Effect of Central Corneal Thickness on the Outcome of Selective Laser Trabeculoplasty: Texas Experience

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ABSTRACT

Objectives: To determine if central corneal thickness influences Intra Ocular Pressure (IOP) lowering response of Selective Laser Trabeculoplasty (SLT) in patients with medically uncontrolled primary open angle glaucoma.

Methods: Consecutive patients who received selective laser trabeculoplasty during May 2011 through June 2013 were enrolled in this retrospective chart review study. Information gathered included age, gender, race, central corneal thickness and type of glaucoma. Number of glaucoma medications, visual acuity, and IOP were assessed before and after treatment.

Results: Data from 48 patients (77 eyes) were used in the analysis. There were no significant differences in the number of glaucoma medications used or visual acuity before or after treatment. IOP measurements decreased 10.3% over preoperative levels through 18-months from a mean preoperative pressure of 18.4 ± 5.5 to 16.5 ± 4.7 mmHg ($P < 0.0005$). The mean central corneal thickness was 533.8 ± 38.0 μm. The treated eyes were divided into two groups by central corneal thickness: thin (<555μm), and thick (>555μm). There was no difference in mean IOPs of the groups preoperatively, but during the 18 months follow-up there was a significant mean change in intraocular pressure within the thin group (-2.5 mmHg, 95%CI [-3.8, -1.2], p=0.0002) but not in the thick group (-1.6mmHg, 95% CI [-3.4, +0.2], p=0.08). However, the difference between the central corneal thickness groups was not statistically significant.

Conclusions: Selective laser trabeculoplasty was more effective in reducing IOP, when used as an adjunct to medical therapy for glaucoma, in patients with thin central corneal thickness (<555μm) than those with thick central corneal thickness (>555μm).

Key words: Central Corneal Thickness (CCT), Intraocular Pressure (IOP), Primary Open Angle Glaucoma (POAG), Selective Laser Trabeculoplasty (SLT).

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Introduction

Selective laser trabeculoplasty (SLT) has been shown to be both an effective and safe method for reducing intra ocular pressure (IOP) in patients with primary open angle glaucoma (POAG)[1-4] and as efficacious as the previous

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laser-procedure of choice, argon laser trabeculoplasty (ALT).[5-7]

It is also well known that a thinner central corneal thickness (CCT) is an important risk factor for development of primary open angle glaucoma (POAG) and increased glaucoma severity.[8-10]

The role of SLT as a first line mode of treatment has been studied in patients with POAG and ocular hypertension with positive results.[11] More recently, Shazly and associates have shown that patients with thinner CCT showed better IOP control when SLT was used as a primary therapy.[12]

However, the interplay between SLT and CCT is not well understood when SLT is used as an adjunct to medical therapy in glaucoma. This information would be useful to predict response to SLT based on CCT. We addressed these questions by retrospectively reviewing the outcome of patients with who had undergone SLT at our institution. We hypothesized that SLT would reduce IOP further when used in conjunction with medical therapy and patients with thinner CCT would show greater IOP reduction.

Methods

After approval by the Institutional Review Board of the University of Texas Southwestern Medical Center (UTSW), a retrospective chart review of consecutive patients who had undergone SLT for open angle glaucoma at the UT Southwestern Medical Center was performed. Medically uncontrolled patients with open angle glaucoma or pseudoexfoliation glaucoma who underwent the procedure between May 2011 and June 2013 and who were older than 18 years of age were included. Patients were excluded if they had: any identifiable secondary glaucoma other than pseudoexfoliation, intraocular surgery (cataract, glaucoma or retina), follow-up data less than 3 months, use of systemic or topical steroids and prior ALT within two years. We adhered to the tenets of the Declaration of Helsinki.

Baseline information gathered included patient age, gender, race, type of glaucoma, number of glaucoma medications used preoperatively, previous ALT, visual acuity, IOP, and CCT. Baseline IOP was defined as the IOP measured immediately prior to performing SLT. Intra-ocular pressure measurements were made using Goldmann applanation tonometry, and the CCT measurements were made using the Corneo-Gage Plus pachymeter (Sonogage, Inc., Cleveland, OH). The observers taking the IOP or CCT measurements were not masked. Eyes were divided into thin cornea if the CCT was less than 500μm, average cornea if between 500-568μm and thick cornea if the CCT was greater than 568μm.

Selective laser trabeculoplasty (SLT) was performed by one surgeon (KSK) in a standard fashion in all cases at UTSW as follows. All patients provided written informed consent after the potential risks, benefits, and alternatives to the procedure were explained. Selective laser trabeculoplasty was delivered with the Selecta II Glaucoma Laser System, a Q-switched 532-nm frequency-doubled Nd: YAG laser (Lumenis Inc., Santa Clara, CA, USA). The subjects were pre-medicated with topical proparacaine 0.5% and apraclonidine 0.5%. A Latina gonio-lens (Ocular Instruments, Bellevue, WA, USA) was placed on the eye coupled with methylcellulose 1%. The helium-neon aiming beam was focused on the pigmented trabecular meshwork with a pre-adjusted spot size of 400 μm. To deliver the least amount of energy possible, the pulse energy was adjusted by increments of 0.1 mJ to the smallest amount until "champagne" bubble formation became just invisible. Each treatment area consisted of non-overlapping laser spots over 180°, 270°, or 360° of the visible angle. Immediately following the conclusion of the procedure, drops of topical apraclonidine 1% and either prednisolone acetate 1% or loteprednol 0.5% were instilled.

Postoperatively, IOP was measured in both eyes at 1 hour. If the IOP was elevated by more than 5 mmHg, the pressure was treated medically and rechecked before discharging the patient. Anterior chamber reaction was assessed by slit lamp bio-microscopy.

Discharge medications included loteprednol 0.5%, fluoromethalone 0.25%, or diclofenac 0.1% four times daily for one week. Patients were continued on their preoperative anti-glaucoma therapy. Follow-up information included IOP measurements at 1 week, and 1-, 3-, 6-, 12-, and 18-months. Additional information gathered were the last recorded IOP

measurement, number of glaucoma medications, visual acuity, and if repeat SLT was performed.
All postoperative complications were documented and treated appropriately.

Statistical Analyses

The statistical analysis was performed using SAS 9.4 (SAS, NC, USA). Descriptive statistical analysis was done to characterize clinical and functional data. Mean values for visual acuity were calculated after transforming the mean angle of resolution values to-log MAR values. A mixed-effects linear model was used to assess trends over the repeated measurements and to compare the means of the two CCT groups. To account for the correlation between paired eyes of one individual, each subject was modeled as a random effect. A mixed effects model for change in IOP was also constructed, modeling CCT as a continuous variable and controlling for preoperative IOP at each follow-up visit. A *P* value less than 0.05 was considered statistically significant.

Results

Out of a total of 107 patients, thirty-two patients were excluded due to insufficient follow-up data (less than 3 months following SLT), and 27 patients were excluded for previous intraocular surgery. Data from the 48 remaining patients were used for the study. Twenty-nine patients had the procedure repeated in the contralateral eye for a total of 77 eyes treated.

Patient demographics and baseline characteristics are listed in Table I. Fourteen patients (29.2%) had ALT prior to receiving SLT. Using the Log MAR scale, the mean preoperative visual acuity was 0.24± 0.4 (range, 0-1.3).

The average number of SLT pulses placed in each treated eye was 79.4 ± 27.3 (range, 50-150), of which only 19 eyes (24.7%) were treated with greater than 100 pulses. Thirty-two eyes (42%) received 180° of treatment, 7 (9%) received 270°, and the remaining 38 (49%) received 360° of treatment.

Two eyes (2.6%) experienced postoperative complications, both of which were anterior chamber inflammation that responded well to topical corticosteroid drops without further sequelae. Five eyes (6.5%) underwent repeat SLT after 1 year.

Table 1: Baseline characteristics of patients (n = 77 eyes of 48 patients)

Variables	
Sex	
Male	16 (33%)
Female	32 (67%)
Age, years	65.2 ± 10.5
Total eyes treated	
Right	40 (52%)
Left	37 (48%)
Race	
White	21 (44%)
Black	22 (46%)
Hispanic	4 (8%)
Other	1 (2%)
Glaucoma type	
Primary open-angle	42 (88%)
Pseudoexfoliation	6 (12%)
Anti-glaucoma medications	1.9 ± 0.8
Intraocular pressure, mm Hg	18.4 ± 5.5
Central corneal thickness, µm	533.8 ± 38.0

Data are presented as the number of patients (%) and mean ± standard deviation

In the follow-up period, patients were using a mean of 1.9 ± 0.8 anti-glaucoma medications with no change in the number of medications from preoperatively (P = 0.69). Latest visual acuity assessed in the postoperative period (mean = 16 months) using the scale above was 0.21 ± 0.2, which was unchanged when compared to the preoperative visual acuity (P = 0.64).

IOP measurements in the follow-up period showed a sustained decrease over preoperative levels (Fig. 1). Each follow-up mean IOP (week 1 to month 18) was decreased compared to baseline (P= 0.0005, time effect from mixed model repeated measures analysis). From a mean preoperative IOP of 18.4 ± 5.5 mmHg, the reduction postoperatively was significant at the 1-week (16.5 ± 4.0mmHg, P < 0.0005), 1-month (16.0 ± 4.7mmHg, P < 0.0002), 3-month (16.4 ± 4.7mmHg, P < 0.0002), 6-month (16.1 ± 4.8mmHg, P < 0.0006), 12-month (16.5 ± 4.7mmHg, P < 0.0004) and 18-month follow up (16.6 ± 4.7 mmHg, P = 0.01).

The mean CCT of the 77 eyes was 533.8 ± 38.0µm. Fifty one eyes (66.2%) had thin cornea, and 26 eyes (33.8%) had thick cornea.

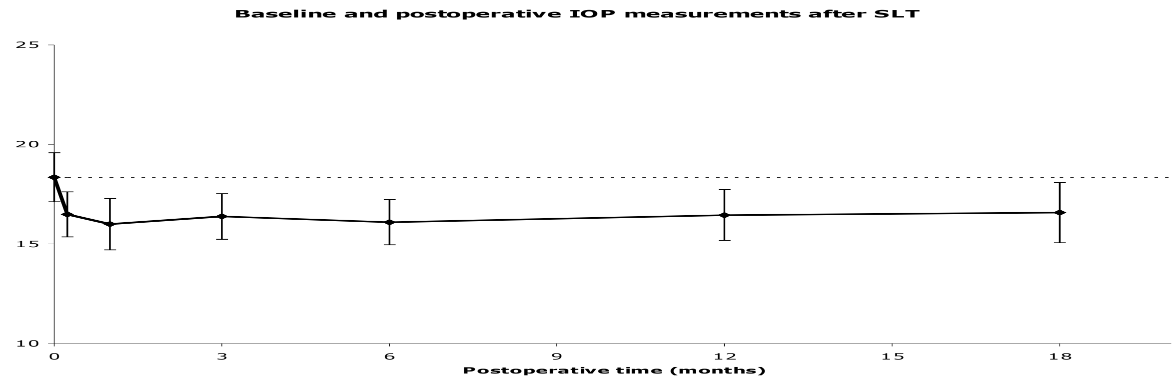

Fig. 1: Mean intraocular pressure at baseline and in the follow-up period. Vertical error bars represent 95% confidence intervals. The dashed line is the baseline mean preoperative intraocular pressure measurement. IOP = intraocular pressure; SLT= selective laser trabeculoplasty. Each follow-up mean IOP (week 1 to 18) was decreased compared to baseline, (*P*=0.0005)

Table II: Effect of CCT on selective laser trabeculoplasty IOP measurements

Variables	Preop	1 wk.	1 mo	3 mo	6 mo	12 mo	18 mo
CCT < 555 N=51 eyes Pts=32	17.6	15.7 (-14.3%)	15.1 (-8.1%)	15.3 (-10.2%)	15.3 (-9.0%)	15.4 (-13.3%)	15.0 (-11.9%)
CCT>=555 N=26 eyes Pts=16	19.8	18.3 (-9.0%)	17.4 (-9.7%)	18.8 (-5.6%)	17.7 (-8.1%)	18.0 (-6.8%)	18.8 (-4.8%)
**P* value between groups	0.07	0.37	0.68	0.34	0.81	0.44	0.64

**P* value comparing the two CCT groups from mixed-effect model repeated measure analysis.
CCT, central corneal thickness; IOP, intraocular pressure; preop, preoperatively; wk, week; mo, month(s); thin group, CCT < 555 µm; thick group, CCT >555 µm; pts, patients.
Results are presented as mean (percent change from baseline)

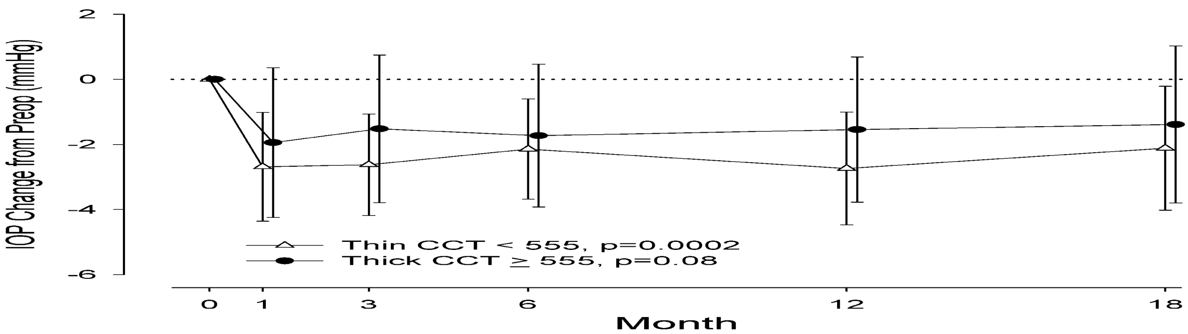

Fig. 2: Intraocular pressure change after selective laser trabeculoplasty from pre-operative value over time (1 week - 18 months) in the two central corneal thickness groups.
Thin CCT = < 555 µm. Thick CCT= > 555 µm. Symbols and error bars represent mean and standard deviation, respectively

The measurements of the IOP at baseline and in the follow-up periods of the two CCT groups are listed in Table II. The baseline IOP in the two groups was similar (*P*=0.07). The thin group had greater reduction of IOP at each visit.

The differences in mean IOP values by CCT groups at baseline and postoperatively were also explored. The changes from baseline were not statistically different among the two CCT groups (*P*=0.37). Fig. 2 illustrates the change of IOP over the 18 months of the study stratified by the two CCT groups.

Treating CCT as a continuous variable and controlling for preoperative IOP as a covariate, we observed significant associations between CCT and change in IOP at month 6 (adjusted regression coefficient (β) =0.06 ΔmmHg/µm, *P*=0.002) and month 12 (β) =0.05, *P*=.008), indicating that larger IOP decreases are associated with lower CCT. Less robust associations were observed at month 1 (β) =0.02, *P*=0.18), month 3 (β) =0.03, *P*=0.055), and month 18 (β) =0.05, *P*=0.052).

Discussion

In our medically uncontrolled patients with glaucoma, we found that SLT reduced preoperative IOP by 10.3% through 18-months of follow-up from the mean preoperative pressure of 18.4 ± 5.5 to 16.5 ± 4.7 mmHg ($P < 0.0005$). These results are in line with the meta-analysis report of several SLT studies which found IOP reduction of 6.9% to 35.9%.[4]

In terms of the role of CCT in influencing the outcome of SLT, we found that in patients with thin CCT (<555µm) there was a significant mean change in IOP during the 18 months follow-up (-2.5mmHg, 95% CI [-3.8, -1.2], p=0.0002) but not in the thick (>555µm) group (-1.6 mmHg, 95% CI [-3.4, +0.2], p=0.08). The pre-op IOPs in both groups were similar but we did not detect any significant difference in the post-SLT IOPs in the thin and thick groups. Larger numbers of patients are needed to address this question. Our results do confirm the findings of Shazly and associates who have shown that eyes with thinner cornea experience greater reduction of IOP following SLT as a primary procedure in patients with POAG and ocular hypertension.[12]

Previous groups have hypothesized that differences in response by corneal thickness to ocular hypotensive medications may be from differences in corneal compliance, lower baseline IOP in thicker corneas, and inherent pharmacokinetic variations.[10,13-14] Although pharmacokinetic differences do not apply directly to SLT, the amount of laser energy that is able to penetrate the cornea to the trabecular meshwork may be influenced by CCT. In our study, this effect could explain why patients with thin corneas had a more robust response to SLT while patients with thick corneas had less response. This would be in agreement with a study that found 180° of SLT to be more effective at lowering IOP than 90° of SLT.[15] Although that study did not investigate whether there was a relationship between the amount of energy delivered per pulse versus IOP reduction, the total amount of energy delivered to the meshwork may play an important role in the efficacy of SLT and may be influenced by CCT. Finally, there may be inherent differences between eyes with a thin CCT versus eyes with a thick CCT in the production and drainage of aqueous humor, that is, patients with thin corneas may have a higher predisposition for increased aqueous humor production or decreased drainage, causing an increased risk for POAG and decreased response to treatment.

Our results are in agreement with much of the literature on the successfulness of SLT in lowering of IOP.[1-7,11-12] Although the difference between the preoperative mean IOP and postoperative measurements were not as large as previous studies, there was a statistically significant decrease in IOP seen during the study follow-up.

Selective laser trabeculoplasty was a safe procedure in our study, with only two patients experiencing complications that were readily treated without sequelae. Additionally, although there was no change in the amount of anti-glaucoma medications used after SLT, it was encouraging that no further anti-glaucoma medications were added and visual acuity remained the same in the follow-up period from preoperatively.

Although this study is limited by its retrospective nature and small sample size in the CCT groups, our results may provide guidance to clinicians in choosing treatment modalities and providing patients with an improved understanding about possible outcomes after SLT. Central corneal thickness may also help to explain the differences in IOP response of some patients to one modality of treatment versus another. Future directions of study include a prospective study to confirm the results of our investigation and whether patients with differences in CCT have structurally different corneo-scleral angles. Thin CCT has been found to be a risk factor for the development of glaucoma, and it remains to be determined if CCT may also serve as a surrogate marker for anatomical differences in angle anatomy.

Conclusion

Our study has demonstrated that SLT is a viable and safe option for patients with medically uncontrolled glaucoma. Patients with CCT <

555µm had significant reduction in IOP over 18 months than those with CCT >555µm. The results comparing both groups were inconclusive because of small number of patients. A larger, prospective study is necessary to answer the influence of CCT and SLT in patients with medically uncontrolled glaucoma.

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