

# Stab incision mitomycin C-assisted rapid trabeculectomy: A 'SMART' trabeculectomy alternative

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**Abstract.** The aim of the present study was to introduce a new modified trabeculectomy technique, stab incision mitomycin C (MMC)-assisted rapid trabeculectomy (SMART), which requires less surgical time and tissue manipulation. A total of 41 eyes with indication for trabeculectomy underwent glaucoma surgery with the SMART technique; superior subconjunctival injection of 0.005 mg MMC mixed with 0.1 ml lidocaine, followed by small, fornix base conjunctival opening. A stab incision was made to enter the anterior chamber 1.5 mm post-limbus using a 2.4 mm cataract knife. Double 0.75 mm punch and peripheral iridectomy were performed. A releasable suture was placed in the scleral opening, and matrix sutures to close conjunctiva. The preoperative mean intraocular pressure (IOP) was 23.8 mmHg, with a mean number of medications of 3.3. The mean follow-up duration was 27.6 months, with a range of 12-46 months. A year post-surgery, the mean IOP was 11 mmHg, with a mean number of medications of 0.7, corresponding to a reduction of 12.8 mmHg in IOP and 2.6 in the number of medications. During follow-up, additional 5-fluorouracil injections were administered when needed. In conclusion, SMART with wound modulation appears to be a safe and quick alternative to classic trabeculectomy. Few minor and no major complications were observed during the first 2.5 years of follow-up, with all eyes maintaining an IOP <15 mmHg.

## Introduction

Conventional filtering surgery is currently the gold standard in surgical management of glaucoma not controlled with medication (1). However, the high risk of potentially vision-threatening peri- and postoperative complications, combined with the failure rates associated with standard

trabeculectomy, delay surgical intervention. Intra-operative complications associated with tissue manipulation, such as inadequate scleral flap thickness and bleeding, may compromise the outcome of the procedure. Postoperatively, hypotony is a common, serious complication, which can persist in a small percentage of cases, and is associated with flat anterior chamber (A/C), corneal edema, cataract formation, maculopathy and loss of vision. Other less common complications, but more difficult in terms of management, include pupillary block, suprachoroidal hemorrhage and aqueous misdirection (2). Fibroblastic proliferation and sub-conjunctival fibrosis are the main challenges during follow up as they lead to trabeculectomy failure. Antifibrotic agents are currently used in an order to control fibrosis and sustain bleb morphology, prolonging the hypotonic effect of the procedure. However, the latter are associated with their own complications, of which late-onset bleb leaks and bleb-related endophthalmitis are the most serious (3,4). In an attempt to design a safe and consistent surgical procedure, the present retrospective study aimed to evaluate the effect and safety of a modified trabeculectomy technique, stab incision mitomycin C (MMC)-assisted rapid trabeculectomy (SMART), in achieving low intraocular pressure (IOP) in primary patients with glaucoma.

## Patients and methods

**Patients.** A total of 41 eyes with indication for trabeculectomy underwent glaucoma surgery (31 eyes isolated glaucoma surgery and 10 eyes combined cataract-glaucoma surgery). Surgery indications were uncontrolled IOP on full medical treatment, severe side effects to glaucoma medication and poor compliance to treatment. Indication for combined phacoemulsification with SMART (phaco-SMART) was Best Corrected Visual Acuity <5/10. All surgical procedures were performed by the same surgeon. There was no significant difference concerning age, sex, preoperative IOP and number of preoperative glaucoma medications between eyes undergoing SMART or phaco-SMART. The primary exclusion criteria were angle closure glaucoma, secondary glaucoma and cases where medical notes were unavailable or incomplete. Patient characteristics are presented in Table I. Informed consent was obtained from all patients prior to surgery and all data were collected according to the principles of The Declaration of Helsinki. The Ethics Committee of The

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Table I. Preoperative and postoperative patient data.

Clinicopathological characteristic	SMART, n=31	phaco-SMART, n=10	P-value	Total, n=41
Sex				
Male, eyes	15	9	-	24
Female, eyes	16	1	-	17
Age, years	72±10.16	70±7.87	0.1051	70.50±9.59
Pre-operative IOP, mmHg	25.50±9.27	18.50±3.57	0.0255	23.80±8.75
Postoperative IOP, mmHg				
1st week	7.10±4.67	5.90±2.88	0.4389	6.80±4.30
1st month	9.00±3.66	11.50±2.99	0.0607	9.60±3.63
3rd month	10.20±4.9	10.90±2.73	0.6554	10.40±4.28
6th month	9.40±4.39	11.90±2.73	0.1013	10.00±4.16
1st year	10.70±3.31	12.00±2.67	0.2588	11.00±3.19
Final visit IOP, mmHg	11.70±3.30	11.80±2.93	0.5982	11.70±3.19
Follow-up time, months	29.30±11.80	22.40±9.99	0.1051	27.60±11.66
IOP decrease <sup>a</sup> , mmHg	13.80±9.73	6.70±4.52	0.0102	12.10±9.44
No. of medications				
Preoperative	3.40±1.38	3.00±1.33	0.4803	3.30±1.36
Postoperative	0.70±1.05	0.60±1.07	0.8407	0.70±1.04
Reduction in no. of medications	2.70±1.87	2.40±1.26	0.6650	2.60±1.73
Complications, n				
Shallow A/C	8	5	-	13
Hypotony	1	0	-	1
Bleb leak	2	0	-	2

<sup>a</sup>Decrease between final visit IOP and preoperative IOP. SMART, stab incision mitomycin C-assisted rapid trabeculectomy; IOP, intraocular pressure; A/C, anterior chamber.

Konstantopouleio-Patission General Hospital approved the present study (reference no. 49/2.2.2017).

**Pre-operative management.** Careful assessment of the ocular surface was performed prior to surgery. All patients were prepared 1 week pre-operatively with fluorometholone drops, adequate lubrication of ocular surface with tear substitutes, as well as proper lid hygiene. Discontinuation of topical treatment and IOP management with Acetazolamide per os was suggested in cases where IOP permitted it.

**Surgical techniques.** Immediately pre-operatively, a single application of 2% pilocarpine was instilled into the operative eye, while typical mydriasis with phenylephrine and tropicamide was performed in the phaco-SMART cases. Following insertion of a lid speculum, topical anesthesia with 0.5% proxymetacaine was administered. A single dose of 0.1 ml lidocaine mixed with 0.005 mg MMC was injected into the superior subconjunctiva, ~8 mm from limbus and evenly spread towards the limbus with a sponge tip up to 2 mm from limbus (Fig. 1). Immediate irrigation followed. A 3.5-mm fornix-based conjunctival opening was made with careful Tenon's capsule separation from episclera as superiorly as possible. Caution of underlying sclera was done in the region where the incision was to be made. A stab incision was performed with a 2.4-mm bevel up slit cataract knife,

entering the A/C 1.5 mm posterior to limbus (Figs. 2 and 3), with slow retraction of the knife and immediate A/C fill with visco-elastic substance through the stab incision. A double punch with the 0.75-mm Kelly punch followed (Figs. 4 and 5). Peripheral iridectomy was performed and one releasable suture (10-0 nylon) was placed to secure the opening (Figs. 6 and 7). Matrix sutures (10-0 nylon) were used to close the conjunctiva (Fig. 8).

In the SMART procedure, a side port was made at the end of the procedure, in order to administer intracameral cefuroxime and for postoperative management if necessary. In the phaco-SMART cases, phacoemulsification was performed with clear cornea incision at 105° and quick chop technique, followed by SMART as described. Closure of incisions was made by stroma hydration. At the end of the procedure, a soft contact lens and a protective shell was applied to all patients.

**Postoperative management.** A strict follow-up schedule and medication scheme was followed in all cases. Follow-up visits were made on the 1st, 3rd, 7th and 15th days, followed by 1st, 3rd and 6th months postoperatively. Follow-up was scheduled as necessary after the initial 6-month period, with a minimum of two visits per year. During follow-up visits, careful evaluation of bleb (position, appearance and vascularity), A/C status, IOP and fundus was performed.



Figure 1. Subconjunctival mitomycin C injection.



Figure 3. Entering the anterior chamber.



Figure 2. Stab incision with the 2.4-mm cataract knife, 1.5 mm posterior to limbus.

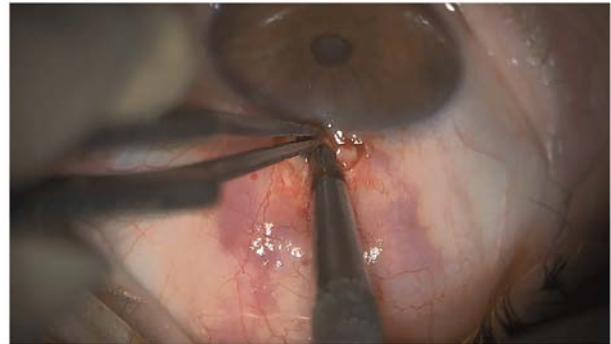


Figure 4. Double punch with the 0.75-mm Kelly punch.

Additional 5-fluorouracil (5-FU) injections were administered when beginning of encapsulation was suspected. The standard protocol for postoperative medication is presented in Table II.

**Statistical analysis.** Student's t-tests and  $\chi^2$  tests were used for comparison of the mean of the variables. The Mann-Whitney U test was performed if data were not distributed normally. The results are presented as the mean  $\pm$  SD and as percentages where appropriate. All statistical analyses were carried out using SPSS 21.0 (IBM, Corp.).  $P < 0.05$  was considered to indicate a statistically significant difference.

## Results

**Hypotonic effect.** There were no intra-operative complications. Operation time from conjunctival opening to closure was  $26.71 \pm 5.55$  min for SMART and  $36.60 \pm 1.95$  min for phaco-SMART cases. The follow-up period ranged from 12-46 months with a mean follow-up of  $27.6 \pm 11.66$  months. Mean IOP during follow-up tended to be lower in the SMART cases but there was no statistically significant difference, compared with phaco-SMART. The mean final IOP was  $11.7 \pm 3.19$  mmHg, which is a reduction of  $12.1 \pm 9.44$  mmHg, compared with the pre-operative IOP. Specifically, at the 12-month follow-up mark, which all patients reached, the mean IOP was  $11 \pm 3.19$  mmHg ( $P < 0.00001$ ) with  $0.7 \pm 1.04$  mean number of medications ( $P < 0.00001$ ), a reduction of  $12.1 \pm 9.44$  mmHg in IOP and  $2.6 \pm 1.73$  in the number of medications.

**Bleb modulation.** During follow-up, 22 out of 31 cases undergoing the SMART procedure needed additional 5-FU injections, (mean  $1.45 \pm 1.87$  injections per eye) compared with 8 out of 10 cases in phaco-SMART (mean  $1.9 \pm 2.57$  injections per eye;  $P = 0.5841$ ). No complaints were reported by the patients concerning 5-FU injections.

**Complications.** Hypotony (defined as IOP  $\leq 2$  mmHg) occurred in one case due to overfiltration of the bleb and was managed with compressive sutures over the conjunctiva. This patient had undergone the phaco-SMART approach; the sutures were removed after 2 weeks and up to 17 months postoperatively with two additional 5-FU injections, IOP remained at 10 mmHg. The most common observation 1st day postoperatively was shallow A/C ( $>1.5$  mm; 13 out of 41 cases). Small choroidal detachment ( $<2$  clock h) was usually observed a few days later (11 of the aforementioned cases), and no choroidal folds or maculopathy occurred in these cases. Typical management of shallow anterior chamber with or without choroidal detachment was reformation of the A/C with viscoelastic substance through the side ports when needed, with none of these patients needing additional intervention in the next follow-up visits. Patient data confirm that visual acuity remained unaffected in these patients, with no impact on postoperative trajectory or final IOP (data not shown). No flat A/C was observed. Wound leak appeared in two cases (on the 1st and 3rd postoperative day) and was managed by resuturing the conjunctiva. No major complications, including persistent hypotony, maculopathy or bleb related complication occurred, with all eyes maintaining an IOP  $< 15$  mmHg (Table I).

Table II. Postoperative medication protocol.

Week post-surgery	Dexamethasone+Chloramphenicol	Dexamethasone (preservative-free)	Bromfenac
Week 1	4 times a day	3 times a day	2 times a day
Week 2	-	6 times a day	2 times a day
Week 3+4	-	5 times a day	2 times a day
Week 5+6	-	4 times a day	2 times a day
Week 7+8	-	3 times a day	-
Week 9+10	-	2 times a day	-



Figure 5. Scleral opening.

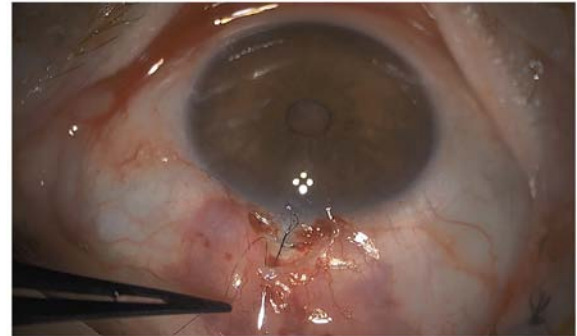


Figure 7. Releasable suture to secure the scleral opening.



Figure 6. Peripheral iridectomy.



Figure 8. Matrix sutures to close the conjunctiva.

## Discussion

Trabeculectomy has undergone many changes since it was first described by Cairns (4) in 1968, with many approaches and modifications to the traditional procedure. The modifications that forged the technique described in the present study aimed to minimize intraoperative tissue handling, as well as pre- and postoperative inflammation.

One of the common causes for trabeculectomy failure is fibrosis due to the wound healing response, appearing as subconjunctival fibrosis of the bleb or as sub-Tenon's encapsulation. It is recognized that an inflamed conjunctiva compromises the success of trabeculectomy, because the conjunctival scarring reaction is already activated (5). A pre-operative adjustment of glaucoma medications has been adopted by many glaucoma surgeons, reducing the number of drops preserved with benzalkonium chloride and/or changing to preservative-free medication, in the weeks prior to surgery (6). Additionally,

evidence suggested that 1-month pre-operative fluorometholone, improved the state of the conjunctiva (7). Hence, careful pre-operative preparation has long been the standard approach with all glaucoma-filtering surgeries.

Antimetabolites are used in various concentrations, usually in the form of sponges, in an attempt to reduce post-operative fibrosis (8). However, their use is not without risks, as bleb infection or leak, hypotony, maculopathy, corneal epithelial toxicity and endophthalmitis have been frequently reported with the intra-operative use of MMC (9). The use of intra-operative MMC in the form of sub-conjunctival injection has been previously described with similar efficacy and safety to MMC-soaked sponges but with a more favorable bleb morphology and a predictable dose of delivery (9,10). In addition, the reduced conjunctival manipulation with injection and shorter waiting time compared with MMC sponges supported the use of this approach in the present



study, as it has been shown to reduce the occurrence of fibrosis (11-17). In the present study, a low MMC concentration (0.005 mg/0.1 ml) was used in an attempt to minimize the side effects of MMC, which is half the minimum dose described in the literature (9,10).

Of note, various types of conjunctival opening formation have been described in the literature, with fornix base opening being associated with less cystic bleb formation (15). The smaller fornix base conjunctival opening used in the present study limits conjunctival manipulation and requires fewer sutures for closure.

Modifications that use a scleral tunnel have been described in the past, with positive results (18-20). Jacob *et al* (21) was the first to describe a stab incision approach, with a 2.8-mm keratome. The technique described in the present study technique differs from this approach, since the 2.4-mm incision, does not include the overlying conjunctiva. Moreover, the formation of a scleral tunnel instead of a scleral flap, as well as the small conjunctival opening contribute to less surgical time in the procedure used in the present study.

In addition, the releasable suture to the scleral incision creates a more guarded environment in order to avoid post-operative hypotony. Regarding the choice of suture, it has been documented that trabeculectomies performed with and without releasable sutures resulted in equivalent efficacy in IOP control, with releasable sutures resulting in a lower incidence of hypotony and flat A/C (22).

The main purpose of close postoperative monitoring is to frequently evaluate bleb morphology and to intervene with bleb needling augmented with 5-FU, if encapsulation is suspected (23). In the present study, most of the patients needed 5-FU injections without needling when encapsulation was suspected or bleb vascularity was increased. All 5-FU injections were performed during the initial 'high-risk' follow-up period (3 months), with three patients having 5-FU injections after the first year, after they underwent phacemulsification in the trabeculectomised eye. Previous studies demonstrated that a timely intervention with 5-FU injections can produce long-term IOP control in a high proportion of patients and appears to play a significant role in avoiding further surgery (24-26).

Shallow A/C and choroidal detachment were associated with a diffuse bleb and low IOP immediately postoperatively. However, no further management was required for these cases as typically the depth of the A/C was normal by the scheduled visit on the 7th postoperative day.

In conclusion, success rates after trabeculectomy with target IOP  $\leq 22$  mmHg  $\leq 86\%$  without medication and 98% with medication have been previously reported (27-30). However, in the present study, all patients had IOP  $\leq 15$  mmHg on the final visit, 63.4% without medication and 36.6% with  $\leq 2$  antiglaucoma agents. In conclusion, SMART with wound modulation appears to be a safe and quicker alternative to classic trabeculectomy. A lower dose of MMC showed good efficiency. Few minor and no major complications were observed during the first 2.5 years of follow-up. All patients showed good IOP control. The primary limitations of the present study are its retrospective, non-comparative design and the small number of patients involved. A larger multicenter prospective study is required to confirm the results described in the present study.

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## Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Authors' contributions

CT conceived and designed the study. AT and GD obtained, analyzed and interpreted the data. AT drafted the manuscript. CT critically revised the manuscript. All authors read and approved the final manuscript.

## Ethics approval and consent to participate

Informed consent was obtained from all patients prior to surgery and all data were collected according to the principles of The Declaration of Helsinki. The Ethics Committee of The Konstantopouleio-Patission General Hospital approved the present study (reference no. 49/2.2.2017).

## Patient consent for publication

The patients provided written informed consent for the publication of any associated data and accompanying images.

## Competing interests

The authors declare that they have no competing interests.

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