

# Comparison of anterior chamber flare among different glaucoma surgeries

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**Purpose:** To compare postsurgical anterior chamber flare (ACF) among conventional (trabeculectomy, LEC) and novel (EX-PRESS Shunt, EXP) filtration surgeries and microhook ab interno trabeculotomy ( $\mu$ LOT), a novel minimally invasive glaucoma surgery (MIGS).

**Subjects and methods:** This retrospective study included 125 primary open angle glaucoma eyes (89 consecutive subjects) treated with  $\mu$ LOT (n=38), LEC (n=12), or EXP (n=75). The intraocular pressure (IOP), numbers of antiglaucoma medication, and ACF at preoperatively and 2 weeks; 1, 3, and 6 months postoperatively were compared among the surgical groups using a mixed-effects regression model.

**Results:** The postoperative IOP ( $p<0.0001$ ) and medication use were significantly ( $p<0.0001$ ) lower in the LEC and EXP groups than with  $\mu$ LOT for up to 6 months postoperatively. The ACF differed significantly ( $p=0.0004$ ) among groups; the ACF was significantly higher ( $p=0.0097$ , post-hoc Student's *t*-test) with  $\mu$ LOT ( $33.6\pm52.8$  pc/msec) than the EXP ( $15.7\pm19.9$  pc/msec) at 2 weeks and was significantly ( $p=0.0111$ , post-hoc *t*-test) lower with  $\mu$ LOT ( $7.9\pm2.0$  pc/msec) than LEC ( $12.0\pm6.1$  pc/msec) at 6 months.

**Conclusion:** Considering our observation, although its clinical significance is unclear, not all MIGS are minimally invasive regarding early postsurgical inflammation.

**Keywords:** anterior chamber flare, trabeculectomy, EX-PRESS shunt, microhook ab interno trabeculotomy, minimally invasive glaucoma surgery, MIGS

## Introduction

Trabeculectomy (LEC) is the standard surgery for glaucoma when the intraocular pressure (IOP) is refractory to medical and laser treatments. Filtration surgery using the EX-PRESS Shunt (EXP) (Alcon Japan, Tokyo, Japan) recently has become an alternative to LEC.<sup>1,2</sup> More recently, trabeculotomy (LOT) and related surgeries, gonioscopy-assisted transluminal LOT,<sup>3</sup> canaloplasty,<sup>4</sup> Kahook dual-blade,<sup>5</sup> and microhook ab interno LOT ( $\mu$ LOT),<sup>6</sup> the so-called minimally invasive glaucoma surgeries (MIGS), are now considered novel glaucoma surgeries. Measurement of anterior chamber flare (ACF) is the established method for estimating postsurgical inflammation;<sup>1,2,7,8</sup> however, few studies have compared postsurgical inflammation between filtration surgeries and MIGS. The current study compared the ACF among conventional (LEC) and novel (EXP) filtration surgeries and novel MIGS (ie,  $\mu$ LOT).

## Subjects and methods

The current study was part of the study protocol titled "Epidemiologic study in ocular morphology and function," that the Ethics Committee of Matsue Red Cross

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Hospital approved. Based on the regulations of the guidelines issued by the Japanese Government, the study protocol did not require each patient's provide written informed consent, instead the protocol was posted at the outpatient clinic to notify the study to the participants. The studies complied with the tenets of the Declaration of Helsinki. This retrospective study included 125 eyes (89 consecutive subjects) treated with  $\mu$ LOT (n=38), LEC (n=12), or EXP (n=75) at Matsue Red Cross Hospital. We searched the division database of Matsue Red Cross Hospital for eyes with glaucoma treated surgically at the hospital between April 2014 and September 2017. The inclusion criteria included primary open-angle glaucoma; patients who underwent one of the three glaucoma surgeries performed by the same surgeon (MT) and did not undergo a simultaneous cataract surgery or other procedures; no history of previous intraocular surgery; no additional glaucoma surgery and other intraocular interventions within 6 months postoperatively; and measurement of best-corrected visual acuity (BCVA), intraocular pressure (IOP), and ACF at all time points (preoperatively; 2 weeks; 1, 3, and 6 months postoperatively). No study eyes had serious surgical complications perioperatively. The decimal BCVA was converted to the logarithm of the minimum angle of resolution VA, the IOP by Goldmann applanation tonometry, and the ACF by the FM-600 laser flare meter (Kowa, Nagoya, Japan). All surgical procedures have been described previously.<sup>9–11</sup>

The age, BCVA, IOP, number of glaucoma medication, and ACF were compared among the three surgical groups by one-way analysis of variance (ANOVA) followed by a comparison between each pair of groups using the post-hoc Student *t*-test. In ANOVA,  $P < 0.05$  was considered significant. In the post-hoc test, based on Bonferroni's method to correct multiple comparisons,  $P < 0.0167$  and  $P < 0.0033$  were considered significant at the probability levels of 5% and 1%, respectively. Sex and eye were compared among the three surgical groups using the chi-square test. To adjust for both eyes inclusion in a subjects, the preoperative BCVA and BCVAs measured at 2 weeks, 1 month (3–5 weeks), 3 months (2–4 months), and 6 months (5–7 months) postoperatively were compared using a mixed-effects regression model in which each patient's identification number was regarded as a random effect and the time period and glaucoma surgical procedure were regarded as a fixed effect. The postoperative changes in the IOP, numbers of antiglaucoma medication, and ACF also were assessed using the mixed-effects

regression model. All continuous data are expressed as the mean  $\pm$  SD. All statistical analyses were performed using the JMP version 11.0 statistical software (SAS Institute, Inc., Cary, NC, USA).

## Results

The demographic data obtained from the subjects included patient age, sex, eye, preoperative and postoperative BCVA, IOP, number of medications, and ACF (Table 1). The mixed-effect regression model showed that the postoperative IOP ( $p < 0.0001$ ) and medication use were significantly ( $p < 0.0001$ ) lower in the LEC and EXP groups than with  $\mu$ LOT for up to 6 months postoperatively and that the ACF differed significantly ( $p = 0.0004$ ) among groups, ie, the ACF was significantly higher ( $p = 0.0097$ , post-hoc *t*-test) with  $\mu$ LOT than the EXP at 2 weeks and was significantly ( $p = 0.0111$ , post-hoc *t*-test) lower with  $\mu$ LOT than LEC at 6 months.

## Discussion

Lower IOP and fewer medications after LEC and EXP than  $\mu$ LOT agreed well with our previous reports.<sup>11</sup> Higher ACF after LEC was reported compared to deep sclerectomy on postoperative day 7,<sup>7</sup> viscocanalostomy on postoperative week 1,<sup>8</sup> and EXP on postoperative days 1, 3, and 10,<sup>1,2</sup> although the difference in the ACF between LEC and these reported surgical procedures disappeared thereafter. Spikes in the ACF after LEC were seen during the early postoperative periods; therefore, the fact that there was no significant difference in ACF between LEC and EXP at postoperative week 2 does not disagree with previous reports. Significantly higher ACF with  $\mu$ LOT than EXP at postoperative week 2 is unique in the literature. Given the use of the ab interno approach to the angles, the MIGS procedures are expected to be less invasive to the ocular surface than filtration surgeries. The number of study eyes were heterogeneous among the surgical groups, therefore no significant difference not necessarily indicate the equivalent; thus this is one of the major limitations of this study. The  $\mu$ LOT group used more antiglaucoma medications than other groups postoperatively. Since some topical medications are known to break the blood-aqueous barrier, it is possible that the use of antiglaucoma medications have some roles on higher ACF in  $\mu$ LOT group. Considering our observation, although its clinical significance is unclear, not all MIGS are minimally invasive regarding early postsurgical inflammation.

**Table 1** Comparisons of subjects' demographic data, best-corrected visual acuity, intraocular pressure, medication, and anterior chamber flare among three surgical groups

	$\mu$ LOT	LEC	EXP	p-value
Numbers Subjects/Eyes	25/38	10/12	54/75	
Age (years) Mean $\pm$ SD 95% CI	55.4 $\pm$ 12.4 50.2–60.5	58.8 $\pm$ 8.1 53.0–64.6	59.8 $\pm$ 8.0 57.7–62.0	0.1533a
Sex, n (%) Male Female	16 (64) 9 (36)	8 (80) 2 (20)	31 (57) 23 (43)	0.3876b
Eye, n (%) Right Left	20 (53) 18 (47)	7 (58) 5 (42)	37 (49) 38 (51)	0.8804b
BCVA (logMAR) (mean $\pm$ SD [95% CI]) Preoperative 2 weeks 1 month 3 months 6 months	–0.04 $\pm$ 0.08 (–0.06–0.01) –0.02 $\pm$ 0.08 (–0.05–0.01) –0.03 $\pm$ 0.08 (–0.06–0.00) –0.04 $\pm$ 0.08 (–0.06–0.01) –0.03 $\pm$ 0.08 (–0.06–0.01)	0.36 $\pm$ 0.48 (0.06–0.66)** 0.35 $\pm$ 0.35 (0.13–0.58)** 0.31 $\pm$ 0.36 (0.08–0.54)** 0.30 $\pm$ 0.36 (0.07–0.53)** 0.29 $\pm$ 0.36 (0.06–0.52)**	0.07 $\pm$ 0.29 (0.00–0.14)### 0.20 $\pm$ 0.36 (0.12–0.28)### 0.12 $\pm$ 0.28 (0.06–0.19)** 0.11 $\pm$ 0.28 (0.05–0.18)**## 0.13 $\pm$ 0.32 (0.06–0.20)*	0.2108c 0.0001a 0.0001a 0.0001a 0.0001a 0.0007a
IOP (mmHg) (mean $\pm$ SD [95% CI]) Preoperative 2 weeks 1 month 3 months 6 months	18.8 $\pm$ 5.2 (17.1–20.5) 14.9 $\pm$ 4.4 (13.4–16.4) 14.5 $\pm$ 3.3 (13.4–15.6) 14.2 $\pm$ 3.1 (13.2–15.2) 14.2 $\pm$ 2.8 (13.3–15.19)	20.1 $\pm$ 7.9 (15.1–25.1) 8.8 $\pm$ 4.7 (5.9–11.8)** 8.2 $\pm$ 3.4 (6.0–10.3)** 8.3 $\pm$ 1.9 (7.1–9.5)** 9.0 $\pm$ 3.7 (6.6–11.4)**	18.1 $\pm$ 6.1 (16.7–19.5) 8.3 $\pm$ 4.1 (7.4–9.3)** 9.4 $\pm$ 3.6 (8.5–10.2)** 10.3 $\pm$ 6.2 (8.9–11.7)** 10.3 $\pm$ 3.9 (9.4–11.2)**	<0.0001c 0.5417a <0.0001a <0.0001a 0.0002a <0.0001a
Medication (mean $\pm$ SD [95% CI]) Preoperative 2 weeks 1 month 3 months 6 months	3.5 $\pm$ 0.9 (3.2–3.8) 2.8 $\pm$ 0.7 (2.6–3.1) 2.8 $\pm$ 0.7 (2.6–3.1) 3.0 $\pm$ 0.7 (2.7–3.29) 3.1 $\pm$ 0.8 (2.8–3.3)	3.6 $\pm$ 0.8 (3.1–4.1) 0 $\pm$ 0** 0.3 $\pm$ 0.9 (–0.3–0.8)** 0.3 $\pm$ 0.9 (–0.3–0.8)** 0.5 $\pm$ 1.2 (–0.2–1.2)**	3.5 $\pm$ 0.8 (3.4–3.7) 0 $\pm$ 0** 0 $\pm$ 0** 0.2 $\pm$ 0.7 (0.0–0.3)** 0.6 $\pm$ 1.2 (0.3–0.8)**	<0.0001c 0.9769a <0.0001a <0.0001a <0.0001a <0.0001a
AC flare (pc/msec) (mean $\pm$ SD [95% CI]) Preoperative 2 weeks 1 month 3 months 6 months	8.1 $\pm$ 2.7 (7.3–9.0) 33.6 $\pm$ 52.8 (16.2–51.0) 9.9 $\pm$ 4.1 (8.6–11.2) 9.1 $\pm$ 4.2 (7.7–10.5) 7.9 $\pm$ 2.0 (7.3–8.6)	11.0 $\pm$ 8.1 (7.2–14.9) 26.5 $\pm$ 29.3 (7.9–45.1) 11.5 $\pm$ 4.5 (8.6–14.3) 10.8 $\pm$ 3.7 (8.4–13.2) 12.0 $\pm$ 6.1 (8.1–15.8)*	8.7 $\pm$ 4.4 (7.7–9.7) 15.7 $\pm$ 19.9 (11.1–20.3)** 9.3 $\pm$ 5.8 (8.0–10.6) 8.4 $\pm$ 4.4 (7.5–9.4) 8.7 $\pm$ 5.4 (7.5–10.0)	0.0004c 0.1129a 0.0316a 0.1946a 0.0386a

**Notes:** The p-values were calculated among the three glaucoma surgeries by one-way analysis of variance for the continuous variables (A) or by the chi-square test for the categorical variables (B). The changes in BCVA, IOP, medication, and AC flare during the postoperative periods are tested by mixed-effect regression model (C). The post-hoc Student's t-test was performed between each pair of surgical groups. \* And \*\* Indicate significance levels of 5% and 1%, respectively, against the  $\mu$ LOT group; and the # and ## indicate significance levels of 5% and 1%, respectively, against the LEC group. In the post-hoc test, based on Bonferroni's method to correct multiple comparisons,  $p < 0.0167$  and  $p < 0.0033$  are considered significance levels of 5% (\* or #) and 1% (\*\* or ##), respectively.

**Abbreviations:**  $\mu$ LOT, microhook ab interno trabeculotomy; LEC, trabeculectomy; EXP, EX-PRESS shunt; SD, standard deviation; 95% CI, 95% confidence interval; BCVA, best-corrected visual acuity; logMAR, logarithm of the minimum angle of resolution; IOP, intraocular pressure; Medication, number of antiglaucoma medication; AC, anterior chamber; and pc, photon counts.

## Disclosure

The microhooks used were co-developed by Masaki Tanito, MD, PhD, and Inami & Co., Ltd. (Tokyo, Japan) and provided by Inami & Co., Ltd. Masaki Tanito reports receiving

royalties and personal fees from Inami & Co., Ltd., during the conduct of the study, and personal fees from Santen, Senju, Otsuka, Novartis, Pfizer, Alcon, Kowa, Nidek, Hoya, Bayer, AMO Japan, Tomey, Glaukos, and Sucampo

Pharma, outside the submitted work. The authors report no other conflicts of interest in this work.

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