation of the inner wall of Schlemm´s canal.
After placing the tensioning suture in all 8 eyes with canaloplasty a distension of the inner wall of schlemm´s canal could be observed, indicating successful distension. Distension was checked next to the sclerectomy site, at 3, 6 and 9 o´clock position. Distension was in all cases highest next to the sclerectomy site, but same at 3, 6 and 9 o´clock position. Distension suture within the lumen of the Schlemm´s canal was visible in all cases.
No device related complication occurred. The device was easy to use with the help of a trained assistance.

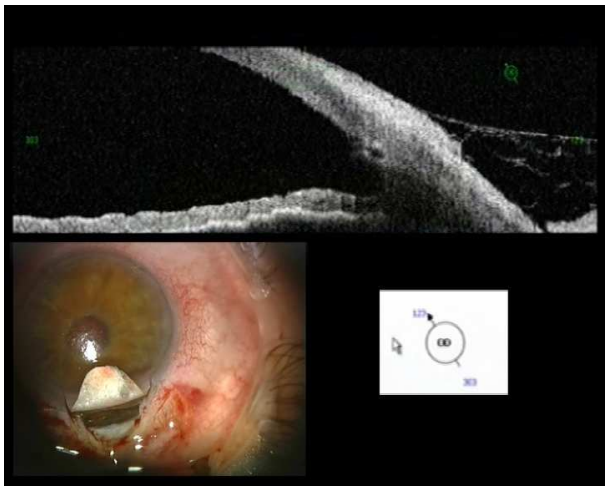

Fig. 30 intraoperative optical coherence tomography next to surgical site
note enlarged Schlemm´s canal with good distension and tensioning suture at the inner wall

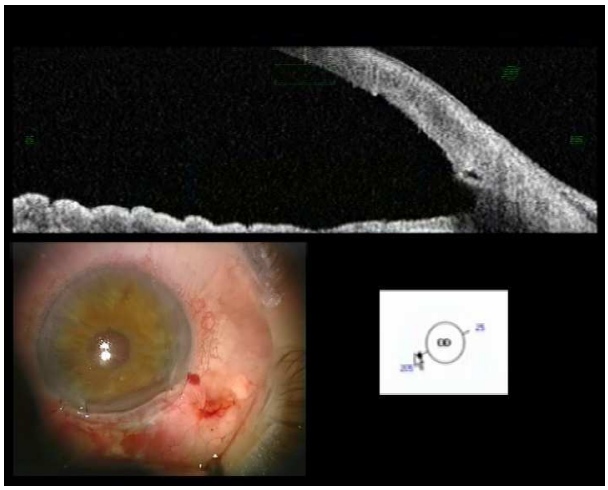

Fig. 31 end of surgery. Intraoperative optical coherence tomography at 9 o´clock
note enlarged Schlemm´s canal with good distension and tensioning suture at the inner wall

Fig. 32 intraoperative optical coherence tomography prior to injection of ophthalmic viscosurgical device

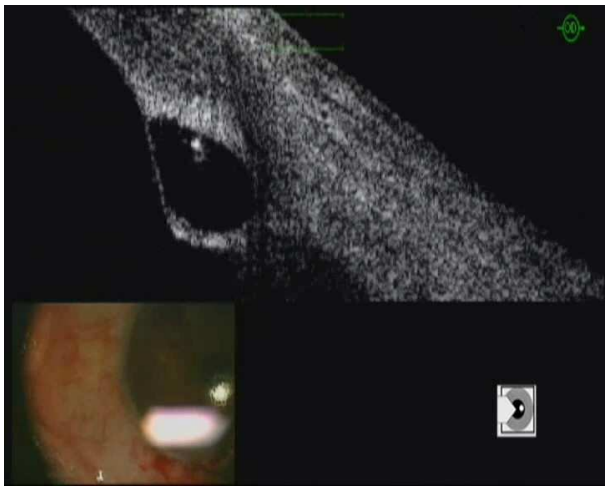

Fig. 33 intraoperative optical coherence tomography after injection of ophthalmic viscosurgical device,
note dilatation of Schlemm´s canal lumen, wire of iTrack visible inside the lumen

5.6. Flow test after incisional glaucoma surgery

Five eyes after previous trabeculectomy have been operated. While two eyes showed a typical pattern of cystic conjunctival bleb, two eyes showed no sign of external filtration and only one eye did show a formation of a subconjunctival bleb with diffuse subconjunctival filtration. Five eyes after deep sclerectomy did show a diffuse subconjunctival filtration with at least in two eyes signs of mixed resorption with trypan blue filling of episcleral veins.
Two eyes after successful canaloplasty showed no sign of subconjunctival filtration but filling of episcleral veins with tryptan blue.
In all eyes with external appearance of trypan blue this occurred in the surgical site or next to the surgical area. No complication related to this flow test occurred.

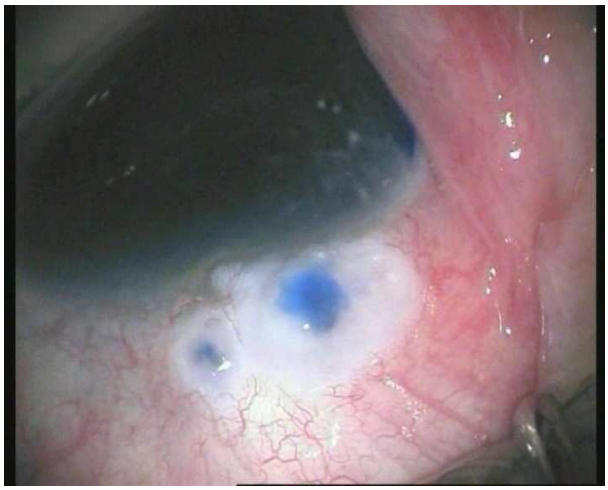

Fig. 34 filling of an avascular cystic bleb after trabeculectomy with no sign of subconjunctival filtration Preoperative intraocular pressure 30mmHg

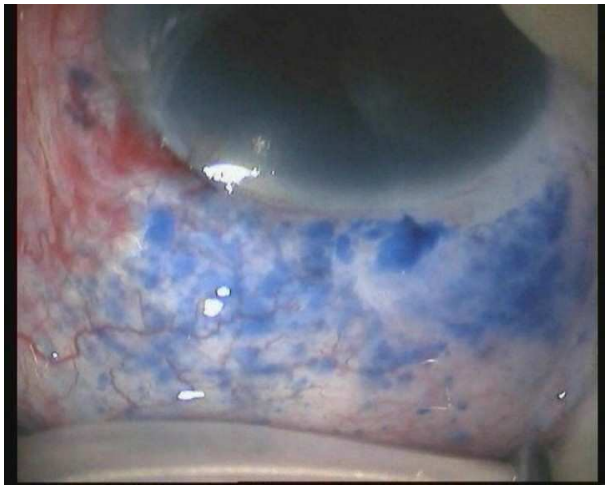

Fig 35 diffuse subconjunctival leackage of tryptan blue after successful trabeculectomy, indicating diffuse subconjunctival filtration, preoperative intraocular pressure 12mmHg

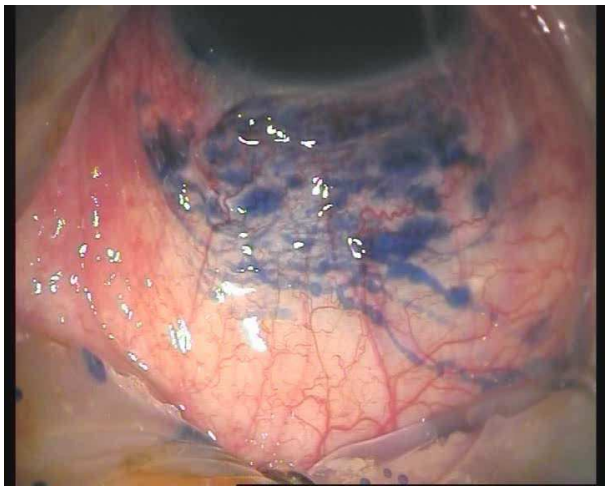

Fig. 36 note intravasal filling of episcleral veins and spots of subconjunctival leckage as a sign of mixed mechanism of aqueous humor drainage after successful deep sclerectomy with SK-Gel, preoperative intraocular pressure 13mmHg

Fig. 37 note light filing of episcleral veins with trypan blue esp. at left side, wit no sign of subconjunctival filtration after successful canaloplasty, preoperative intraocular pressure 12mmHg

5.7. Glaucolight and Scharioth´s glaucoma forceps

After more then 12 months of processing and testing a new catheter for canaloplasty was developed and is now commercially available.
This device is called Glaucolight. It is a specially designed lightfiber with an atraumatic tip design for smooth transfer through the Schlemm´s canal. Its outer diameter is only 150µm. This small diameter allows flexible 360° followability of the Schlemm´s canal. The material is ductile. Bending the tip reduces the risk for misdirection of the catheter during the passage through Schlemm´s canal. It has an integrated battery powered red LED light source. The LED is switched on simply by pressing a contact on the case. The battery lasts for several hours. The illuminated tip indicates the position of the catheter in the Schlemm´s canal during the passage. The special suture fixation notch at the distal end of the fiber assures a firm fixation of the stretching-suture in combination with minimizing injury effect of the suture knot to the wall of Schlemm´s canal during the withdrawn. The clip attached to the light source is used to fix the catheter to the sterile patients drape next to surgical area during the procedure.

Fig. 38 Glaucolight (DORC, The Netherlands) with integrated battery powered LED light source and clip

Fig. 39 pressing at sensor of the sterile case for illuminating the fiber

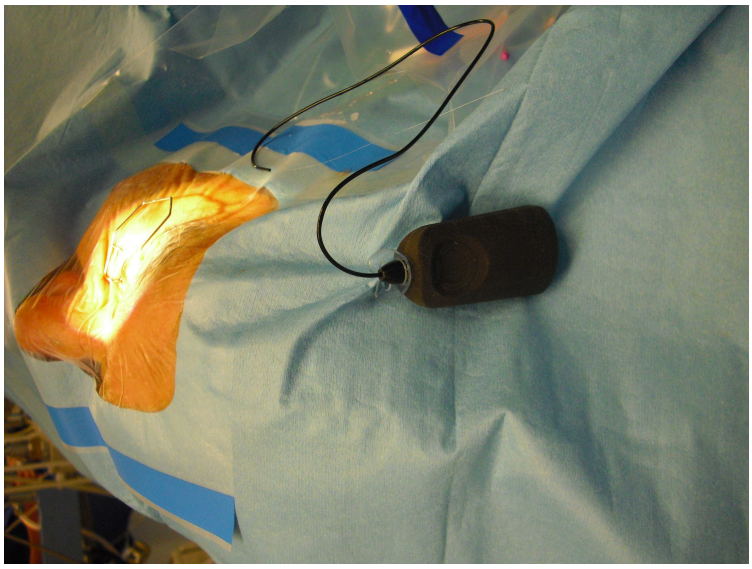

Fig. 40 Glaucolight attached to the sterile patients cover just next to the surgical area

During the testing period 22 eyes have been operated with this new device and in all cases a successful 360° cannulation could be performed. No complication related to the device occurred. The passage through the Schlemm´s canal was found smooth and atraumatic.

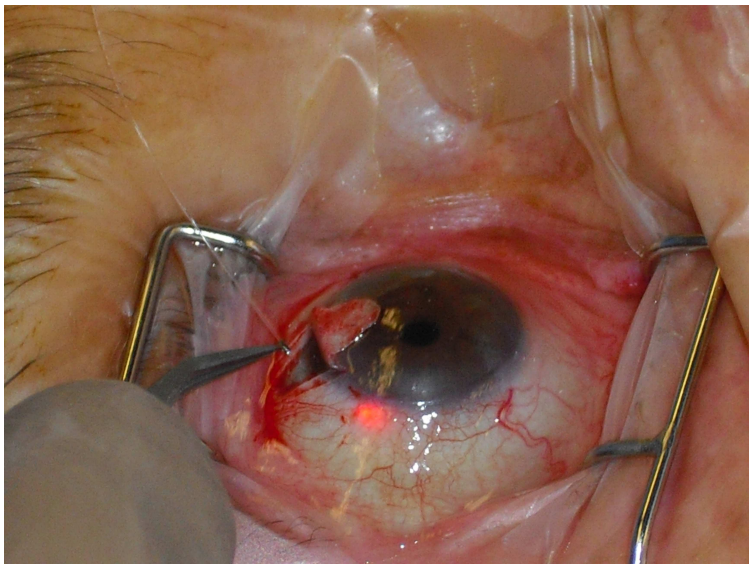

Fig. 41 manipulating the Glaucolight with the new designed forceps within the Schlemm´s canal, note the intense transscleral illumination of the Glaucolight tip

The forceps developed for modern glaucoma procedures is a modified tying forceps with an enlarged tip with a groove for easier and safer grasping of the catheter during cannulation. This atraumatic tip could also be used during the procedure for atraumatic but safe manipulation of the scleral flap.

The distal end of the forceps has a special marker for blunt marking of a parabolic 5x5mm superficial scleral flap. The special design of this marker allows observation of the episcleral vessels during marking to select an adaequate area for dissection. This reduces the need for diathermy during flap preparation.

Fig. 42 New glaucoma forcpes with special designed tip for better control of glaucoma surgery fibers and atraumatic grasp of ocular tissue, parabolic marker at distal end for marking the superficial scleral flap

6. Discussion

Deep sclerectomy has an effect on filtration, hence its success is vulnerable to scarring and will be positively influenced by the use of antimetabolites and theoretically by a device implanted within the scleral bed. These so-called space maintainers are either absorbable implants which degrade within several months or nonabsorbable persisting devices. Judging from our years of experience with implantation of the devices in glaucoma surgery, we assumed that both the absorbable and the nonabsorbable implant lower IOP approximately to the same level. Therefore we had no preference for a certain device. Also, there were no special indications or circumstances where we expected one device to perform better than the other. We compared SK-Gel versus T-Flux in different patients with and without combined phacoemulsification. Deep sclerectomy was performed with a relatively good success rate at 12 months postoperative and with not difference between both implants. Therefore, over the years we accumulated some patients who required glaucoma surgery on both eyes and who happened to be implanted with both devices. Our retrospective analysis of the patients who received SK-GEL in one eye and T-Flux in the contralateral eye (second study) bore the opportunity to compare both devices regarding their IOP-lowering effect. The intraindividual comparison limits the effect of confounding variables, e.g. the influence of individual variations in the inflammatory reaction or fibrotic response after deep sclerectomy. Moreover, all eyes underwent simultaneous phacoemulsification, precluding a systematical bias because of a possible IOPlowering effect of phacoemulsification. Only very few studies with an intraindividual control have been performed up to now and only few studies have a comparably long follow-up with implants in deep sclerectomy. Furthermore, to our knowledge there are only two studies comparing the efficacy of absorbable versus nonabsorbable implants. The results showed no difference in IOP in all 4 groups. And Mansouri et al. **55** compared a nonabsorbable polymethylmethacrylate implant versus an absorbable collagen device for a mean observation period of 20 months. The effect on IOP and the rate of complications were the same in both groups. Theoretically, in the long term absorbable implants like SK-GEL might work less well than nonabsorbable devices. The implantation of a nonabsorbable device could create an intrascleral space by permanently preventing adhesion between the scleral flap and the scleral bed. Dahan et al. **56** carried out ultrasound biomicroscopy (UBM) investigations and

confirmed a permanent intrascleral space surrounding the T-Flux implant. On the other hand, the rationale for the absorbable implant is that it can maintain the surgically created intrascleral space for several months during the period of maximum postoperative inflammation and scarring. It is assumed that by the time the implant dissolves, the healing process is already completed. **57** Chiou et al. **58** investigated the scleral space by UBM several months after implantation of a collagen implant. They observed that the implant dissolved slowly, within 6 to 9 months, and was replaced by new autologous scleral tissue, yet leaving a tunnel. The lifespan of SK-GEL is not clear but it is estimated to be at least as long as for the collagen implant. Marchini and associates **59** were unable to determine the lifespan of the SK-GEL as it is nearly undetectable by UBM, in contrast to a collagen implant. In glaucoma revision surgery we extracted a hardly dissolved SK-GEL device which we had placed there more than one year before. In our patients, preoperative mean IOP was lower than in some of the studies cited. Ten patients in the SK-GEL group and 12 patients in the T-Flux group had IOP meeting the criteria of a "qualified" success even before surgery. In these cases, indications for surgery were borderline IOP and progression of glaucoma despite an IOP below or equal to 21mm Hg. Of those patients with a preoperative IOP <21 mm Hg, there was one patient in each group who still required medical glaucoma therapy after surgery. Setting a stricter cut-off IOP of <16 mmHg to define success, 10 patients (58.8%) in the T-Flux® group and 9 (52.9%) patients in the SK-GEL group showed a qualified success and 9 (52.9%) and 7 patients (41.1%) respectively, a complete success. We consider these results as being comparable for both groups. Concerning complications during surgery, we could finish all interventions as planned; none of them had to be transformed to a trabeculectomy despite microperforations of the trabeculo-Descemet's membrane. Postoperatively we did not see any iris incarceration. During the postoperative period there was no need for goniopuncture or needling, and no antifibrotic agents were employed, unlike in other studies. **60** In one patient a cyclocryocoagulation was performed for an uncontrollable rise in IOP. Most of our patients did not require postoperative antiglaucoma treatment; in less than 20% per group a permanent medical treatment was necessary after surgery. Phacoemulsification can be done simultaneously in glaucoma patients suffering from additional cataract, avoiding the need of a second surgery. However, the contribution of lens removal to the IOP-lowering effect of a combined cataract-glaucoma surgery is unclear. Due to the fact that all eyes underwent phacoemulsification in our study, all eyes did benefit from a possible IOP-lowering effect. A cataract extraction without filtering surgery may result in a decrease of IOP in healthy eyes and to a lesser extent in some eyes with glaucoma. **61**

Lens extraction may cause an increase in the depth of both the central and the peripheral anterior chamber.

Our next study analyzed the effect of a novel approach in nonpenetrating glaucoma surgery called canaloplasty. To our knowledge this study is one of the largest controll of canaloplasty alone in a very selected population of open-angle glaucoma patients with no previous intervention. Thus we operated on virgine eyes, this should be the very best selection for this type of surgery we expected a high success rate regarding 360° cannulation and intraocular pressure lowering effect.
Only very few information were available about this technique when we started our study. **52**
The intraoperative experience and the postoperative course met our expectations. There was additional intraocular pressure lowering effect compared to classic deep sclerectomy and reduced need for postoperative intervention.
Our results were comparable to results of other studies on iTrack assisted canaloplasty. **52, 53**

As an unreported postoperative finding almost all eyes had some amount of intracameral bleeding. We believe that this is a result of the tensioning suture which prevents collapse of Schlemm´s canal in the early postoperative period during a possible hypotonic phase. The reflux bleeding from episcleral veins to collector channels, Schlemm´s canal and finally into the anterior chamber might indicate a successful surgery. Thus it should not be considered a complication.

Main drawback of iTrack assisted canaloplasty are the high costs. Therefore we tried to perform a canaloplasty with the help of a blunt tipped 6x0 polypropylane suture. A very similar approach has been used for 360° trabeculotomy in congenital dysgentic glaucoma. **50**
We found it possible to cannulate the entire Schlemm´s canal with this technique even if it required a relatively long learnig curve and until the tip of the suture was not exposed on the opposite site it was unclear wether the suture took the right way or perforated and went suprachoroidal. This problem has been addressed by a previous publication. **61**
In our experience a thin catheter with illuminated tip but without lumen would be sufficient to perform canaloplasty with high success rate.

Result of ten years intensive work in the field of nonpenetrating glaucoma surgery and the cooperation with an innovative company was the development of a new improved fiber for

canaloplasty and a special designed forceps. Limited experience with the new device suggests at least the same success rate for canaloplasty as with iTrack. Special features of this new device (Glaucolight, DORC, The Netherlands) seem to improve the safety of this surgerical approach and to reduce surgical time and costs of the procedure.
Further studies are needed to compare both catheters and the effect of OVD 360° injection within the Schlemm´s canal.

Optical coherence tomography with a modified time domain OCT with 1300µm wavelength mounted to a standard operating microscope was performed during various ophthlomosurgical procedures. Handling was relatively easy with the help of our assisting staff. During glaucoma surgery new information regarding the size of the lumen of Schlemm´s canal and the distension were found. Main advantage of this new technology was the non-contact approach in contrast to competting high resolution ultrasound imaging. Additionally, the surgeon hands were kept free for intraopertive surgical manipulations. We expected to see the Schlemm´s canal prior to manipulations. This was not possible in our study. We believe that an improved system using spectral domain and possibly a slightly different wathlength would increase resolution and could make the untouched Schlemm´s canal visible. This could lead to a new understanding of the pathology of open-angle glaucoma since there is some evidence that in some patients with open-angle glaucoma the Schlemm´s canal might be collapsed. These patients should then preferably be treated with canaloplasty.

There is still controversy about the possible mechanism of aqueous outflow after incisonal glaucoma surgery. All previous studies used indirect methods to analyze the outflow after nonpenetrating glaucoma surgery. Optical coherence tomography and high resolution ultrasound biomicroscopy cannot directly show the aqoueous flow.
To our knowledge this study using intracameral trypan blue after incisional glaucoma surgery is the first study proving aqueous outflow long term after incisional glaucoma surgery. Our expectation that in failed trabeculectomy with cystic bleb no filtration was detectable was met, whereas in a succeful trabeculectomy a nice diffuse subconjunctival filtration zone was proven. Surprisingly in deep sclerectomy with SK-Gel implantation and intraoperative watertight flap closure we found signs of mixed resortion, eighter subconjunctival and intavasal. In our explanation a postoperative swelling of the implant may cause in some cases an insufficient closure of the superficial flap resulting in subconjunctival aqueous humor flow

and resorption. This seems not to cause failure in all cases. But the risk for late fibrosis and late failure due to stopped subconjunctival filtration should be theoretically increased.
Our findings regarding canaloplasty were new. Here in two eyes we could prove exclusive drainage through the natural outflow system via Schlemm´s canal, collector channels and episcleral veins with no sign of subconjunctival filtration suggesting that it could be possible to re-establish the natural outflow.

7. Conclusion

In conclusion, the results of our retrospective analysis confirm the results of other studies, in that in open-angle glaucoma a deep sclerectomy with implantation of a device in combination with phacoemulsification lowers IOP in a clinically relevant way over a long period.
We proved that the effect of deep sclerectomy with implantation of a device is independent from the absorbable or nonabsorbable property of the implant, while the risks of a combined surgery are few when performed by an experienced surgeon.

Peripheral anterior synechiae could cause failure in nonpenetrating glaucoma surgery. We developed a new technique for release of goniosynechiae in the area of the descemetic window and could prove that with this new surgical technique deep sclerectomy could be performed successfully in case of peripheral anterior synechiae.

Canaloplasty is a new effective bleb-independent intraocular pressure lowering-procedure with a very low complication rate. Longer follow-up is needed to understand the long term success rate and effects of the tensioning suture on intraocular tissue.
The commercially available catheters for canaloplasty (Glaucolight, DORC, The Netherlands and iTrack, iScience, USA) reduces surgical time and improves the safety of the procedure. But canaloplasty can be performed even without the need of this expensive device with the help of a self made catheter (blunt tipped polypropylene suture 6x0). The procedure was successful even without injection of ophthalmic viscosurgical device throughout the entire Schlemm´s canal. Our new forceps simplifies intraoperative manipulations.

Intraoperative optical coherence tomography is a new technique to visualize intraocular structures with very high resolution. This technology could be helpful in modern glaucoma surgery as well as other ophthalmic surgical techniques (i.e. refractive intraocular implants, corneal surgery, femtosecond-assisted cataract surgery). We could show that this new system is able to image intraoperative the Schlemm´s canal and distension of the inner wall of Schlemm´s canal during canaloplasty. Further development of this system with higher resolution and improved recording speed is recommended. Faster computer technology could lead to three dimensional imaging with new options in ophthalmic surgery and diagnostics.

To prove the concept of bleb-independent glaucoma surgery we have developed the intraoperative flow test with trypan blue. With this test the outflow of aqueous humor after incisional glaucoma surgery was directly visualized. At least in some eyes we could prove the bleb independent character of canaloplasty.

Nonpenetrating bleb independent glaucoma surgery is possible, has a very low complication rate and could lead to re-establishing the natural outflow in patients with open-angle glaucoma.

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9. Awards

Video Award at the Video Film Festival during 15th Congress of German Ophthalmic Surgeons, 2002, Nuernberg, Germany
for
Non-penetrating Glaucoma Surgery in Case of Goniosynachiae

and

Video Award at the Video Film Festival during XXVIII Congress of the European Society of Cataract and Refractive Surgeons, 2010, Paris, France
for
Optical Coherence Tomography Assisted Anterior Segment Surgery

10. Publications

List of publications directly related to the subjects of the Thesis:

1. Wiermann A. Zeitz O. Jochim E. Matthiessen L. Wagenfeld P. Galambos G. **Scharioth G.** Mathiessen N. Klemm K. : A comparision between absorbable and non-absorbabale scleral implants in deep sclerectomy (T-Flux and SK-Gel). *Opthalmologe.* 2007;104(5):409-414 **(IF: 0.791)**

2. **Scharioth G.B.** Pavlidis M., Sutureless intrascleral posterior chamber intraocular lens fixation", *Journal Cataract and Refractive Surgery* 2007 Nov., 33(11):1851-4. **(IF: 2.497)**

3. Schreyger F. **Scharioth G.B.** Baatz H. : SK-Gel implant versus T-Flux implant in the contralateral eye in deep sclerectomy with phacoemulsification: Long-term follow-up. *The Open Ophthalmology Journal.* 2008;2:57-61

4. Mirshahi A. **Scharioth G.B.** : Non-penetrating glaucoma surgery with goniosynechiolysis ab interno: a surgical technique. *European Journal of Ophthalmology.* 2009;19 (2):147-150 **(IF: 0.887)**

5. **Scharioth G.B.** Craven R. : Trabecular Bypass Surgery. in *Surgical Techniques in Ophthalmology – Glaucoma Surgery*, 304-307, Jaypee Brothers Medical Publisher Ltd.

6. **Scharioth G.B.** : From Deep Sclerectomy to Canaloplasty – Re-establishing the Natural Outflow. in *Surgical Techniques in Ophthalmology – Glaucoma Surgery*, 308-317, Jaypee Brothers Medical Publisher Ltd.

7. **Scharioth G.B.** : Combined Cataract and Nonpenetrating Glaucoma Surgery. in *Video Atlas of Advanced Ophthalmic Surgeries*, Slack Incorporated, USA

8. **Scharioth G.B.** : Canaloplasty. in Jaypee´s *Video Atlas of Ophthalmic Surgery* Vol. 2, Jaypee Brothers Medical Publisher Ltd,

9. **Scharioth G.B.** : Management of Glaucoma Combined with Cataract – Blebless Surgical Techniques, *Ophthalmology News*, Sept 2010, 25-26

10. **Scharioth G.B.** Raak P. Skribek A. Kolozsvári L. : A természetes csarnokvíz elfolyás műtéti helyreállítása – Összefoglalás, *Szemészet*, 2010, in print

11. **Scharioth G.B.** Kolozsvári L. Mirshahi A. : Management of Juvenile-Onset Glaucoma and Cataract in a Patient with Oculocutaneous Albinism, *Techniques in Ophthalmol*. 2010, in print

List of presentations directly related to the subjects of the Thesis:

1. Drüsedau M. **Scharioth G.B.** Bull H. v. Wolff K.D. von Barsewisch B. : A comparision of combined cataract and glaucoma surgery: viscocanaolostomy-phacoemulsification versus trabeculectomy-phacoemulsification, 97th German Society of Ophthalmology, 1999, Berlin, Germany
2. **Scharioth G.B.** Combined phaco and non-penetrating glaucoma surgery. Phaco Caravan, 2001, Marocco.
3. **Scharioth G.B.** Non-penetrating glaucoma surgery with SK Gel implantation. X.AMO Meeting, 2001, Zermatt, Switzerland.
4. **Scharioth G.B.** Combined phaco and non-penetrating glaucoma surgery. Video, Annual Meeting of American Society of Cataract and Refractive Surgeons, San Diego, USA.
5. **Scharioth G.B.** Non-penetratining glaucoma surgery with implants. XI. AMO Meeting, 2002, Zermatt, Switzerland.
6. **Scharioth G.B.** Combined phaco and non-penetrating glaucoma surgery. International Meeting on non-pentrating glaucoma surgery, 2002, Recklinghausen, Germany
7. **Scharioth G.B.** Kombinierte Glaukom- und Kataraktchirurgie. Phakozirkel, 2002, Budapest, Hungary.
8. **Scharioth G.B.** Non-Penetrating Glaucoma Surgery in Case of Goniosynechiae. Video, 15th Congress of German Ophthalmic Surgeons, 2002, Nuernberg, Germany.
9. **Scharioth G.B.** Non-penetrating glaucoma surgery - state of the art. Meeting of Hungarian Society of Ophthalmology, 2003, Miskolc, Hungary.
10. **Scharioth G.B.** Non-penetrating Glaucoma Surgery. Ophthalmic Surgery Meeting, 2005, Szombathely, Hungary.
11. Cseke I. **Scharioth G.B.** : A mély sclerectomia tanulási tapasztalatai. Annual Congress of the Hungarian Ophthalomolgical Society, 2006, Sopron, Hungary
12. Cseke I. **Scharioth G.B.** : Deep Sclerectomy - Experience of the Learning Period. 5th Congress of the Romanian Society of Ophthalmology, 2006, Sinaia, Romania.
13. Scharioth G.B. Non-Penetrating Glaucoma Surgery. 5th Congress of the Romanian Society of Ophthalmology, 2006, Sinaia, Romania.
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15. **Scharioth G.B.** Intraindividueller Vergleich von T-Flux- und SK-Gel-Implantat bei nicht-penetrierender Glaukom-OP kombiniert mit Phakoemulsifikation. 169. Versammlung des Vereins Rheinisch-Westfälischer Augenärzte, 2007, Mülheim a. R., Germany.
16. **Scharioth G.B.** Iridolenticular block in heavy solicone oil. III. Vitreoretinal Symposium, 2007, Lodz, Poland.
17. **Scharioth G.B.** Non-penetrating Glaucoma Surgery. Zeiss ViP Meeting, 2007, LaRochelle, France
18. **Scharioth G.B.** Implantate in der nicht-penetrierenden Glaukomchirurgie. 20. Internationaler Kongress der Deutschen Ophthalmochirurgen, Nürnberg, Germany.
19. Pavlidis M. **Scharioth G.B.** : Die Bewertung des Sehnerven und der retinalen Nervenfaserschicht beim chronischen Offenwinkelglaukom. 20. Internationaler Kongress der Deutschen Ophthalmochirurgen, 2007, Nürnberg, Germany.
20. **Scharioth G.B.** Pavlidis M. : Hilfe! Mein Glaukompatient sieht schlechter – Diagnostik und Therapie von subjektiven Sehverschlechterungen beim chronischen Offenwinkelglaukom. 20. Internationaler Kongress der Deutschen Ophthalmochirurgen, 2007, Nürnberg, Germany.
21. **Scharioth G.B.** Catheterless Viscocanaloplasty. Annual Congress of Hungarian Ophthalmological Society, 2007, Debrecen, Hungary.

22. **Scharioth G.B.** Catheterless Viscocanaloplasty. 6th Congress of Romanian Society of Ophthalmology, 2007, Sinaia, Romania.
23. **Scharioth G.B.** Non-Penetrating Glaucoma Surgery. 6th Congress of Romanian Society of Ophthalmologiy, 2007, Sinaia, Romania.
24. **Scharioth G.B.** From Deep Sclerectomy to Canaloplasty – Is it possible to re-establish the natural outflow ?!. Meeting of Pondycherry Association of Ophthalmologists, 2007, Pondicherry, India
25. **Scharioth G.B.** Canaloplasty", 170. Versammlung des Vereins Rheinisch-Westfälischer Augenärzte, 2008, Wuppertal Germany.
26. Pavlidis M. **Scharioth G.B.** Baatz H. : Iridolentikularer Block nach Pars plana Vitrektomie mit schwerem Silikonöl", 170. Versammlung des Vereins Rheinisch-Westfälischer Augenärzte, 2008, Wuppertal Germany.
27. **Scharioth G.B.** Catheterless Canaloplasty. 21st Congress of German Ophthalmic Surgeons, 2008, Nuernberg, Germany.
28. **Scharioth G.B.** Implants in Non-penetrating Glaucoma Surgery. 21st Congress of German Ophthalmic Surgeons, 2008, Nuernberg, Germany.
29. **Scharioth G.B.** A New Look Inside: Intraoperative Online Anterior Segment OCT. Poster, XXVI. European Society of Cataract and Refractive Surgeons, 2008, Berlin, Germany
30. **Scharioth G.B.** Canaloplasty – Re-Establishing the Natural Outflow. Video, XXVI. European Society of Cataract and Refractive Surgeons, 2008. Berlin, Germany
30. **Scharioth G.B.** OCTAASS – OCT assisted anterior segment surgery. 7th Congress of Romanian Society of Ophthalmology, 2008, Sinaia, Romania.
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32. **Scharioth G.B.** Catheterless Canaloplasty. 3rd International Meeting on Innovative Glaucoma Surgery, 2008, Recklinghausen, Germany
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35. **Scharioth G.B.** New developments in glaucoma surgery. Meeting of University of Szeged, 2009, Hungary
36. **Scharioth G.B.** Non-penetrating Glaucoma Surgery (Canaloplasty). Instructional Course, 4th International Congress on Glaucoma Surgery, 2009, Geneva, Switzerland
37. **Scharioth G.B.** iStent trabecular micro-bypass and concurrent cataract surgery: 24 months result. 4th International Congress on Glaucoma Surgery, 2009, Geneva, Switzerland
38. **Scharioth G.B.** Gibt es in der Glaukomchirurgie einen Goldstandard?. Hamburger Glaukomtag des Universitätsklinikum Eppendorf, 2009, Hamburg, Germany
40. **Scharioth G.B.** Canaloplasty. Hamburger Glaukomtag des Universitätsklinikum Eppendorf, 2009, Hamburg, Germany
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45. **Scharioth G.B.** The management of advanced glaucoma with penetrating and non penetrating techniques. Instructional course, XXVII. European Society of Cataract and Refractive Surgeons, 2009, Barcelona, Spain
46. **Scharioth G.B.** Management of juvenile-onset glaucoma and cataract in a patient with oculocutaneous albinism. Poster, XXVI. European Society of Cataract and Refractive Surgeons, 2009, Barcelona, Spain
47. **Scharioth G.B.** Kanaloplastik – 3 Jahre Erfahrung. Augenchirurgentreffen Zermatt, 2010, Switzerland
48. **Scharioth G.B.** Optical coherence tomography assisted anterior segment surgery. 14th ESCRS Winter Meeting, 2010, Budapest, Hungary
49. **Scharioth G.B.** Kearney J. Stegmann R. Peckar C. Schlemm Canal Surgery. Instructional course, Annual Meeting of American Society of Cataract and Refractive Surgeons, 2010, Boston, USA
50. **Scharioth G.B.** Optical coherence tomography assisted anterior segment surgery. Video, Annual Meeting of American Society of Cataract and Refractive Surgeons, 2010, Boston, USA
51. **Scharioth G.B.** Is it possible to re-establish the natural outflow?. 2nd International Meeting Eye Microsurgery Today, 2010, Prishtina, Kososvo
52. **Scharioth G.B.** Optical coherence tomography assisted anterior segment surgery. Poster, World Ophthalmology Congress, 2010, Berlin, Germany
53. **Scharioth G.B.** Tryptane blue flow test after incisional glaucoma surgrey. World Ophthalmology Congress, 2010, Berlin, Germany
54. Mirshai A. **Scharioth G.B.** : Combined phacoemulsification and non-penetrating glaucoma surgery (NPGS) with goniosynechiolysis ab interno. World Ophthalmology Congress, Berlin, Germany
55. **Scharioth G.B.** Glaucolight. at Eurotimes Satellite Education Programme “Innovative Glaucoma and DMEK Surgery” at XXVIII Congress of the European Society of Cataract and Refractive Surgeons, 2010, Paris, France
56. **Scharioth G.B.** Optical coherence tomography assisted anterior segment surgery. Video, Video Award 3rd place Category Innovative Techniques at XXVIII Congress of the European Society of Cataract and Refractive Surgeons, 2010, Paris, France

List of papers not directly related to the subjects of the Thesis

1. Mirshahi A. **Scharioth G.B.** Baatz B. : White planar deposits on the retina. *Ophthalmologe*. 2004 Dec., 101(12):1236-8. **(IF: 0.466)**
2. **Scharioth G.** Mirshahi A. Schreyger F. Baatz H., Macular Translocation after Photodynamic Therapy: A Case Report. *Klinische Monatsblätter für Augenheilkunde* 2005 Jul., 222(7): 586-9. **(IF: 0.412)**
3. Mirshahi A. **Scharioth G.** de Ortueta D. Baatz H., Posterior segment complications of laser in situ keratomileusis (LASIK). *Klinische Monatsblätter für Augenheilkunde*; 2006 Sep., 223(9):721-5. **(IF: 0.679)**
4. A. Mirshahi A. **Scharioth G.B.** Klais Ch. Baatz H. : Enhanced visualization of acute macular neuroretinopathy by Heidelberg Retina Tomography. *Clinical & Experimental Ophthalmology.* 2006 Aug., 34(6):596-599. **(IF: 1.247)**
5. Baatz H. Lange S. Buchner H. **Scharioth G.S**. : Pseudoangiitis in bilateral ocular ischemia. *Ophthalmologe*, 2007 Mar., 104(3):243-5. **(IF: 0.791)**
6. Tatar O. Adam A. Shinoda K. Eckert T. **Scharioth G.B.** Klein M. Yoeruek E. Bartz-Schmidt K.U. Grisanti S. : Matrix metalloproteinase in human choroidal neovascular

membranes excised following verteporfin photodynamic therapy. *British Jorunal of Ophthalmology*, 2007 Sep., 91(9):1183-9. **(IF: 2.689)**
7. Baatz H. **Scharioth G.B.** deOrtueta D. Pavlidids M. : Age Distribution of Patients Presenting with Uveitis, *The Open Ophthalmology J*., 2007, 1, 23-24.
8. Baatz H. Darawsha R. Ackermann H. **Scharioth G.B.** deOrtueta D. Pavlidis M. Hattenbach L.O. : Phacoemulsification does not induce neovascular age-related macular degeneration, *Investigative Ophthalmology and Visual Science*, 2008 Mar., 49(3):1079-83. **(IF: 3.582)**
9. **Scharioth G.B.** : April consultation # 2, J Cataract Refract Surg. 2008 Apr;34(4):537-9. **(IF: 2.508)**
10. Baatz H. Darawsha R. Scharioth G.B. deOrtueta D. Ackermann H. : Visual acuity after cataract surgery in patients with age-related macular degeneration, *Ophthalmologe*. 2008 May 18 **(IF: 0.791)**
11. Tatar O., Youeruek E., Szurmann P., Bartz-Schmidt K.U.; Tübingen Bevacizumab Study Group, Adam A. Shinoda K. Eckardt C. Boeyeden V. Claes C. Pertile G. **Scharioth G.B.** Grisanti G. : Effect of bevacizumab on inflammation and proliferation in human choroidal neovascularization, *Arch Ophthalmol.* 2008 Jun;126(6):782-790. **(IF: 3.102)**
12. **Scharioth G**., deOrtueta D. : New IOL fixation techniques – intrascleral, *Video Journal of Cataract and Refractive Surgery*, Vol XXIV, Issue II, 2008
13. Tatar O. Shinoda K. Kaiserling E. Claes C. Eckardt C. Eckert T. Pertile G. Boeyeden V. **Scharioth G.B.** Yoeruek E. Szurmann P. Bartz-Schmidt K.U., Tuebingen Bevacizumab Study Group, Grisanti S. : Implications of bevacizumab on vascular endothelial growth and endostatin in human choroidal neovascularisaton, *Br J Ophthalmology*. 2009 Feb; 93(2): 159-165. **(IF: 2.917)**
14. Tatar O. Adam A. Shinoda K. Kaiserling E. Boeyden V. Claes C. Eckardt C. Eckert T. Pertile G. **Scharioth GB.** Yoeruek E. Szurman P. Bartz-Schmidt KU. Grisanti S. : Early effects of intravitreal triamcinolone acetonide on inflammation and proliferation in human choroidal neovascularisation, *Arch Ophthalmol.* 2009 Mar; 127 (3):275-81 **(IF: 3.859)**
15. Mirshai A. **Scharioth G.B.** : Submaculäre Blutungen: Operative Therapie, *Ophthalmo-Chirurgie 2009* Sept; 2:311-316
16. **Scharioth G.B.** Pavlidis M. : Nahtlose intrasklerale Hinterkammerlinsen-Fixation: Langzeitergebnisse, *Ophthalmo-Chirurgie* 2009 Sept; 2:322-324
17. **Scharioth G.B.** : Transconjunctival 25 gauge vitrectomy, *Video Journal of Vitreoretinal Surgery*, 2009, Issue# 1
18. Baddon CJA. **Scharioth GB.** Prasad S. : Intrascleral Sutureless Posterior Chamber Intraocular Lens Fixation Using Sceral Tunnels, *Techniques in Ophthalmol.* 2009 June; 7(2):56-59
19. Pavlidis M. **Scharioth G.** Ortueta DD. Baatz H. : Iridolenticular Block in Heavy Silicone Oil Tamponade, *Retina.* 2009 Dec.; **(IF: 2.932)**
20. **Scharioth G.B.** Prasad S. Georgalas I. Tataru C. Pavlidis M. : Intermediate results of sutureless intrascleral posterior chamber intraocular lens fixation, *Journal Cataract and Refractive Surgery.* 2010 Feb; 36(2):254-259 **(IF: 2.745)**
21. **Scharioth G.B.** : Bimanual Torsional Phaco. in *Video Atlas of Advanced Ophthalmic Surgeries,* Slack Incorporated, USA
22. **Scharioth G.B.** : Triamcinolone-Assisted Peeling of Epimacular Membrane. in *Video Atlas of Advanced Ophthalmic Surgeries*, Slack Incorporated, USA
23. **Scharioth G.B.** : Intrascleral PC IOL Fixation. in *Jaypee´s Video Atlas of Ophthalmic Surgery Vol. 2*, Jaypee Brothers Medical Publisher Ltd,
24. **Scharioth G.B.** : Triamcinolon Assisted ILM-Peeling. in *Jaypee´s Video Atlas of Ophthalmic Surgery Vol. 2*, Jaypee Brothers Medical Publisher Ltd,
25. **Scharioth G.B.** : Intraocular IOL Refolding for Explantation. in *Jaypee´s Video Atlas of Ophthalmic Surgery Vol. 2*, Jaypee Brothers Medical Publisher Ltd,

26. **Scharioth G.B.** : Transconjunctival 25 G Pars Plana Vitrectomy. in *Jaypee´s Video Atlas of Ophthalmic Surgery Vol. 2*, Jaypee Brothers Medical Publisher Ltd,
27. Prasad S. Kumar B.V. **Scharioth G.B.** : Needle-guided intrascleral fixation of posterior chamber intraocular lens for aphakia correction. *Journal of Cataract and Refractive Surgery*, Jun;36 (6): 1063, author reply **(IF: 2.497)**
28. Baatz H. Raak P. de Ortueta D. Mirshahi A. **Scharioth G.B.** : Practical significance of critical fusion frequency (CFF) : Chronological resolution of the visual system in different diagnosis" *Ophthalmologe*, Jun 2010, 107:715-719 **(IF: 1.0)**

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