Predictors of selective laser trabeculoplasty success in open angle glaucoma or ocular hypertension: Does baseline tonography have a predictive role?

Authors:

Pouya Alaghband[1,2] MD, FRCOphth

Elizabeth Galvis[1] MSC

Arij Daas[1,2] MD

Anindyt Nagar[1] MBBS

Laura Beltran-Agullo[3] MD

Anthony P. Khawaja[4] PhD, FRCOphth

Saurabh Goyal[1,2] MBBS, MS, DNB, FRCOphth

Kin Sheng Lim[1,2] MD, FRCOphth (corresponding author)

1. St Thomas' Hospital, London, United Kingdom

2. King's College London, London, United Kingdom

3. Institut Català de la Retina, Barcelona, Spain

4. NIHR Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, London, UK Moorfields Eye Hospital, London, United Kingdom

This work was presented at the annual Association of Research in Vision and Ophthalmology (ARVO) 2012, Fort Lauderdale, FL, USA

Financial support: KSL is funded by the NIHR, Biomedical Research Centre, Guy's & St Thomas' NHS Foundation Trust, London, UK

No conflicting relationship exists for any author

Contributorship: PA and KSL conceived the study. PA, EG, LBA and SG have collected and collated the data. PA has performed data analysis. All authors have contributed equally to manuscript preparation.

Running Head: SLT and its success determinants- IOP versus tonographic outflow facility

Corresponding author’s email address: shenglim@gmail.com

Address: KCL Frost Eye Research Department, St Thomas’ Hospital, Westminster Bridge Road, London, United Kingdom,

SE1 7EH

Abbreviations: IOP (intraocular pressure), OHT (ocular hypertension), POAG (primary open angle glaucoma), TOF (tonographic outflow facility), SLT (selective laser trabeculoplasty), AGIS (advanced glaucoma intervention study), GLT (glaucoma laser trial), LiGHT (selective laser trabeculoplasty versus eye drops or first line treatment of ocular hypertension and glaucoma), ACD (anterior chamber depth), AXL (axial length), CCT (central corneal thickness), HVF (Humphrey visual field)

Synopsis

This study demonstrated that only pre-treatment IOP (and not TOF) is the only determinant of success after primary SLT therapy. Perhaps there is resistance at the level of Schlemm’s canal.

Abstract

Background

The determinants of success of SLT in treatment naïve open angle glaucoma(OAG) and ocular hypertension(OHT) patients have not been understood fully. Therefore, we have conducted this study to explore the predictors of success.

Methods

This is a retrospective review of a pre-existing database of patients who had received primary SLT at St Thomas' Hospital, London, UK. Patients with OAG and OHT who had received primary 360º SLT treatment and had reliable baseline tonographic outflow facility with minimum of one year of follow up. Univariate and multivariate analyses were performed to find the determinants of success.

Results

One hundred and seventy-four patients between August 2006 and February 2010 had received primary 360º SLT treatment and had baseline tonographic outflow facility measurement. Of these, 72 subjects fulfilled the eligibility criteria.

In multivariate regression analysis, the only variable associated with success was baseline IOP (R^2 =0.32, beta=-0.51, p<0.001, 95% CI= -2.02 - -0.74).

Conclusion

To our knowledge, this is the only study investigating the pre-treatment TOF (measured with electronic Shiøtz tonography) and IOP as determinants of success 12-month's post 360º SLT in treatment naïve OAG and OHT patients. This study demonstrated that pre-treatment IOP (and not TOF) is the only determinant of success after primary SLT therapy.

Wise and Witter [1] first described argon laser trabeculoplasty (ALT) in 1970's. Since then several seminal clinical trials including the Advanced Glaucoma Intervention Study (AGIS) [2] and Glaucoma Laser Trial (GLT) [3] have shown the effectiveness of this treatment modality. Later in 1990's Latina and colleagues [4] devised a new technique called selective laser trabeculoplasty (SLT) which is gentler and repeatable but as effective to ALT. Subsequently, numerous studies demonstrated benefits of this procedure [5-7]. Most recently published study on SLT versus eye drops as the first line treatment of ocular hypertension and glaucoma (LiGHT) has confirmed that SLT is an effective first-line treatment for open angle glaucoma and OHT [5]. However, the response rate to SLT was reported to be only 74% according to LiGHT trial. It is not clear why the rest of (26%) patients do not respond to primary SLT treatment.

Previous studies have indicated that pre-treatment intraocular pressure (IOP) is the strongest factor in predicting IOP reduction post SLT in patients who were on medical therapy. Mao et al,[8] investigated the predictors of success after 180º SLT treatment. In that study the baseline IOP was the only determinant of success.

Ayala and associates,[9] in a retrospective report assessed 120 patients with primary open angle glaucoma (POAG) and ocular hypertension (OHT), who had uncontrolled IOP despite medical therapy. All cases had undergone 90º SLT. It was confirmed that higher pre-treatment IOP, age and the amount of laser energy determine the time to failure. All aforementioned studies, however, were undertaken in previously medically treated eyes.

In our previous publications,[10,11] we demonstrated that IOP reduction was not fully explained by the amount of outflow facility enhancement at 3 months post SLT. However, Gulati et al.[12] reported that lower baseline aqueous outflow facility (measured by fluorophotometry and pneumatonometry) is significantly associated with IOP 3-month post SLT.

We sought to investigate the predictive role of baseline electronic Shiøtz tonographic outflow facility (TOF: a method that has been shown to be the most consistent way to measure outflow facility[13]) in patients with open angle glaucoma (OAG) and OHT who received primary 360º of SLT treatment.

To our knowledge, this is the first study exploring the predictive role of IOP and tonographic outflow facility using electronic Shiøtz tonography after 360º SLT in treatment naïve patients with OAG and OHT with one year follow up.

Materials and methods

This is a retrospective review of a pre-existing database of patients who had received primary SLT (as first line therapy) from August 2006 till February 2010 at St Thomas' Hospital, London, UK. The ethical approval was obtained from the local ethics committee. An informed consent form was sought prior to the study. The study conformed with the Tenants of Helsinki. Treatment naïve patients with newly diagnosed OAG or OHT (who required to have IOP reduction) with a reliable baseline tonographic outflow facility and minimum follow up of 12 months with available IOP measurements post treatment, were included in the final analysis.

Baseline characteristics of patients were documented including age, gender and ethnicity. All subjects had a comprehensive ophthalmic examination including visual acuity, gonioscopy, axial length and anterior chamber depth (measured using IOL Master, Carl Zeiss Meditec Inc., Dublin, CA), central corneal thickness (CCT) (CCT; Pachmate DGH 55, DGH Technology, Inc., Exton, PA), IOP, disc assessment and Humphrey visual field (Humphrey automated white-on white, 24-2 SITA-standard; Carl Zeiss Meditec Inc., Dublin, CA). Total laser energy was documented.

The tonographic facility of outflow was measured at baseline from the rate of decay of IOP in the supine position during application of a recording electronic Schiøtz tonometer probe over a period of 4 minutes with various weights depending on the starting IOP [14]. The 'R' values of the curve at every 30 seconds time point were manually entered into the McLaren tonography computer program[15]. This program fits a second-degree polynomial by the least squares to nine data points. It then determines the best-fit values for time 0 and time 4 minutes by extrapolation [10,11].

Treatment

The SLT protocol is described in detail in our previous publications[10,11]. But in brief, it comprised pre-treatment with pilocarpine 2% and Apraclonidine 1% drops followed by laser treatment to 360° of the trabecular meshwork. SLT treatment was performed using the Ellex Solo machine (Ellex, Adelaide, Australia), spot size of 400-μm, duration 3 nanoseconds. Starting energy level was 0.6 mJ. Energy level was titrated at three o'clock position up to the point where champagne bubbles or minimal blanching was visible. Approximately 100 treatment spots were applied to each eye. Magna view gonioscopy lens (Ocular instruments, Bellevue, Washington, USA) was used to visualise the trabecular meshwork during SLT application. All patients had a standardised postoperative regime of Dexamethasone 0.1% eye drops (Maxidex, Alcon Laboratories, UK) four times a day for 5 days.

Baseline IOP was the average of two IOP measurements using Goldmann applanation tonometry (GAT) prior to SLT therapy. The success (responders) was defined as 20% or greater IOP reduction from the baseline without additional IOP-lowering medications and/or repeat glaucoma laser/surgical procedures at one-year post treatment.

Data Analysis

The data was analysed using statistical software SPSS 23.0 (SPSS, IBM, Chicago, IL, USA). A Shapiro Wilk "*W*" value of >0.05 was an evidence of normal distribution. Paired Student *t* tests were used to compare IOP before and after treatment and baseline TOF. A p value <0.05 was considered statistically significant. The 95% confidence interval was also calculated for each parameter. The univariate regression analysis was performed by including patient's AXL, ACD, CCT, HVF, total laser energy, baseline IOP and TOF. Only if $p<0.1$ for each variable, then they were entered into a multivariate regression analysis in order to build a prediction model for success of the SLT treatment.

Results

One hundred and seventy-four eyes of 174 patients between August 2006 and February 2010 were identified to have primary SLT treatment and baseline tonographic outflow facility measurement. Eighteen eyes had <360º SLT treatment, 67 individuals had less than 12 months follow up and 17 cases had unreliable tonography.

Only 72 eyes of 72 patients had 360˚ SLT and reliable baseline tonographic outflow facility with at least 12-months' follow up and IOP measurements.

All Schiøtz tonography tracings were graded by two examiners (PA and LBA) before the analysis. Only one eye per patient was included in the final analysis. If both eyes were eligible, one eye was randomly chosen (Excel random number generator, Microsoft Office, 2016).

The average (±SD) age of the sample was 59±12.8 years. Thirty-eight participants were male. Black (African-Caribbean): White Caucasian: Asian ratio was 47: 23: 2. Forty-six eyes (63.9%) had POAG, 23 had OHT (32%) and 3 had pigment dispersion syndrome with OHT (4.2%).

The baseline characteristics of participants (based on their response to SLT) are shown in Table 1.

Table 1. Baseline characteristics of participants

	Responders (n=54)	**Non-responders (n=18)**	**P value**	**95% Confidence interval**
Age, years	59.3±13.6	58.3±10.4	0.7	-6.09, 7.9
Visual acuity (logMAR)	0.00 (-0.2-0.5)	0.00 (-0.2-1.0)	0.1	-0.17, 0.02
CCT, μm	544±35	533±58	0.3	-11, 33
ACD, mm	3.17±0.4	3.3±1.2	0.3	-0.4, 0.12
AXL, mm	23.8±1.1	23.8±1.2	0.9	-0.7, 0.7
CD ratio	0.7(0.2-0.9)	0.6(0.2-0.95)	0.4	--------
HVF, MD•	-4.8±5.9	-6.1±4.9	0.4	-1.99, 4.5
Total laser energy, mJ	99±18	103±13	0.5	-13, 7
IOP, mmHg	25.0±4.0	24.6±3.0	0.4	-1.2, 2.9
One-year Post op IOP, mmHg	16.2±2.7	21.9±2.8	<0.001	-7.2, -4.2
TOF, μl/mmHg/min, (Range)	0.12±0.06 (0.02-0.29)	0.11±0.06 (0.05-0.28)	0.7	-0.03, 0.04

CCT: central corneal thickness, ACD: anterior chamber depth, AXL: axial length, CD ratio: cup disc ratio, HVF: Humphrey visual field, MD: mean deviation, IOP: intraocular pressure. TOF- Tonographic outflow facility

The distribution of IOP and TOF in each group is illustrated in Figure 1 and 2.

The success rate based on 20% or greater IOP reduction one-year post SLT, in this cohort was 75%.

The IOP changes at 1, 3, 6 and 12 months postop is shown in Figure 3. The IOP and TOF were not linearly significantly associated (Spearman rho=-0.84, p=0.482).

We used univariate regression analysis including ACD (p=0.2), AXL (p=0.2), CCT-(p=0.2), HVF (p=0.2), total laser energy (p=0.3), baseline IOP (p=0.02) and TOF (p=0.5) to compare with 12 months IOP. The only variable with p<0.1 was IOP. It was then entered in multivariate regression model. The baseline IOP was the only parameter which remained significantly associated with IOP at 12 months (R^2 =0.32, beta=-0.543, p<0.001, 95% CI= -2.1, -0.8).

Additionally, we analysed responders (IOP reduction >20% without any hypotensive medications or any further intervention) separately and performed univariate analysis using baseline TOF and IOP. The association between baseline vs 12 months IOP was statistically significant (p=0.05) but TOF was only weakly associated with 12-month IOP (p=0.5). Furthermore, in multivariate regression analysis, the only association that remained statistically significant was baseline IOP (R^2 =0.32, beta=-0.51, p<0.001, 95% CI= -2.02, -0.74). Similar analysis was performed for non-responders. Neither baseline IOP nor TOF were associated with 12-month IOP reduction (p=0.06).

Discussion

This is the first study investigating the predictive role of baseline IOP and tonographic outflow facility using electronic Shiøtz tonography in patients with OAG and OHT who had received 360˚ SLT therapy as a primary treatment in the medium-term. Overall, we demonstrated that baseline IOP prior to delivery of the treatment can strongly be associated with the SLT treatment success (i.e. IOP reduction 20% or greater). However, the response to SLT at one-year was not statistically associated with pre-treatment TOF. The success rate based on 20% or greater IOP reduction without any IOP-lowering medication or additional glaucoma laser/surgical therapy from baseline at 12-months' post procedure was 75%. This is in agreement with most of the available literature including the LiGHT trial[5,8,9,16,17].

Mao and associates [8] defined success as greater or equal to 20% IOP reduction at 6 months after 180˚ SLT. They studied 268 eyes of 158 patients who may have had pervious glaucoma laser procedure i.e. argon laser trabeculoplasty or failed medical therapy. They demonstrated that baseline IOP can predict the success of SLT therapy at 6 months. In our study of SLT treatment of naïve cases who had 360˚ SLT, our findings (in medium term follow up) were in agreement with the aforementioned study. We found that baseline pre-treatment IOP was statistically associated with 12-months IOP reduction post SLT. Other studies of 180˚ SLT with medium or long-term follow up [18,19] corroborated our results in terms of prognostic role of pre-treatment IOP in SLT success. Lee et al [20], in a small prospective study of 51 eyes of 33 patients (they included both eyes in their analysis), investigated the effect of 360˚ SLT and continued medical therapy in a group of Chinese patients. They defined success as ≥20% IOP reduction at 1-month post SLT. The higher pre-treatment IOP was associated with greater SLT success. In our study, we included only one eye per patient who received 360˚ SLT with at least 12 months follow up. We found that baseline IOP, is the only determinant of success post SLT as a primary treatment in patients with OAG and OHT. This finding is supported by the result of the LiGHT trial. Garg and associates showed that the only determinant of SLT success was the pre-treatment IOP [5,21].

Brubaker and colleagues [22] assessed the effect of ALT (argon laser trabeculoplasty) on aqueous humor dynamics. They demonstrated a meaningful IOP reduction at 3-month post procedure. This was associated with an improvement of TOF from 0.11±0.05 µl/min/mmHg to post-treatment value of 0.18±0.08-µl/min/mmHg ($p<0.001$). However, other aqueous humor dynamic parameters remained unchanged post ALT treatment. In our previous studies on the effect of SLT on outflow facility [10,11], we demonstrated that indeed SLT improved post SLT tonographic outflow facility (baseline of 0.08±0.07 vs 0.17±0.09 µl/min/mmHg, $p<0.001$). We found 29% IOP reduction post SLT with 37.5% TOF enhancement. Based on the Goldmann's equation, the amount of IOP reduction was not fully explained by TOF improvement. This finding is congruent with other similar studies [22-24].

Gulati et al. [12] showed that calculated uveoscleral outflow, episcleral venous pressure and aqueous flow rate remained unchanged 3-month post SLT. They demonstrated that higher baseline aqueous flow rate, lower fluorophotometric/pneumatonometric outflow facility and lower uveoscleral outflow were associated with IOP lowering effect of SLT. However, association between outflow facility and IOP lowering effect of SLT was in disagreement with our findings. This disparity may be due to inclusion of glaucoma suspect cases and the follow-up was only 3 months in the Gulati et al. study. Additionally, they utilised fluorophotometry/pneumatonography to measure outflow facility which are known to be less reproducible with higher variability of measurements compared to Shiøtz tonography[13]

This controversy, begs the question of what might be the explanation for non-response after application of SLT? If trabecular meshwork (TM) is the primary site of pathology in POAG, then variation in TOF in POAG patients would be expected to primarily reflect variation in TM resistance. In turn, we would then expect TOF to predict response to TM-targeted therapies such as SLT. However, there is a growing evidence that POAG affects post-TM structures as well. The post-TM aqueous outflow pathway is limited by the resistance of structures including Schlemm's canal and collector channels [25,26]. Supporting this are the floor effects seen in outcomes of surgical TM-bypass procedures [27,28]. Additional evidence for the role of post-TM structures in IOP regulation comes from a large genome-wide association study which identified genetic variants that predict IOP in population [29]. The lymphangiogenesis biological pathway was the most significantly enriched pathway underlying IOP variation [29]. The lymphangiogenic factors, including *ANGPT1* and *VEGF-C*, appear to affect Schlemm's canal and collector channels (which have a lymphatic phenotype), but not TM [30-33]. This suggests that a proportion of high IOP in populations is due to Schlemm's canal or collector channel pathology, rather than TM pathology. We would not expect TM-targeted therapies, such as SLT, to be effective in this instance. Therefore, TOF alone would be unlikely to predict response to SLT, as a low TOF may be reflecting post-TM pathology and not solely TM pathology.

To our knowledge, this is the only study using electronic Shiøtz tonography investigating the TOF and IOP as a determinant of success at 12 month's post 360º SLT in treatment naïve patients.

The limitations of our study included: absence of 12 months post SLT, TOF measurement, perhaps the study might have been underpowered for some of the variables, the IOP data beyond 3 months post SLT were collected from the notes which is subject to bias and finally the included cases were treatment naïve OHT or mild to moderate OAG only. This means the result of this study may not be generalisable to other groups of patients.

In summary, the current study demonstrated that pre-treatment IOP is the only determinant of success after SLT therapy. Pre-treatment TOF cannot reliably predict the SLT outcome.

References:

1. Wise JB, Witter SL. Argon Laser Therapy for Open-Angle Glaucoma. *Arch Ophthalmol* 1979;**97**:319.

2. Ederer F, Gaasterland D, Dally L, *et al.* The advanced glaucoma intervention study (AGIS)-13. Comparison of treatment outcomes within race: 10-year results. *Ophthalmology* 2004;**111**:651–64.

3. Beckman H, Meinert C, Ritch R, *et al.* The Glaucoma Laser Trial (GLT). 2. Results of argon laser trabeculoplasty versus topical medicines. The Glaucoma Laser Trial Research Group. *Ophthalmology* 1990;**97**:1403–13.

4. Latina M, Park C. Selective targeting of trabecular meshwork cells: in vitro studies of pulsed and CW laser interactions. *Exp Eye Res* 1995;**60**:359–71.

5. Gazzard G, Konstantakopoulou E, Garway-Heath D, *et al.* Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial. *Lancet* 2019;**6736**:1–12.

6. Damji KF. II. Selective Laser Trabeculoplasty: A Better Alternative. *Surv Ophthalmol* 2008;**53**:646–651

7. Bovell AM, Damji KF, Hodge WG, *et al.* Long term effects on the lowering of intraocular pressure: Selective laser or argon laser trabeculoplasty? *Can J Ophthalmol* 2011;**46**:408–13.

8. Mao AJ, Pan X-J, McIlraith I, *et al.* Development of a prediction rule to estimate the probability of acceptable intraocular pressure reduction after selective laser trabeculoplasty in open-angle glaucoma and ocular hypertension. *J Glaucoma* 2008;**17**:449–54.

9. Ayala M, Chen E. Predictive factors of success in selective laser trabeculoplasty

(SLT) treatment. *Clin Ophthalmol* 2011;**5**:573–6.

10. Goyal S, Beltran-Agullo L, Rashid S, *et al.* Effect of primary selective laser trabeculoplasty on tonographic outflow facility: a randomised clinical trial. *Br J Ophthalmol* 2010;**94**:1443–7.

11. Beltran-Agullo L, Alaghband P, Obi A, *et al.* The effect of selective laser trabeculoplasty on aqueous humor dynamics in patients with ocular hypertension and primary open-angle glaucoma. *J Glaucoma* 2013;**22**:746–9.

12. Gulati V, Fan S, Gardner BJ, *et al.* Mechanism of action of selective laser trabeculoplasty and predictors of response. *Investig Ophthalmol Vis Sci* 2017;**58**:1462–8.

13. Lim KS, Nau CB, O'Byrne MM, *et al.* Mechanism of action of bimatoprost, latanoprost, and travoprost in healthy subjects. A crossover study. *Ophthalmology* 2008;**115**:790–5.

14. Grant WM. Clinical Measurements of Aqueous Outflow. *Arch Ophthalmol* 1951;**46**:113–31.

15. Brubaker RF, Schoff EO, Nau CB, *et al.* Effects of AGN 192024, a new ocular hypotensive agent, on aqueous dynamics. *Am J Ophthalmol* 2001;**131**:19–24.

16. Realini T. Selective laser trabeculoplasty: a review. *J Glaucoma* 2008;**17**:497–502.

17. Kennedy J, SooHoo J, Kahook M, *et al.* Selective laser trabeculoplasty: an update. *Asia Pac J Ophthalmol* 2016;**5**:63–9.

18. Martow E, Hutnik CML, Mao A. SLT and adjunctive medical therapy: a prediction rule analysis. *J Glaucoma* 2011;**20**:266–70.

19. Miki A, Kawashima R, Usui S, *et al.* Treatment Outcomes and Prognostic Factors of Selective Laser Trabeculoplasty for Open-angle Glaucoma Receiving

Maximal-tolerable Medical Therapy. *J Glaucoma* 2016;**25**:785–9.

20. Lee JW, Liu CC, Chan JC, *et al.* Predictors of success in selective laser trabeculoplasty for primary open angle glaucoma in Chinese. *Clin Ophthalmol* 2014;**8**:1787–91.
21. Garg A, Vickerstaff V, Nathwani N, *et al.* Primary Selective Laser Trabeculoplasty for Open Angle Glaucoma and Ocular Hypertension: Clinical Outcomes, Predictors of Success and Safety from the Laser in Glaucoma and Ocular Hypertension (LiGHT) Trial. *Ophthalmology* 2019;**126**:1238–49.
22. Brubaker R, Liesegang T. Effect of Trabecular Photocoagulation on the Aqueous-Humor Dynamics of the Human eye. *Am J Ophthalmol J* 1983;**96**:139–47.
23. Bergea˚ B, Svedbergh B. Primary argon laser trabeculoplasty vs. pilocarpine. Short-term effects. *Acta Ophthalmol* 1992;**70**:454–60.
24. Thomas JVJ, Simmons RRJ, Belcher CDC. Argon laser trabeculoplasty in the presurgical glaucoma patient. *Ophthalmology* 1982;**89**:187–97.
25. Carreon T, van der Merwe E, Fellman RL, *et al.* Aqueous outflow - A continuum from trabecular meshwork to episcleral veins. *Prog Retin Eye Res* 2017;**57**:108–33.
26. Swaminathan SS, Oh D-JJ, Kang MH, *et al.* Aqueous outflow: Segmental and distal flow. *J Cataract Refract Surg* 2014;**40**:1263–72.
27. raven ER, Katz LJ, Wells JM, *et al.* Cataract surgery with trabecular micro-bypass stent implantation in patients with mild-to-moderate open-angle glaucoma and cataract: Two-year follow-up. *J Cataract Refract Surg* 2012;**38**:1339–45.
28. Pfeiffer N, Garcia-Feijoo J, Martinez-de-la-Casa JM, *et al.* A Randomized Trial of

a Schlemm's Canal Microstent with Phacoemulsification for Reducing Intraocular Pressure in Open-Angle Glaucoma. *Ophthalmology* 2015;**122**:1283–93.

29. Khawaja AP, Cooke Bailey JN, Wareham NJ, *et al.* Genome-wide analyses identify 68 new loci associated with intraocular pressure and improve risk prediction for primary open-angle glaucoma. *Nat Genet* 2018;**50**:778–82.

30. Thomson BR, Souma T, Tompson SW, *et al.* Angiopoietin-1 is required for Schlemm's canal development in mice and humans. *J Clin Invest* 2017;**127**:4421–36.

31. Souma T, Tompson SW, Thomson BR, *et al.* Angiopoietin receptor TEK mutations underlie primary congenital glaucoma with variable expressivity. *J Clin Invest* 2016;**126**:2575–87.

32 Kizhatil K, Ryan M, Marchant JK, *et al.* Schlemm's canal is a unique vessel with a combination of blood vascular and lymphatic phenotypes that forms by a novel developmental process. *PLoS Biol* 2014;**12**:e1001912.

33 Aspelund A, Tammela T, Antila S, *et al.* The Schlemm's canal is a VEGF-C/VEGFR-3-responsive lymphatic-like vessel. *J Clin Invest* 2014;**124**:3975–86.

Figure 1. The distribution of baseline intraocular pressure in the successful vs treatment failure group

Figure 2. The distribution of baseline topographic outflow facility in the successful vs treatment failure group

Figure 3. The IOP changes at 1, 3, 6 and 12 months postop

Figure 1. The distribution of baseline intraocular pressure in the successful vs treatment failure group

Figure 2. The distribution of baseline topographic outflow facility in the successful vs treatment failure group

Figure 3. The IOP changes at 1, 3, 6 and 12 months postop