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# Predictors of Success in Selective Laser Trabeculoplasty for Normal Tension Glaucoma

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**Abstract:** To determine the predictors of success for selective laser trabeculoplasty (SLT) in normal tension glaucoma (NTG).

This prospective cohort study recruited subjects with unilateral or bilateral NTG on medication. All subjects received a single session of 360° SLT treatment. SLT success was defined as IOP reduction ≥20% at 1-month. The following covariates were analyzed via univariate and multivariate analyses: age; sex; lens status; presenting, pre-SLT, and post-SLT IOP's; number and type of medications; SLT shots and energy; and pre-SLT investigations.

In 60 eyes of 32 subjects with NTG, there were 30 right eyes and 28 left eyes. The success rate of SLT was 61.7%. Using 3 types of anti-glaucoma medications (coefficient = −2.2, OR = 0.1, $P = 0.02$) and a thicker retinal nerve fiber layer thickness (coefficient = −0.04, OR = 0.96, $P = 0.04$) were associated with failure (univariate analysis). In multivariate analysis, a higher pre-SLT IOP (coefficient = 1.1, OR = 3.1, $P = 0.05$) and a lower 1-week IOP (coefficient = −0.8, OR = 0.5, $P = 0.04$) were associated with success.

SLT was successful in over 60% of treated NTG patients. A higher pre-SLT IOP and a greater IOP reduction at 1-week post-SLT were predictors of a successful outcome.

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**Abbreviations**: ALT = argon laser trabeculoplasty, IOP = intraocular pressure, NTG = normal tension glaucoma, RNFL = retinal nerve fiber layer, SLT = selective laser trabeculoplasty.

## INTRODUCTION

Selective laser trabeculoplasty (SLT) works just as well in IOP-lowering as anti-glaucoma medication and argon laser trabeculoplasty (ALT)[1,2] but only utilizing 1% of the energy in ALT hence making it a safer treatment for open angle glaucoma.[3–12]

While SLT is safe and almost free of permanent damages to the trabecular meshwork and cornea,[13] not everyone that is being treated responds. Recently, in a series of 83 eyes, SLT was found to be effective in normal tension glaucoma (NTG), lowering the IOP by an additional 20% from pre-SLT levels with 27% less medication use at 6 months while maintaining a 30% reduction from baseline IOP.[14]

Much work has been done to identify the factors that predict SLT success including: an absence of IOP-lowering medication prior to laser[15–17] and a higher pre-SLT IOP.[18] Conflicting results have been reported for angle pigmentation,[6,7] while other factors like diabetes, central corneal thickness, lens status, and angle status were not found to influence SLT success.[19] There is limited information in the literature investigating variables that predict SLT outcomes in NTG.

## METHODS

This prospective cohort study sequentially recruited subjects from the ophthalmology clinic of a university hospital, Queen Mary Hospital, Hong Kong Special Administrative Region, China, during September 2011 to September 2012. The study included subjects with NTG currently on anti-glaucoma medication. Subjects were excluded if they had pre-existing corneal pathology or scars, previous ALT or SLT treatment, or if they defaulted follow-up. A single session of SLT was performed by a single surgeon (JWYL) using a Q-switched Nd:YAG laser (Ellex Solo™, Ellex Medical Pty. Ltd., Adelaide, SA, Australia), for 360° in all patients with an initial energy of 0.8 mJ and titrated until bubble formation was just visible. For those with bilateral disease, both eyes were treated in the same laser session. In all treated eyes, a single drop of brimonidine (Alphagan P, Allergan, Inc., Waco, TX) was instilled immediately after SLT and a dexamethasone 0.1% and neomycin 0.5% combination eye drop (Dexoptic-N by Ashford Laboratories Pvt. Ltd., Santacruz (West), Mumbai, India) was used twice daily for 1 day and was continued for a few more days only if anterior chamber reaction was detected during follow-up. Patients returned for follow-up on Day 1, 1 week, 1 month, and 3 months after SLT. Patients continued the same anti-glaucoma drug regime for the first month after SLT and medication was subsequently titrated to achieve individual target pressures as per the recommendations from The Collaborative Normal Tension Glaucoma Study, aiming at a 30% reduction from presenting IOP.[20]

The following parameters were recorded during the study: age, sex, lens status (phakic or pseudophakic), presenting IOP without medication, pre-SLT IOP, post-SLT Day 1 IOP, post-SLT 1 week IOP, number of anti-glaucoma medications, number of SLT shots, average laser energy used, pre-SLT average retinal nerve fiber layer (RNFL) via a Spectralis Optical Coherene Tomography, pre-SLT Visual Field Index on Humphrey Field Analyzer (Humphrey Instruments, Inc., Zeiss Humphrey, San

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Leandro, CA), pre-SLT endothelial cell count via a non-contact specular microscopy (Noncon ROBO-CA by Konan Medical USA, Inc., Irvine, CA), pre-SLT central corneal thickness via videokeratography (Orbscan® IIz by Bausch & Lomb, Rochester, NY), pre-SLT Snellen visual acuity, pre-SLT spherical equivalent via kerato-refractometer (Topcon KR-8900 by Topcon Europe Medical B.V., Capelle a/d Ijssel, Netherlands), and the type of anti-glaucoma eye drops used pre-SLT (B-blocker, carbonic anhydrase inhibitor, prostaglandin analog, alpha agonist, or pilocarpine). All IOP readings were measured via Goldmann applanation tonometry by a single investigator and trained optometrists measured all other ocular parameters.

This study adhered to the tenets of the Declaration of Helsinki. Informed patient consent and approval by the Institutional Review Board were obtained prior to study commencement. The authors declare no financial or proprietary interests. The study was conducted without funding.

## Definition of Success

The definition of SLT success was determined as a 20% or more reduction in IOP at 1 month after SLT as compared to the pre-SLT IOP. The 1 month IOP was selected as all anti-glaucoma medications were kept unchanged until 1 month after SLT; after which, anti-glaucoma medications were titrated to achieve individual target pressures so the IOP's measured beyond 1 month will not solely represent the efficacy of SLT.

## Statistics

The association of the 24 covariates (Table 1) with SLT success was analyzed in the NTG group using univariate logistic analysis and multiple regression analysis were used. The high collinearity among the covariates hindered the interpretation of traditional multiple logistic regression. To overcome this, variable selection by elastic net approach was first conducted to opt out redundant covariates where the estimates of coefficients equaled to zero prior to multiple regression analysis.

We performed both the univariate and multivariate regression analysis for the following 3 datasets separately: (1) both eyes, (2) right eyes only, and (3) left eyes only. We found that the significant variables detected from the right and left eyes were different, signifying that each eye has a unique underlying distribution, which was different from the other side eye. Furthermore, the analysis using data from both eyes was the most comprehensive in including all variables that were significant when using just the right or left eyes alone. Hence, we adopted the methodology of including both eyes in the dataset as this reveals all the possible significant variables.

Correlations were expressed in coefficients and odds ratio (OR) and a $P < 0.05$ was considered as statistically significant. All means were expressed as mean ± standard deviation.

# RESULTS

In 60 eyes of 32 subjects with NTG, there were 30 right eyes and 28 left eyes. Twenty-eight subjects received bilateral SLT treatment. The mean age was 67.4 ± 12.3 years.

The mean IOP at initial presentation prior to starting anti-glaucoma medication was 17.4 ± 2.7 mm Hg. The pre-SLT IOP was 16.0 ± 2.1 mm Hg while on 1.7 ± 1.0 types of anti-glaucoma eye drops. The mean average RNFL thickness was 66.2 ± 15.1 μm.

The mean SLT shots applied was 185.4 ± 27.5 per session using a mean power of 1.0 ± 0.08 mJ. The mean IOP at 1 month after SLT was 12.5 ± 2.1 mm Hg representing an IOP reduction of 21.5 ± 11.4%. The success rate of SLT (eyes with IOP reduction ≥20%) was 61.7% (37/60).

Using univariate analysis, the following parameters were significantly associated with SLT failure: using 3 anti-glaucoma eye drops prior to SLT (coefficient = −2.2, OR = 0.1, $P = 0.02$) and a thicker RNFL (coefficient = −0.04, OR = 0.96, $P = 0.04$). In multivariate analysis, a higher pre-SLT IOP (coefficient = 1.1, OR = 3.1, $P = 0.05$) and a lower 1-week IOP (coefficient = −0.8, OR = 0.5, $P = 0.04$) were associated with SLT success (Table 1).

# DISCUSSION

Identification of factors that predict success is important for SLT because not everyone that is being treated responds in the same manner; the success rate for SLT in open angle glaucoma ranges from 65% to 100%.[3–12] We noted slightly lower success rate (61.7%) than what has been reported in the literature primarily because our population consisted of subjects with normal/low IOP and as we have demonstrated in multivariate analysis that SLT success was correlated with a higher pre-treatment IOP. This finding was consistent with other reports that reported associations of higher IOP with SLT success[18] with OR in the range of 1.3[21] to 1.58[22] for open angle glaucomas. We report an OR of 3.1 when using a higher pre-SLT IOP as a predictor of success.

A lower IOP in the earlier phase (1-week) following SLT was also a significant predictor for success. This was consistent with the findings of a larger series including primary open angle glaucomas that reported a similar association with IOP 1 day following SLT.[23] A greater IOP reduction in the early periods following SLT may represent a higher level of metalloproteinases, cytokines, and macrophages, which have been proposed to be the biological agents responsible for IOP-lowering.[24]

The results from our study suggest that the number of anti-glaucoma medication use prior to SLT may influence its success. It was found that using 3 types of anti-glaucoma eye drops prior to SLT was associated with a higher failure rate ($P = 0.02$). We postulate that those using multiple anti-glaucoma medications were likely to have a lower pre-SLT IOP hence, less success with SLT because of this indirect association with pre-treatment IOP. The influence of medication on SLT has been controversial. While some have suggested that SLT response is better for those without prior medication use,[15,16] others have reported no differences in outcome with anti-glaucoma medication use[25] and it has even been suggested that SLT may have an additive effect with anti-glaucoma medication.[26] In a recent study on the predictors of SLT in Chinese POAG, the use of a topical carbonic anhydrase inhibitor prior to laser was found to be associated with greater success (coefficient = 1.7; OR: 6.0; $P = 0.003$).[27]

A thicker average RNFL thickness was weakly associated with a higher failure rate for SLT. This observation was consistent with that of a larger series involving primary angle open angle glaucomas, where it was postulated that those with a higher IOP may present with more advanced RNFL thinning, hence those with a thicker RNFL (less RNFL damage) may be those with a lower or better IOP control and hence, poorer response to SLT, another indirect association between pre-SLT IOP and SLT response.

Our study was limited by the fact that the 1-month IOP was used as a reference of SLT success, a longer time period following SLT would have been more ideal. However, the

**TABLE 1.** Univariate and Multivariate Regression Analyses of the Covariates Affecting SLT Success in NTG

| | Univariate Logistic Analysis | | | | Multiple Regression | | | |
|---|---|---|---|---|---|---|---|---|
| | *P*-Value | Coefficient Estimates | Standard Deviation | Odds Ratio | *P*-Value | Coefficient Estimates | Standard Deviation | Odds Ratio |
| Age | 0.15 | −0.03 | 0.02 | 0.97 | 0.12 | −0.31 | 0.20 | 0.73 |
| Sex | 0.46 | −0.39 | 0.53 | 0.68 | 0.86 | 0.38 | 2.13 | 1.46 |
| Pseudophakic | 0.31 | −0.74 | 0.73 | 0.48 | 0.14 | 5.22 | 3.57 | 184.52 |
| Phakic | 0.40 | 0.51 | 0.62 | 1.67 | 0.42 | −1.93 | 2.41 | 0.15 |
| Presenting IOP (without medication) | 0.68 | −0.04 | 0.10 | 0.96 | 0.45 | −0.26 | 0.35 | 0.77 |
| Pre-SLT IOP | 0.17 | 0.18 | 0.13 | 1.19 | 0.05* | 1.12 | 0.57 | 3.08 |
| Day 1 IOP post-SLT | 0.97 | 0.00 | 0.11 | 1.00 | 0.16 | −0.83 | 0.59 | 0.43 |
| 1 Week IOP post-SLT | 0.20 | −0.09 | 0.07 | 0.91 | 0.04* | −0.77 | 0.37 | 0.46 |
| 1 Type of anti-glaucoma medication | 1.00 | 0.00 | 0.53 | 1.00 | 0.51 | 3.03 | 4.64 | 20.73 |
| 2 Type of anti-glaucoma medication | 0.09 | 1.00 | 0.61 | 2.71 | 0.11 | 15.63 | 9.78 | 6147411.00 |
| 3 Type of anti-glaucoma medication | 0.02* | −2.22 | 1.13 | 0.11 | 0.78 | 2.25 | 8.13 | 9.48 |
| 4 Type of anti-glaucoma medication | 1.00 | 0.00 | 0.95 | 1.00 | 0.23 | 12.71 | 10.59 | 330773.20 |
| SLT shots | 0.57 | 0.01 | 0.01 | 1.01 | 0.45 | −0.06 | 0.07 | 0.95 |
| SLT energy | 0.45 | 0.01 | 0.01 | 1.01 | 0.64 | 0.03 | 0.07 | 1.03 |
| Pre-SLT RNFL | 0.04* | −0.04 | 0.02 | 0.96 | 0.27 | −0.10 | 0.09 | 0.90 |
| Pre-SLT VFI on HVF | 0.57 | −0.01 | 0.01 | 0.99 | 0.87 | 0.01 | 0.05 | 1.01 |
| Pre-SLT endothelial cell count | 0.99 | 0.00 | 0.00 | 1.00 | 0.57 | 0.00 | 0.00 | 1.00 |
| Pre-SLT central corneal thickness | 0.98 | 0.00 | 0.01 | 1.00 | 0.91 | 0.00 | 0.03 | 1.00 |
| Pre-SLT Snellen VA | 0.47 | 0.80 | 1.13 | 2.23 | 0.63 | −2.89 | 6.04 | 0.06 |
| Pre-SLT spherical equivalent | 0.08 | −0.11 | 0.07 | 0.89 | 0.74 | −0.16 | 0.49 | 0.85 |
| Pre-SLT use of prostaglandin analogs | 0.75 | 0.17 | 0.53 | 1.18 | 0.25 | −3.10 | 2.71 | 0.05 |
| Pre-SLT use of β-blockers | 0.32 | −0.55 | 0.56 | 0.58 | 0.14 | −9.01 | 6.07 | 0.00 |
| Pre-SLT use of carbonic anhydrase inhibitors | 0.91 | 0.07 | 0.58 | 1.07 | 0.97 | 0.12 | 3.32 | 1.13 |
| Pre-SLT use of alpha agonist | 0.23 | −0.73 | 0.60 | 0.48 | Excluded from multivariate logistic analysis | | | |

* Statistical significance.

1-month period was selected based on previous knowledge that even the 2-week post-SLT IOP was already predictive of future IOP control[28] as well as to be compliant with the clinical practice at our center of adjusting patients' medication regimen for those with suboptimal response to SLT at 1 month following treatment. The results in this study were derived from a population of medically treated NTG subjects that received adjuvant SLT and may not be generalizable to naive eyes or those with other forms of glaucoma.

To the best of our knowledge, this is one of the few and more comprehensive analyses on the predictors of success in NTG. In summary, SLT was successful in over 60% of NTG patients. A higher pre-SLT IOP and a greater IOP reduction at 1-week post-SLT were predictors of success while using 3 types of anti-glaucoma eye drops and a thicker RNFL were associated with SLT failure.

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