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Efficacy of 180 versus 360 Degrees of Selective Laser Trabeculoplasty on Lowering Intraocular Pressure

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Efficacy Of 180 Versus 360 Degrees Of Selective Laser Trabeculoplasty On Lowering Intraocular Pressure

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ABSTRACT

EFFICACY OF 180 VS. 360 DEGREES OF SELECTIVE LASER TRABECULOPLASTY ON LOWERING INTRAOCULAR PRESSURE. Robert H. McGlynn (Sponsored by M. Bruce Shields). Department of Ophthalmology, Yale University, School of Medicine, New Haven, CT

The purpose of this study was to determine if the application of 360° of selective laser trabeculoplasty (SLT) to the trabecular meshwork (TM) is more effective than 180° in the lowering of intraocular pressure (IOP) in glaucoma. This issue was addressed in the form of a retrospective chart review of patients treated consecutively with SLT for primary open angle glaucoma, pseudoexfoliation glaucoma or ocular hypertension. Patients were treated with either 180° of SLT by Dr. Wand or 360° by Dr. Martone using a 532nm, Q-switched, frequency doubled Nd:Yag laser. Only the initial treatment with SLT of a given eye was analyzed. There were 108 patients per group. Patient age, type of glaucoma, history of previous argon laser trabeculoplasty (ALT), number of medications, lens status and visual acuity pre-and post-treatment and the number and power of laser spots were compared between the treatment groups. The mean IOP from three consecutive visits prior to treatment was compared with post-operative IOPs measured at 1 hour, 6 weeks, and 3 months. Patients were classified as responders if the three month postoperative IOP was reduced by more than or equal to 3 mmHg compared to baseline.

At three months post-op the 360° group had a response rate of 60% and a mean IOP drop of 3.6 mmHg (17.8%). The 180° group had a response rate of 29% with a mean IOP drop of 1.5 mmHg (7.5%). The number of pre- and post-treatment medications, eye treated, gender, phakic status, number of spots delivered and pre-op IOP were equivalent for the two study groups. The 180° group subjects had more overall energy delivered during treatment and had had previous ALT more frequently than the 360° group. The 180° group also was significantly older and was less likely to have non-open angle glaucoma.

This study suggests that with a 2.1 mmHg greater drop in IOP and 31% greater response rate at three months post-op 360 degrees of SLT is more effective in lowering intraocular pressure than 180 degrees.

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INTRODUCTION

Argon Laser Trabeculoplasty

Histopathology and Mechanism

Argon Laser Trabeculoplasty (ALT) was shown by Wise and Witter to be an effective treatment for lowering intraocular pressure (IOP) open angle glaucoma (OAG) in 1979 (1). ALT employs the application of argon laser burns to the trabecular meshwork (TM) in the anterior chamber angle of the eye. These burns cause coagulative damage to uveoscleral meshwork, disruption of the trabecular beams and heat-induced damaged to surrounding collagen fibers (2). The precise mechanism of action is unknown but one theory, known as the mechanical theory, is that the thermal energy causes coagulation and, hence, contraction of the areas of application. This contraction causes shrinkage of the inner TM ring applying traction on the intervening meshwork and Schlemm's canal. The traction causes separation of the trabecular sheets and prevents the collapse of Schlemm's canal, therefore facilitating outflow of aqueous humor and lowering IOP. Similar histopathological changes in the ultrastructure of the TM as those produced by ALT have been documented after the application of 1064 nm neodymium:yittrium-aluminum-garnet (Nd:YAG) and diode lasers (3,4). Another theory, the cellular theory, postulates that ALT causes increases in both cell division (5) and phagocytic activity (6) in the trabecular endothelial cells. This is thought to cause clearing of debris from the trabecular meshwork as well as stimulate growth of healthy trabecular tissue, thus facilitating aqueous outflow. Furthermore, ALT has been shown to induce expression and secretion of IL-1 and TNFalpha (7). This in turn leads to increased

expression of stromelysin in trabecular cells which plays an important role in remodeling of the trabecular extracellular matrix and increasing aqueous outflow.

Clinical Efficacy

ALT was shown in the Glaucoma Laser Trial (GLT) to produce lower IOP, better visual acuity and better optic disc status in treated eyes when compared to eyes treated medically when employed as the initial treatment of glaucoma (8). In the seven year follow-up of the GLT study initial treatment with ALT was again found to be as, if not more, efficacious than initial medical treatment of glaucoma with an average IOP reduction of 7-10 mmHg (9). That IOP reduction was 1.2 mmHg greater than that demonstrated by the primary medical treatment group. Despite these findings ALT is most commonly used after medical options have been explored without resulting in adequate IOP control in hopes of postponing or eliminating the need for filtering or cyclodestructive surgery. While ALT has proved to be an effective treatment, long term failure of IOP control is common. One study reported that ALT controlled IOP in one-third of patients after a five year follow-up (10). Defining success of treatment as a 3 mmHg decrease in IOP or more, another study found that 21% of subjects treated with ALT were successes after five years (11). The failure of IOP control is hypothesized to be due to destruction of the uveoscleral meshwork from thermal damage and membrane formation from migrating endothelial cells over the TM in between laser applications (12, 13). In addition to long-term treatment failure, ALT can also produce significant side effects in treated individuals. These side effects include post-op IOP spikes, iritis and peripheral anterior synechiae (14, 15). The amount of energy delivered during treatment correlated with the incidence of these side-effects but did not effect the long-term

reduction in IOP (16, 17). Seeking to reduce the frequency of these side-effects led investigators to attempt to lower the total amount of energy delivered to the TM without losing efficacy of the treatment.

Selective Laser Trabeculoplasty

Selective Thermolysis

Selective Laser Trabeculoplasty (SLT) is a newer technique that uses an Nd:YAG laser to selectively target pigmented trabecular cells without causing widespread thermal damage to the trabecular meshwork. This technique was developed by Latina and Park in 1995 by applying lasers pulses of various frequencies, duration and power to a mixed cell culture of pigmented and non-pigmented TM cells (18). They found that with lasers capable of pulses in the sub-microsecond range it was possible to define a range of energy pulses in which pigmented TM cells could be selectively damaged and killed while leaving adjacent non-pigmented TM cells unharmed. The theory upon which SLT is based and which makes this selective killing possible is called selective thermolysis. The brevity of the laser pulses is critical to produce selective thermolysis because in order to specifically target pigmented TM endothelial cells the pulse duration must be shorter than the thermal relaxation time of melanin. Thermal relaxation is the time required for a chromophore to convert electromagnetic energy into thermal energy. At pulse durations less than the thermal relaxation time, energy is deposited in the melanin granules faster than it can diffuse. The thermal energy is therefore limited to the pigmented granules in the TM endothelial cells with very little dissipated to surrounding structures, limiting their damage.

The thermal relaxation time of melanin is approximately 1 μsec explaining why pulse durations below this threshold allowed for selective targeting. When cultures irradiated using a low energy, q-switched, frequency doubled Nd:YAG laser emitting at 523 nm in 10 nsec pulses were examined the damage was strictly limited to lysosomes containing pigment granules. This was seen as fractured melanin granules and ruptured lysosomal membranes on transmission electron microscopy. At pulses that approached this threshold, such as the 1 μsec pulses of the pulsed dye laser used in this study, damage was seen to subcellular organelles surrounding the pigment granules in addition to the granules themselves. This gave evidence of the importance of thermal diffusion in the production of collateral damage to surrounding structures. At the light microscopy level, the damage induced by these two lasers was so subtle that it was difficult for the investigators to distinguish irradiated areas by phase contrast microscopy. Using stains to identify compromised cells they found non-pigmented cells remained viable even when all of their adjacent pigmented cells had been killed. Cultures irradiated with longer pulse durations at energies above the threshold that caused cell damage showed complete vaporization of both pigmented and non-pigmented cells at the burn sites.

The q-switched, frequency doubled Nd:YAG laser application delivers about 0.6 – 1.0 mJ per pulse which is 1% of what traditional ALT delivers at 60-100 mJ per pulse. SLT is able to be applied over a much larger area because spatial targeting is unnecessary. SLT is usually applied with a spot size of 400 μm versus the 50 μm spot size in ALT. Coupling the lower amount of energy delivered in SLT with a larger spot size over which this energy is applied leads to a far lower fluency (energy/area) in SLT when compared with ALT. Due to the low fluency required together with the approximately 1mm tissue penetration and relative transparency of collagen in the trabecular beams to 523 nm light, it was hypothesized that the

results found on the two dimensional cell cultures could be applied to the three dimensional trabecular meshwork with similar selectivity.

Histopathology

Microscopic studies have subsequently shown the selectivity of SLT when applied to human eyes. Scanning electron microscopy (SEM) performed on the TM after application of ALT showed crater formation with evidence of coagulative damage at the base and edges (2). This was seen in the form of whitening and bleb formation. There was also disruption of the collagen scaffolding and trabecular beams with debris from these structures in the adjacent intratrabecular spaces. SEM on SLT treated specimens, on the other hand, showed minimal mechanical disruption of the collagen scaffolding and trabecular beams with no evidence of crater formation or coagulative damage. Transmission electron microscopy (TEM) on ALT specimens showed similar disruption of trabecular beams and collagen scaffolding immediately surrounding the laser lesions. Additionally, trabecular endothelial cells were found to be disrupted with many of them appearing to be detached from the trabecular beams. The pigment granules within these cells were rounded and intact. SLT specimens examined with TEM showed no disruption of the TM which was lined with a continuous layer of trabecular endothelial cells. In contrast to the ALT treated specimens many of the intracytoplasmic pigment granules in the SLT treated specimens were cracked and fragmented as Latina and Park (18) found in cell culture. This is precisely where SLT is designed to interact. Many of these endothelial cells were also vacuolated. The Kramer et al. study (2) study involved ALT using the standard energy delivery levels of 60 – 100 mJ/pulse. A more recent study examined the effect of lower energy ALT (46 mJ/pulse) versus standard SLT application to the TM of

eyes one to five days prior to enucleation for malignant melanoma of the choroid (19). This study found that both treatments caused disruption of the trabecular beams and desquamation of endothelial cells but that the extent of this damage was less after SLT. They also found that long-spacing collagen was better preserved after SLT.

Mechanism of Action

The lack of coagulative damage induced by ALT suggests that any IOP reduction caused by SLT is due to the selective killing of pigmented trabecular meshwork cells and the biologic response that ensues. Multiple biologic reactions have been documented and all of them can be at least partially attributed to the induced expression of various cytokines after SLT.

Cytokine Production and Endothelial Cell Permeability

As with ALT, SLT has been shown to increase expression of IL-1 and TNF-alpha with the addition of IL-8 (20). These cytokines are important in the recruitment of macrophages which may help to clear debris from the TM and facilitate aqueous outflow. A study by Alvarado et al. (20) found that SLT applied to trabecular meshwork cells in culture produces increased levels of these cytokines in the culture medium. When endothelial cells from the TM and Schlemm's canal were incubated with this culture medium it was found that it significantly altered their genetic expression. The increase in cytokine activity and altered expression of genes occurs simultaneously with an increased rate of conductivity of aqueous humor across monolayers of these two cell types. This increased conductivity is also reproducible by administering exogenous IL-1 alpha and beta, TNF-alpha and IL-8 to these

cellular monolayers. This is an important finding because the endothelial cells of Schlemm's canal form the last barrier of the outflow tract and exert important control over how much aqueous humor leaves the eye and enters the venous circulation. If SLT produces the same four-fold increase in conductivity in Schlemm's canal endothelial cells in vivo that it produces in vitro it could explain much of the IOP reduction seen clinically.

Extracellular Matrix Remodeling

The TM extra-cellular matrix has been shown to be both increased and modified in primary open angle glaucoma (POAG) (21, 22). This is thought to be another pivotal factor in the outflow resistance and elevated IOP in this condition. The normal turnover of the TM extra-cellular matrix is partially governed by the activity of metalloproteinases (MMPs) (23, 24). The activity of MMPs, in turn, is increased by the cytokines IL-1 and TNF-alpha (25, 26, 27). The ratio of MMP concentration to the concentration of their inhibitors' is also increased by these cytokines. These inhibitors are called tissue inhibitors of metalloproteinases, or TIMPs. MMP-2 is the predominant gelatinase in the aqueous humor and its inhibitor, TIMP-2, is up regulated in POAG (28). This imbalanced ratio of MMP-2 to TIMP-2 is thought to be responsible for the decreased collagenase activity of aqueous humor from POAG eyes in vitro (29). The increased expression of cytokines after SLT could be influencing the ratio between these two factors and inducing remodeling of the extracellular matrix in the TM. This finding is similar to the finding of increased expression of stromalysin, another MMP, due to increased IL-1 and TNF-alpha activity after ALT (27).

Endothelial Cell Repopulation

Another one of the main factors that is thought to contribute to the etiology of POAG is the relative dearth of endothelial cells in the TM when compared to healthy controls. The endothelial cells in the TM and Schlemm's canal undergo mechanical deformation due to stretching when IOP is elevated (30). This mechanical stretching has been shown to induce various changes in signal transduction, genetic expression and permeability in the anterior segment of the human eye (31, 32). Among the up regulated genes are PIP 5K1C, VIP, tropomodulin, and MMP2 which are known to influence outflow resistance. A similar increase in MMP-2 as well as a decrease in TIMP-2 in TM endothelial cells due to mechanical stretch have been found in other studies (33). This increased expression of MMP-2 was shown to correlate with the ability of eyes challenged with increased flow rates to restore IOP to normal levels after a couple of days (34). This effect was hypothesized to be a result of pruning of the TM extracellular matrix and subsequent reduction in outflow resistance. The decreased cellularity of the TM in POAG when compared to age matched normal controls (35) may lead to increased IOP due to an inability of the present cell population to generate equivalent levels of these factors in response to a given IOP as would be produced by a normally populated TM. This decreased cellularity of TM endothelial cells may also contribute to elevated IOP by not being able to produce sufficient concentrations of cytokines to adequately alter the permeability of the Schlemm's canal's endothelial cells. The importance of this is that laser treatments have been shown to increase cell division in the TM (5). This is likely to be at least partially due to the ability of cytokines to act as growth factors for TM endothelial cells. SLT, by inducing cytokine expression, may be triggering a repopulation of the TM endothelial cells and therefore restoring the ability of this cell population to adequately

respond to increases in IOP. The new population of TM cells could then secrete factors important in the regulation of the permeability of Schlemm's canal endothelial cells and in the proper turnover in the TM extracellular matrix.

There is one more piece of evidence that supports the importance of the biological response induced by SLT in lowering IOP. This evidence comes from a study that found that untreated eyes contra lateral to SLT treated eyes exhibit a statistically significant pressure reduction (36). This study found a 9.7% IOP reduction in these untreated eyes at 6 months. A mechanical mode of action is ruled out in the contra lateral eye as the laser was not applied there. This suggests that the inflammatory cascade induced in the treated eye has some crossover effect in the untreated eye.

In summary, there is strong evidence that SLT is inducing biological responses in the TM that are responsible for IOP reduction. These mechanisms are the increased expression of cytokines, increased permeability of the endothelial cells in the TM and Schlemm's canal, remodeling of the extracellular matrix of the TM and repopulation of TM endothelial cells. All of these mechanisms influence each other and the induction of cytokine expression plays a potential role in modulating all of them.

Clinical Efficacy

Clinical trials thus far conducted have shown reasonable response rates, effective IOP reduction and minimal side effects. The first study to look at the clinical applicability of this procedure was published in 1998 (36). This study included a total of 53 eyes with uncontrolled open-angle glaucoma (OAG) treated with 180° degrees of SLT followed for 26 weeks. They found that 70% of the treated subjects had a reduction of IOP of greater than 3

mmHg with an average drop of 4.6 mmHg (18.7%) after 26 weeks. The magnitude of this reduction was uninfluenced by previous treatment with ALT. This demonstrated that effective, clinically significant IOP reduction could be accomplished without inflicting coagulative damage to the trabecular meshwork. Interestingly, this study also found that there was a statistically significant, albeit less extensive, 9% reduction in the IOP of the fellow untreated eyes in these subjects. Subsequently there have been many other studies published addressing the clinical efficacy of SLT. These results are summarized in Table 1. Overall, the response rate to SLT was 63.1% with a range from 14-88% at a mean follow-up time of 19.4 months. The mean decrease in IOP was 6.18 mmHg (2.1-10.6) with a percentage decrease of 26.0% (11.9-39.9). When only the studies that reported follow-up periods of longer than one year are included in these figures the mean response rate was 60.2% with a mean IOP drop of 5.7 mmHg (2.1-8.6) reflecting a 24.0% drop (11.9-35.1). These are significant responses and the majority are either similar to or better than outcomes reported for ALT (9, 10, 11).

Table 1

Summary of studies reporting efficacy of SLT

	Sample	Baseline IOP (mmHg)	Follow-up	Response Rate	IOP Reduction (mmHg)
Latina et al. (36)	50 POAG 3 PG	24.6	26 weeks	70%	4.6 (18.7%)
Lanzetta et al. (37)	8 POAG	26.6	6 weeks		10.6 (39.9%)
Kim et al. (38)	16 POAG	24.4	1 year		4.9 (20.2%)
Gracner (39)	50 POAG	22.5	6 months	88%	5.1 (22.5%)
Gracner (40)	10 CG 10 POAG	23.6 22.8	12 months 13.5 months	64% 78%	7.4 (31.4) 8.0 (35.1%)
Melamed et al. (41)	45 POAG (primary Tx)	25.5	18 months		7.7 (30%)
Cvenkel (42)	44 POAG	25.6	1 year	62%	4.7 (18.6%)
Lai et al. (43)	29 POAG/OHT	26.8	5 years		8.6 (32%)
Best et al. (44)	269 POAG/LTG/OHT	22.7	2 years		2.7 (12.1%)

Table 1 continued					
Kano et al. (45)	67 POAG	22.4	6 months	68.7% at 1 mo.	4.4 (19.6%)
Hodge et al. (46)	72 POAG/PXG/PG	23.8	1 year	59.7%	5.8 (24.4%)
Kajiya et al. (47)	17 POAG	22.8	6 months		6.7 (29.4%)
Jindra (48)	283 POAG (primary Tx) 43 POAG (repeat Tx)	21.1 23.7	4.8 months 3.5 months		7.4 (35%) 8.2 (35%)
Song et al. (58)	94 POAG/PXG/PG/LTG	17.6 68.7+	14.5 months	14%	2.1 (11.9%)

Table 1. Summary of studies reporting efficacy of SLT. Abbreviations: SLT, selective laser trabeculoplasty; IOP, intraocular pressure; POAG, primary open angle glaucoma; CG, capsular glaucoma; OHT, ocular hypertension; LTG, low-tension glaucoma; PXG, pseudoexfoliation glaucoma; PG, pigmentary glaucoma.

SLT vs. ALT

Clinical trials that have compared ALT to SLT have also shown that the two treatments have similar efficacy. A study comparing 154 patients treated with ALT to 41 patients treated with SLT, all on maximal medical therapy, found that there was no significant difference in success of treatment at an average follow-up time of 34.4 months (11). This equivalence was found two separate criteria for success: one was and IOP reduction of greater than 20% of baseline IOP (P=0.12) and the second was an IOP reduction of greater than 3 mmHg (p=0.20). There was no significant difference in the percentage reductions in IOP with 27.1% and 23.5% decreases in the SLT and ALT groups respectively (P=0.75). Other studies comparing SLT to ALT are summarized in table 2. Briefly, over an average follow-up period of 5.6 months these three studies reported an average IOP reduction of 4.8 mmHg (2.85-6.9) for SLT and 5.0 mmHg (2.63-6.6) for ALT. This corresponded to percentage reductions of 20.9% (13.4-29.2) for SLT and 22.0% (13.0-29.2) for ALT. None of the IOP reductions differed significantly in any of the three studies. This establishes that SLT is a viable treatment alternative to ALT. In fact, it may offer some advantages such as a decreased incidence of

complications and a potential for repeatability that make it a more attractive treatment option when compared to ALT. These issues will be discussed in greater detail below.

Table 2						
Summary of studies comparing efficacy of SLT vs. ALT						
	SLT Sample	ALT Sample	Follow-up	SLT IOP Reduction	ALT IOP Reduction	P-Value
Martinez de la Casa et al. (49)	20 POAG	20 POAG	6 months	5.4 mmHg (22.2%)	4.6 mmHg (19.5%)	0.81
Damji et al. (50)	18 POAG	18 POAG	6 months	5.0 mmHg (21.9%)	4.8 mmHg (21.3%)	0.97
Popiela et al. (51)	27 POAG	27 POAG	3 months	2.85 mmHg (13.4%)	2.63 mmHg (13.0%)	0.84
Pirnazar et al. (52)	30 POAG	27 POAG	12 months	6.9 mmHg (29.2%)	6.6 mmHg (29.2%)	0.86
Tabak et al. (53)	22 patients	17 patients	4 weeks	3.84 mmHg (17.7%)	6.5 mmHg (26.8%)	Not significant

Table 2. Summary of studies comparing efficacy of SLT vs. ALT. Abbreviations: SLT, selective laser trabeculoplasty; ALT, argon laser trabeculoplasty; IOP, intraocular pressure; POAG, primary open angle glaucoma.

SLT After ALT

Due to the fact that SLT does not cause coagulative damage to the TM, it offers the possibility of benefiting patients who have failed previous ALT. SLT can be applied without causing further scarring and potential outflow obstruction as is thought to be a possible problem with repeat ALT treatments. A study conducted examining the effect of repeat ALT treatments on 40 eyes of 37 patients found a greater than 3 mmHg drop in IOP response rate of 32% (54). At 1.75 years 14% of these patients continued to have successful control of IOP. This study concluded that although it is a safe option to repeat ALT, the likelihood of success is low.

A study that addressed the question of the relative efficacy of repeat ALT treatments and SLT after previous ALT found that there was not significant difference between the two

at the 5 year follow-up (11). They found that there was no difference in the response rates when success was defined as a reduction of IOP greater than 3 mmHg (P=0.35) or greater than 20% (P=0.21). It should be noted that 6 patients (14.6%) in the SLT group and 16 patients (10.4%) in the ALT group had previously received 180 degrees of ALT. These 22 patients were included in the no prior treatment groups during analysis. This was done with the rationale that the treatment was a primary treatment because the surgeon treated the previously untreated 180 degrees of the TM. In the other studies mentioned below these patients would have been included in the repeat treatment groups. Differing from these findings, Damji et al. found that patients with previous failed ALT had a greater reduction in IOP with SLT (6.8 mmHg, 29.8%) than with repeat ALT (3.6 mmHg, 16.0%) (P= 0.01) after 6 months (50).

Another study that compared pressure reduction and response rates of SLT either as the primary laser treatment or after previous ALT found that there was no difference in IOP reduction in these two groups (36). They reported 5.8 mmHg (23.5%) and 6.0 mmHg (24.2%) reductions in IOP at 26 weeks in the primary SLT and previous ALT groups, respectively. Both groups had a 3 mmHg IOP reduction response rate of 70%. Similarly, Chen et al. that IOP reduction is independent of previous ALT treatments (55).

Repeat SLT Treatments

SLT has been shown to be as effective as ALT with less histological damage to the trabecular meshwork. Additionally, the efficacy of SLT has been demonstrated in patients with previous ALT. These two facts have lead to the promise of SLT being a repeatable treatment. Repeat ALT is not favored due to the permanent changes it causes on the first

application and the mixed findings on its long term efficacy. There is not yet much data supporting the clinical repeatability of SLT. One study found that response rates on repeat SLT always exceeded 50%, in some cases by a considerable amount (56). This study was conducted on a mixed group of glaucoma patients with a mean time of 12 to 15 months between SLT treatments. In a small sample of patients that had received a third SLT treatment they found a 100% response rate with an average pressure reduction of 10.8 mmHg. They also found that the degree of pressure reduction and 3 mmHg IOP reduction response rate was positively correlated with having a baseline IOP of greater than 21 mmHg. Another study compared 283 primary to 43 repeat SLT treatments and found that there was a 35% reduction in IOP in both groups (48). All of these studies concur in their findings that, when repeated, SLT is effectively lowers IOP.

SLT as Initial Therapy

The Glaucoma Laser Trial Follow-up Study established ALT as a viable first line treatment option for POAG. Despite this it continues to be employed after medical therapy has failed to control IOP in order to avoid the need for incisional pressure lowering surgery. Given the equivalent efficacy of SLT and ALT, it follows that SLT may be viable option for primary treatment of POAG as well. In fact, there have been studies that support this hypothesis. One study examined the response of 45 eyes with either POAG or ocular hypertension with a mean baseline IOP of 25.5 mmHg to primary treatment with SLT (41). At 18 months follow-up the mean drop in IOP was 7.7 mmHg (30%) with 43 of the 45 eyes responding with a greater than 20% reduction. Forty of the eyes had an IOP reduction of greater than 5 mmHg. Another study compared 283 primary to 43 repeat SLT treatments and

found that there was a 35% reduction in IOP in both groups. The initial treatment group had and IOP reduction of 7.4 mmHg from 21.1 to 13.7 mmHg. The repeat group had a drop of 8.2 mmHg from 23.7 to 15.5 mmHg. One additional study on 29 newly diagnosed patients randomized one eye of each patient to receive SLT and the other medical treatment (43). The baseline IOPs were 26.8 and 26.2 mmHg in the SLT and medication groups respectively ($p=0.62$). At the end of the five year follow-up the mean pressure drops were 8.6 (32.1%) and 8.7 (33.2%), respectively ($P=0.95$). They also had similar failure rates of therapy as defined as an IOP of greater than 21 mmHg at five years of 17.2% and 27.6%, respectively ($P=0.53$). Eight of the SLT eyes (27.6%) required medications to keep their IOP below this threshold but the SLT group required less medications at the five year follow-up (0.46-0.55) compared to the medications group (1.45-1.63) ($P<0.001$). In summary, these studies suggest that as with ALT, SLT is an effective initial treatment for POAG.

Adverse Effects

SLT administers 1% of the energy delivered by ALT. This most likely accounts for its relatively lower complication rate than ALT. In the Glaucoma Laser Treatment Follow-up Study (9) 34% of subjects had an IOP rise more than 5 mmHg after treatment. Following SLT, two studies reported incidence of IOP rises greater than 5 mmHg at 25% (41) and 11% (36). Martinez-de-la-Casa et al. found that the degree of IOP elevation immediately following SLT was lower than that occurring after ALT, although this difference was not significantly different (49). This same study compared the anterior chamber reaction after SLT and ALT. At 1 hour after treatment the SLT group had significantly less flare than the ALT group using a laser flare meter (13.3 vs. 20.7 photons/ms, $P=0.003$). Alternatively, Damji et al. reported an

increased anterior chamber reaction after SLT when considering the number of cells observed ($p<0.001$) (50). Another study reported that 83% of subjects had a mild to moderate anterior chamber reaction after SLT but that the usually decreased within 24 hours with no persistent cases of iritis (36).

The incidence of pain after SLT has been reported at 15% of patients (36). Another study described significantly less pain after SLT when compared to ALT (49). The GLT group observed that 34% of patients receiving ALT had formation of peripheral anterior synechiae (PAS) (9). These PAS did not have any effect on pressure control, number of medications needed or need for pressure reducing surgery. In their original clinical study Latina et al. reported that there was no evidence of any PAS formation (36). Other possible side effects are non-specific conjunctivitis and corneal edema but these are usually mild and transient occurrences.

Variables Influencing Outcome of SLT

ALT has previously been shown to produce a greater IOP decrease in eyes with a higher initial pressure (57). Studies on SLT have thus far returned mixed results. One study from Japan found that lower baseline IOP was predictive of SLT success (45). Another study found precisely the opposite with a greater success rate in patients with higher baseline IOP (58). An observational case study series found increased degree of TM pigmentation has been found to result in greater risk of complications, including post-op IOP spikes after SLT (59). Despite this increased rate of adverse effects another study found that TMs with greater degrees of pigment have significantly greater reductions in IOP at 7 month follow-up (55). This study also found that patients with pseudoexfoliation have an increased response to SLT.

The number of medications that a patient is on has also shown to have an effect on the outcome of ALT with the presence of fewer medications producing statistically significant better outcomes (60). This has also been found with SLT (58).

The type of medications an eye is treated with has also proved to be important in the outcome of SLT. Eyes treated with prostaglandins have been reported to have a diminished response to SLT. In one study there was a trend towards subjects on prostaglandins having a higher failure rate after SLT (58). Another study found an increased percentage of patients on prostaglandins were not responsive to SLT (Bryce A. Ford MD, personal communication, 2005). They found that 76% of responders (41/54) were taking prostaglandins, compared to 91% of non-responders (49/54) ($p=0.039$). This decreased response rate may in part be due to the fact that both prostaglandins and SLT are thought to act on the aqueous outflow tract. PGs have been shown to induce increased expression of MMP-1,-2 and -3 both in vitro and in vivo (61). In vivo, this induction corresponded with a decreased concentration of types I, III and IV collagen, which are some of the TM extracellular matrix substrates which the MMPs degrade. As discussed above, SLT has been shown to act on this same pathway. The population of MMPs may be depleted by prostaglandin treatment precluding SLT from acting on this pathway. Another possibly redundant mechanism between these two treatments is that they both act by recruiting inflammatory cells. Prostaglandins may be precluding the ability of SLT to cause a cellular response. Despite the idea that steroids may interfere with the inflammatory cascade and thus diminish the efficacy of SLT, this has proved to be either unfounded (62) or possibly beneficial (63).

Degrees of TM Treated with SLT

SLT has a lot of evidence supporting its use as a treatment for open angle glaucoma, possibly as a first line treatment. This said it still remains a relatively new technique for which the optimal amount of power delivered and extent of the trabecular meshwork that should be treated still remains to be determined. These issues have been addressed in previous studies although the question has not been sufficiently resolved. With ALT the amount of energy delivered correlates with the incidence of post-op IOP spikes, iritis and peripheral anterior synechiae although this was not thought to influence the long-term reduction in IOP (14, 15, 16). A study comparing the degrees of the TM treated with ALT showed a greater success rate in eyes treated with 100 spots over 360 degrees (group 1, 26 eyes) when compared to eyes treated with 50 spots over 180 degrees (group 2, 20 eyes) (64). The baseline IOP in group one was 35.9 mmHg and 36.3 mmHg in group 2. Success was defined as a reduction of IOP to below 22 mmHg. At 12 months group 1 and group 2 had success rates of 69% and 15%, respectively.

Thus far there have been three studies examining the issue of the degree of the TM that should be treated with SLT. One study by Chen et. al. found that 90 and 180 degrees of SLT had equivalent efficacy (55). Both groups were composed of 32 eyes that were followed up for 7 months. The baseline IOPs were 25.44 and 26.06 for the 90 and 180 degree groups, respectively. The overall IOP reductions were 7.01 mmHg (27.6%) and 6.16 mmHg (23.6%), respectively (P=0.21). There was no significant difference between the IOPs at 1, 4 or 7 months. There was also a similar rate of treatment failure with 15 of the 32 patients in the 90 degree group requiring repeat SLT or trabeculectomy by the 7 month follow-up and 13 of the 32 in the 180 degree group.

The second study by Nagar et. al. compared the relative efficacies of latanoprost and 90, 180 and 360 degrees of SLT in 167 patients with either POAG or ocular hypertension (65). There were 39, 35, 49 and 44 patients in these groups, respectively. At an average follow-up time of 10.3 months they found that the 360 degree group had success rates of 82% (greater than 20% reduction) and 59% (greater than 30% reduction). The success rates in the 180 degree group were 65% and 48%, as defined by these two criteria ($P<0.1$). While these response rates trended towards being more efficacious with 360 degrees than 180 degrees they did not reach statistical significance. Furthermore they found that 360 and 180 degree treatments had a greater response rate than 90 degrees ($P<0.05$), which was generally not effective. Latanoprost had response rates of 90% and 78% which were significantly higher than 90 ($p<0.001$) and 180 ($P<0.02$) degrees but were statistically equivalent to those of 360 degrees ($P<0.5$). Adverse events including, IOP spikes, transient uveitis and ocular pain were more common in the 180 and 360 degree group compared to 90 degrees but only reached statistical significance in a couple of instances. These instances were that ocular pain was more common ($P>0.001$) and mean IOP at 1 hour was higher ($P<0.05$) after 360 degrees than after 90 degrees of SLT.

The last study compared 19 eyes that received 180 degrees and 17 that received 360 degrees of SLT (66). The mean baseline IOP was 20.6 mmHg in the 180 degree group and 21.7 mmHg in the 360 degree group. The mean change in IOP was 1.7 mmHg (8.3%) in the 180 degree group and 4.5 mmHg (20.7%) in the 360 degree group ($p=0.15$) at three months.

Of these three studies, one showed no effect due to the extent of TM treated with SLT, another showed 360 degrees to be superior to 180 and 90 degrees and a third found a non-significant trend of 360 degrees being more efficacious than 180 degrees. As discussed

above, ALT had a more robust IOP response when applied over 360 degrees of the TM than after 180 degrees. SLT and ALT have been shown to have similar response rates and efficacy in many respects and these three studies suggest that they both have better efficacy when more of the TM is treated, although this is not yet established. In order to address this question we conducted a retrospective chart review of 108 patients treated with 180 degrees versus 108 patients treated with 360 degrees of SLT.

MATERIALS AND METHODS

Patient Selection

A retrospective chart review of patients with primary open angle glaucoma, pseudoexfoliation glaucoma and glaucoma suspects treated with SLT was conducted. Patients at the Hamden Eye Center were treated between January 22, 2004 and September 8, 2005 with 360 degrees of SLT by Dr. James Martone. Patients at the University of Connecticut were treated between September 5, 2002 and August 5, 2004 with 180 degrees of SLT by Dr. Martin Wand. Patients were selected at the discretion of these physicians for SLT because they were felt to have IOPs above their goal pressures. Therefore patients were included who had either failed to control IOP adequately on maximum medical therapy, opted for SLT treatment over medical treatment or were intolerant of medications. After obtaining permission from Yale University School of Medicine Human Investigations Committee the charts of patients treated consecutively during these periods were reviewed and their eyes were included in the study if they met the inclusion criteria. The inclusion criteria were: (1) eyes had to have POAG, pseudoexfoliation glaucoma or be glaucoma suspects, (2) the eye had to have undergone its first time treatment with SLT, (3) eyes had to have at least three pre- and post-operative IOP measurements with the last one being at least 3 months after treatment. Exclusion criteria were: (1) prior treatment with SLT, (2) prior pressure lowering surgery including trabeculectomy, cyclodestructive therapy and peripheral iridotomies, (3) inadequate pre-operative data, (4) inadequate post-operative follow-up. Patients who had undergone prior ALT were included in this study. Patient information including age, type of glaucoma, history of previous ALT, phakic status and pre- and postoperative visual acuity and number and type

of medications was collected. In addition, which eye was treated, the number and power of laser spots, three consecutive pre-operative IOP measurements and two post-operative measurements at 6 weeks and three months were collected for both eyes.

Operative Technique

Dr. Martin Wand

Patients were treated preoperatively with pilocarpine 2% and anesthetized with topical anesthetic. SLT was applied with a Lumenis Selecta 532nm, Q-switched, frequency doubled Nd:Yag laser with a 3 nsec pulse duration using a slit lamp delivery system, a Latina goniolens and methylcellulose. The TM was targeted using a helium-neon targeting beam. An average of 103 spots were delivered over 180 degrees of the TM with a spot size of 400 μm. This spot size was adequate to irradiate the entire anteroposterior width of the TM. The energy level was initially set at 0.8 mJ and increased in 0.1 mJ increments until small bubbles appeared. The rest of the TM was irradiated at this energy level. The total amount of spots, the average energy per spot and the total amount of energy delivered were recorded. Post-operatively patients were treated with pilocarpine 2% and prednisolone. They were then treated with a topical NSAID QID for 5 days while continuing on their prior pressure lowering medication regimen.

Dr. James Martone

Patients were treated preoperatively with pilocarpine 2% and apraclonidine 0.5%. They were anesthetized with topical properacaine 0.5%. SLT was applied with a Lumenis

Selecta 532nm, Q-switched, frequency doubled Nd:Yag laser with a 3 nsec pulse duration using a slit lamp delivery system, a goniolens and methylcellulose. The TM was targeted using a helium-neon targeting beam. An average of 104 spots were delivered over 360 degrees of the TM with a spot size of 400 μm. This spot size was adequate to irradiate the entire anteroposterior width of the TM. The energy level was initially set at 0.8 mJ and increased in 0.1 mJ increments until blanching or small bubbles were observed. The energy was then backed off 0.1 mJ and the rest of the TM was irradiated at this energy level unless blanching or bubbling was again observed in which case the energy was lowered another 0.1mJ. The total amount of spots, the average energy per spot and the total amount of energy delivered were recorded. Post-operatively patients were treated with diclofenac 0.1% ophthalmic solution QID for four days while continuing on their prior pressure lowering medication regimen.

Postoperative Follow-up

Patients were seen by their respective treated physicians at 6 weeks and 3 months post-operatively. At these visits a slit lamp examination of the anterior segment and an IOP measurement using a Goldman applanation tonometer were performed. At the three month follow up a follow-up visual acuity assessment was performed and the total number of medications was recorded. Throughout the follow-up period patients' antiglaucoma medications were adjusted as needed to control IOP.

Success Criteria

The primary outcome measure of this study was to compare the IOP reductions at three months after 180 and 360 degrees of SLT. In addition to reporting mean IOP reduction

and percentage reduction of the two groups two sets of success criteria were defined that divided the treatments groups into responders and non-responders. These two success criteria were 3 mmHg and 20% reductions of IOP from baseline values at three months.. Baseline IOP was determined by averaging the three consecutive IOP measurements immediately preceding the SLT administration. These criteria were chosen because historically they have been the benchmarks by which success of laser trabeculoplasty treatments have been judged.

Statistical Analysis

All data was analyzed using SAS version 9.1 published by SAS Publishing Cary, NC. Visual acuity values were transformed into a logarithmic scale prior to analysis using the conversion chart described in table 3 (67).

Table 3			
Snellen to Logarithmic Conversion Chart			
LogMAR	Snellen	LogMAR	Snellen
-0.30	10	0.70	100
-0.20	12.5	0.76	114
-0.10	16	0.80	125
0.00	20	0.88	150
0.10	25	0.90	160
0.18	30	1.00	200
0.20	32	1.10	250
0.30	40	1.18	300
0.40	50	1.20	320
0.48	60	1.30	400
0.50	63	1.60	800
0.54	70	2.00	2000
0.60	80	3.00	20000

Table 3. Chart used to convert Snellen chart measurements of visual acuity into a logarithmic scale.

RESULTS

Patient Demographics

A total of 216 eyes from 195 patients were included in the final analyses. Table 4 presents the baseline descriptive statistics of the patients in both treatment arms. Patients in the 180° group were significantly younger than the 360° group with a mean age of 70.417 years versus 74.296 years (P=0.0176). Distribution of gender and which eye was treated were equivalent between both groups (P=0.0525, P=0.2760, respectively). Glaucoma type composition of the two groups differed, with 99 patients in the 360° group and 106 patients in the 180° group having primary open angle glaucoma (P=0.0303). The remaining patients in these two groups were composed of either pseudo-exfoliation glaucoma or were glaucoma suspects. A statistically equivalent number of patients had previous cataract surgery and intra-ocular lens placement in both groups with 28 and 32 patients (P=0.5434) in the 360° and 180° groups, respectively. A total of 43 patients in the 180° group had received prior ALT application which was significantly more than the 18 patients in the 360° group (P=0.0002). Both groups had equivalent pre-operative visual acuity with means of 0.2615 and 0.2726 (P=0.7242) in the 360° and 180° groups, respectively. Both groups were on statistically equivalent number of medications pre-operatively (P=0.6148). See figure 1 for graphic representation of number of medication administered to patients in both groups. Of these medications the 180° group was on significantly more prostaglandins with 86 patients taking them pre-operatively compared with 59 patients in the 360° group (P<0.0001).

Table 4				
Summary of patient demographics				
Factor		**360°**	**180°**	**comments**
Age (years)				
		74.296 +/- 10.493	70.417 +/- 13.122	P=0.0176
Gender				
	Male	37 (34.26%)	51 (47.22%)	P=0.0525
	Female	71 (65.74%)	57 (52.78%)	
Eye				
	OD	52 (48.1%)	60 (55.6%)	P=0.2760
	OS	56 (51.9%)	48 (44.4%)	
Glaucoma type				
	POAG	99 (91.7%)	106 (98.1%)	P=0.0303
	PXG	7 (6.5%)	2 (1.9%)	
	GS	2 (1.9%)	0 (0%)	
Lens Status				
	Phakic	80 (74.07%)	76 (70.37%)	
	Psuedophakic	28 (25.93%)	32 (29.63%)	P=0.5434
Previous ALT				
	No	88 (83.02%)	65 (60.19%)	
	Yes	18 (16.98%)	43 (39.81%)	P=0.0002
Pre-op Visual Acuity				
		0.2615 +/- 0.2413	0.2726 +/- 0.2172	P=0.7242
No. of Meds, Pre-op				
	0	12 (11.11%)	6 (5.56%)	
	1	16 (14.81%)	19 (17.59%)	
	2	29 (26.85%)	30 (27.78%)	
	3	28 (25.93%)	26 (24.07%)	
	≥4	23 (21.30%)	27 (25.00%)	P=0.6148
Prostaglandin Treatment				
	No	49 (45.37%)	21 (19.63%)	
	Yes	59 (54.63%)	86 (80.37%)	P<0.0001

Table 4. Summary of patient demographics. All values given +/- standard deviation. Abbreviations: OD, right eye; OS, left eye; POAG, primary open angle glaucoma; PXG, pseudoexfoliation glaucoma; GS, glaucoma suspect; ALT, argon laser trabeculoplasty. Visual acuity values were transformed into a logarithmic scale prior to analysis.

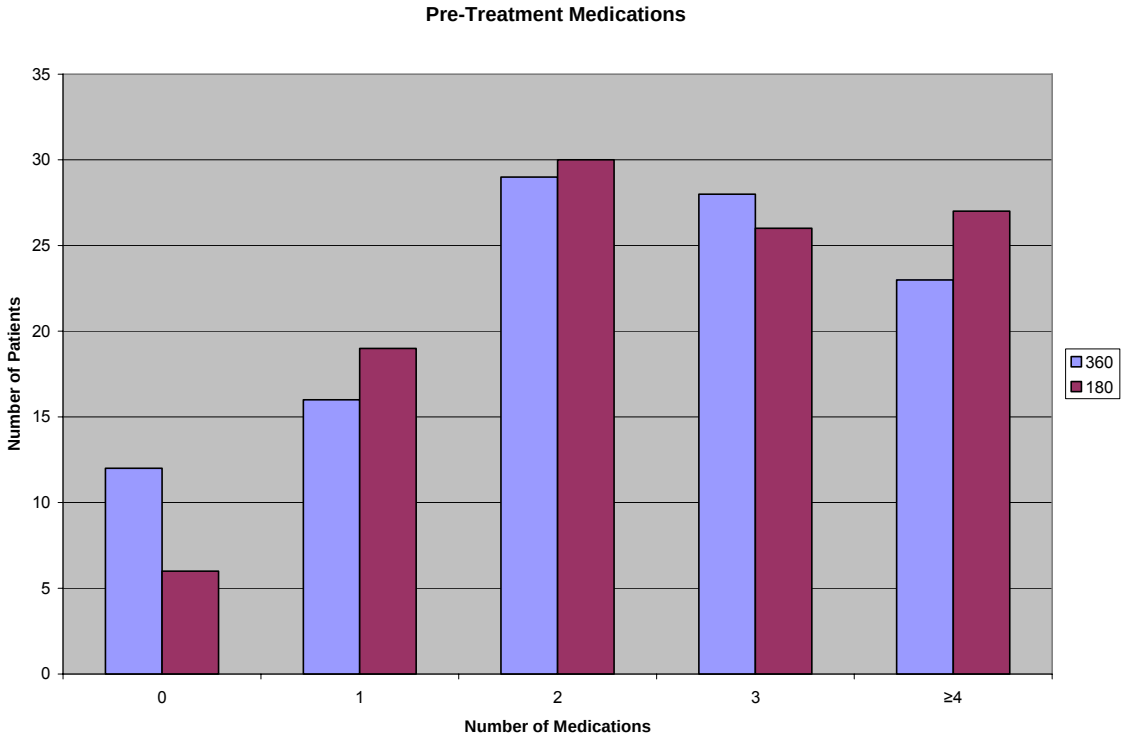

Figure 1. Number of intraocular pressure lowering medications patients were taking prior to treatment with SLT in both 180 and 360 degree subgroups. There was not a statistically significant difference in the number of medications the two treatment groups were receiving (P=0.6148).

Post-operative results are summarized in table 5. Both treatment arms received an equivalent number of SLT spots (P=0.7695). The spots applied to the 180° group were significantly more powerful than the 360° group and therefore they received more overall power (107.38 mJ vs. 91.406 mJ, P<0.0001). Post-operatively both groups had an equivalent decrease in the mean number of medications administered (-0.009 vs. -0.114, 360° vs. 180° respectively, P=0.2499) and were therefore still on comparable numbers of medications (P=0.3620). Both groups also had a statistically equivalent reduction in visual acuity with a reduction of 0.0164 in the 360° group and 0.0069 in the 180° group (P=0.6455).

Table 5				
Results				
Factor		**360°**	**180°**	**Comments**
No. of Spots Delivered				
		103.8 +/- 13.291	103.14 +/- 19.268	P=0.7695
Power Delivered (mJ)				
		91.406 +/- 10.634	107.38 +/- 31.311	P<0.0001
No. of Meds, Post-op				
	0	16 (14.95%)	9 (8.57%)	
	1	13 (12.15%)	19 (18.10%)	
	2	28 (26.17%)	26 (24.76%)	
	3	24 (22.43%)	30 (28.57%)	
	≥4	26 (24.30%)	21 (20.00%)	P=0.3620
Mean No. of Med. Reduction				
		-0.009 +/- 0.5745	-0.114 +/- 0.7379	P=0.2499
Post-op VA Reduction				
		-0.0164 +/- 0.1748	-0.0069 +/- 0.124	P=0.6455
Pre-op IOP (mmHg)				
		19.299 +/- 4.1638	18.54 +/- 4.4992	P=0.1994
Post-op IOP (mmHg)				
	1 hour	17.028 +/- 6.5245	19.093 +/- 5.9351	P=0.0158
	6 weeks	16.213 +/- 5.2025	16.278 +/- 5.3927	P=0.9285
	3 months	15.747 +/- 4.5132	17.111 +/- 5.6739	P=0.0518
Contra lateral Pre-op IOP				
		16.758 +/- 3.8582	16.75 +/- 4.7814	P=0.9896
Contra lateral Post op IOP				
	6 weeks	16.198 +/- 5.1798	15.954 +/- 5.3396	P=0.7337
	3 months	15.657 +/- 4.1674	16.574 +/- 5.4141	P=0.1648
Δ IOP at 3 mos. (mmHg)				
	Unadjusted	-3.552 +/- 3.6703	-1.492 +/- 4.1139	P<0.0001
	Adjusted	-3.4540	-1.5274	P=0.0020
Δ IOP at 3 mos. (percentage)				
	Unadjusted	-17.8 +/- 17.804	-7.456 +/- 23.436	P=0.0003
	Adjusted	-17.8835	-7.3684	P=0.0016

Table 5. Summary of treatment results. Change in IOP Adjusted values determined by regression analysis. All values given +/- standard deviation. Abbreviations: VA, visual acuity, IOP, intra-ocular pressure, Δ IOP, change in intra-ocular pressure.

Pre-operative intra-ocular pressure was statistically equivalent for both treatment arms with a mean IOP in the 360° group of 19.299 mmHg and 18.54 mmHg in the 180° group

(P=0.1994). Pre-operative IOPs were also statistically equivalent in the contra lateral, untreated eye with measurements of 16.758 mmHg and 16.75 mmHg in the 360° and 180° groups, respectively (P=0.9896). One hour post-operatively, the mean IOP in the 360° group was significantly lower than in the 180° group with measurements of 17.028 mmHg and 19.093 mmHg, respectively (P=0.0158). At the 6 week and 3 month time points the mean IOPs were statistically equivalent (P=0.9285 and P=0.0518, respectively) for both treatment arms (see figure 2).

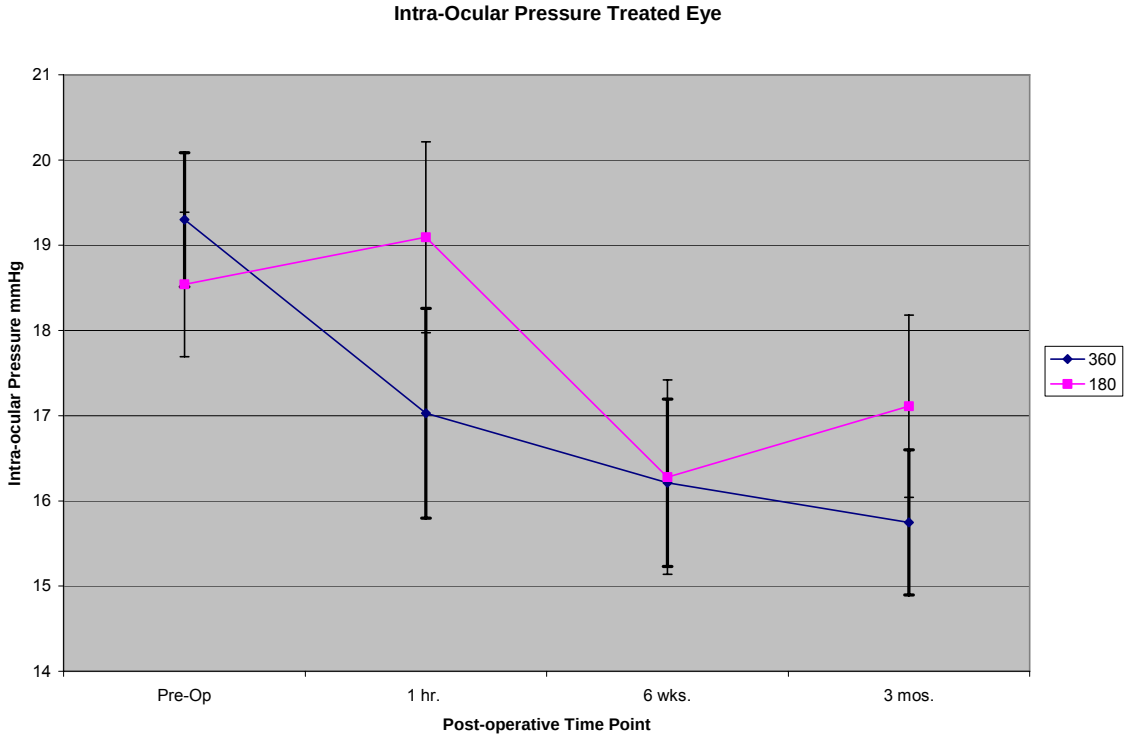

Figure 2. Pressure curves of the treated eyes in the 180° and 360° treatment subgroups including pre-treatment, one hour, six week and three month measurement values(mmHg). Pre-treatment values were determined by taking the average of intraocular pressure readings from the day of treatment and two visits prior to the day of treatment. The difference in intraocular pressures were only statistically significant at the one hour post-treatment time point (P=0.1994, P=0.0158, P=0.9285, P=0.0518). Error bars represent the 95% confidence intervals.

In the contra lateral, untreated eye the mean IOPs were also statistically equivalent at the 6 week and 3 month time points (P=0.7337, P=0.1648, respectively) for both treatment arms (see figure 3).

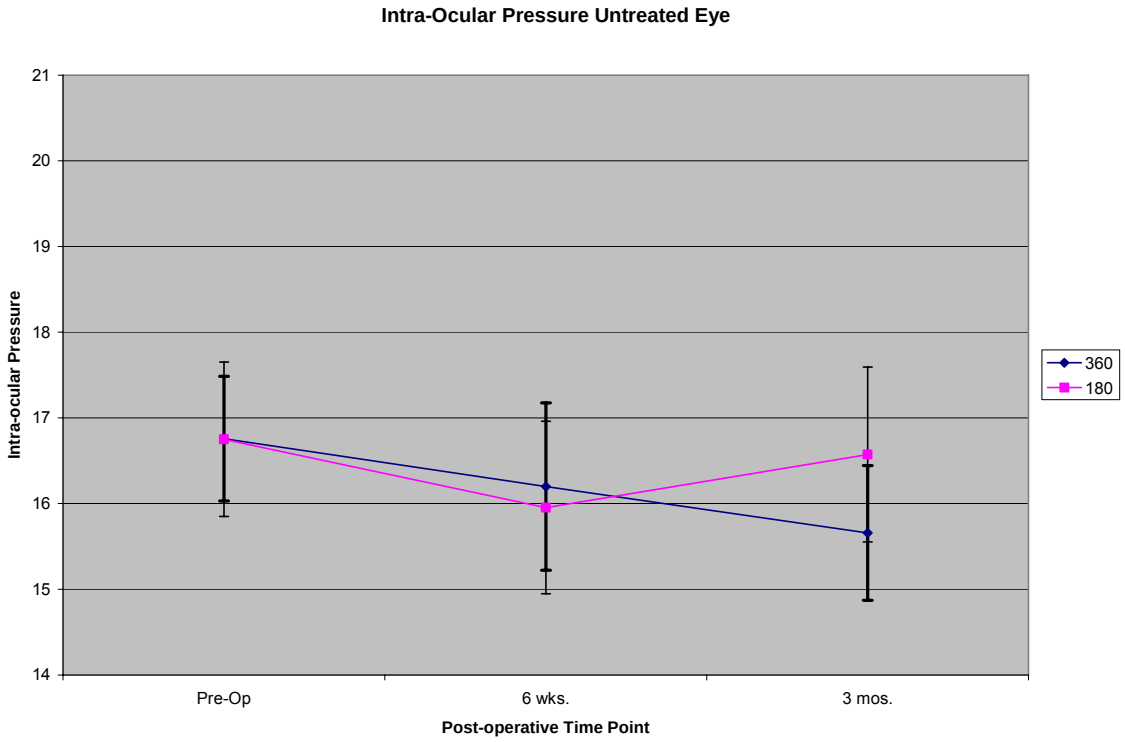

Figure 3. Pressure curves of the eyes contra lateral to the treated eyes in the 180° and 360° treatment subgroups including pre-treatment, six week and three month measurement values (mmHg). Pre-treatment values were determined by taking the average of intraocular pressure readings from the day of treatment and two visits prior to the day of treatment. There were no statistically significant differences in intraocular at any of the time points (P=0.9896, P=0.7337, P=0.1648). Error bars represent the 95% confidence intervals.

While the measured IOPs were equivalent for both treatment arms at the 3 month time point, the overall changes in IOP were not. The baseline-adjusted reduction in IOP for the 360° group was 3.552 mmHg and 1.492 mmHg for the 180° group (P<0.0001). The baseline-adjusted reductions in IOP in terms of percentage points were 17.8% and 7.456% in the 360° and 180° groups, respectively (P=0.0003).

Regression analyses were performed on three month IOP reductions in terms of mmHg as well as percent change in order to adjust outcomes for differences in age, overall power delivered, gender, type of glaucoma, presence of prior ALT and prostaglandin treatment. In analysis of maximum likelihood estimates, prostaglandins were shown to have a significant negative correlation with reduction of IOP (P=0.0305). The remaining factors were not found to have significant correlations with IOP reduction. After the results were re-calculated in the regression analyses taking into account these variables, the reduction in IOP for the 360° group was 3.4541 mmHg and 1.5274 mmHg for the 180° group (P=0.0020). The adjusted reductions in IOP in terms of percentage points were 17.8834% and 7.3684% in the 360° and 180° groups, respectively (P=0.0016).

Two different criteria were established to judge the success of each one of the treatment protocols. One was a greater than 3 mmHg reduction in IOP and the other was a greater than 20% reduction in IOP. The success rates for reduction of IOP greater than 3 mmHg at one hour were 55 and 25 (P<0.0001) for the 360° and 180° groups, respectively. At 6 weeks the rates were equivalent at 57 and 43 (P=0.0561). At 3 months the 360° group again had a significantly better response rate with 65 patients successfully treated compared with 31 in the 180° group (P<0.0001). The 360° group had significantly better response rates at all three time points for the greater than 20% reduction of IOP criteria. At the one hour time point the success rates were 47 and 18 (P<0.0001), At 6 weeks they were 50 and 32 (P=0.016) and at three months they were 55 and 23 (P<0.0001) for the 360° and 180° groups, respectively. The results are graphically represented in figure 4.

Table 6				
Treatment Success Rates				
>3mmHg Responders				
	1 hour	55 (50.93%)	25 (23.15%)	P<0.0001
	6 weeks	57 (52.78%)	43 (39.81%)	P=0.0561
	3 months	65 (60.19%)	31 (28.70%)	P<0.0001
>20% Responders				
	1 hour	47 (43.52%)	18 (16.67%)	P<0.0001
	6 weeks	50 (46.30%)	32 (29.63%)	P=0.016
	3 months	55 (50.93%)	23 (21.30%)	P<0.0001

Table 6. Treatment success rates for both >3mmHg and >20% IOP reduction criteria.

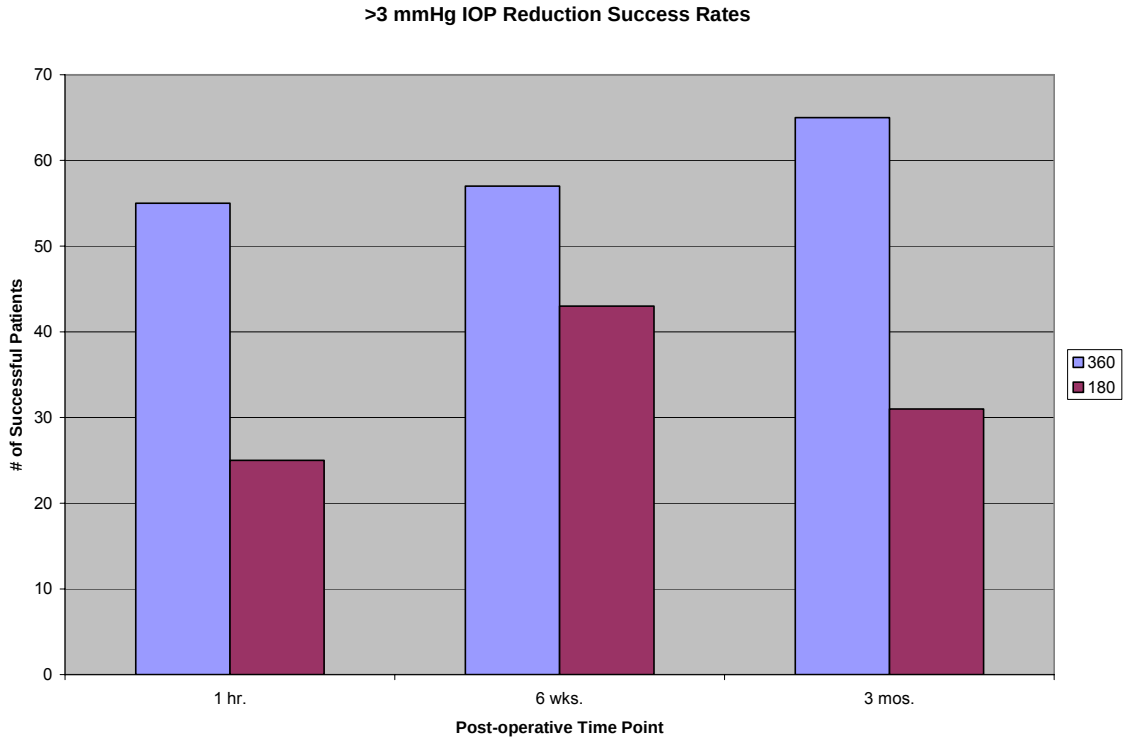

Figure 4. Treatment success rates for >3 mmHg reduction in IOP. The 360° group had significantly higher response rates at the 1 hour and three month time points (P>0.0001, P>0.0001) and marginally significant at six weeks (P=0.0561).

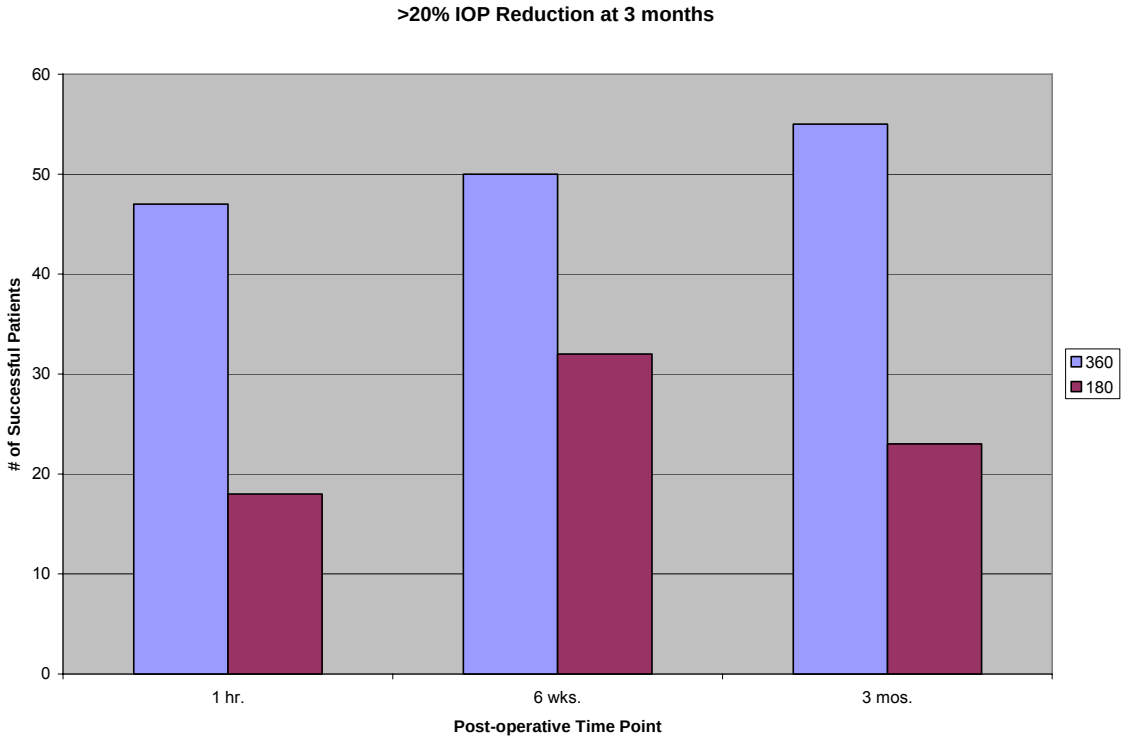

Figure 5. Treatment success rates for >20% reduction in IOP. The 360° group had significantly higher response rates at all three time points (P>0.0001, P=0.0160, P>0.0001).

Success rates at 3 months for the 3 mmHg criteria, broken down by presence or absence of prior prostaglandin treatment and ALT, were also determined. These results are displayed in table 7. Fifty-nine patients in the 360° group were on prostaglandins with a success rate of 33 (55.93%) vs. 23 (26.74) for the 86 of the patients in the 180° group who were on prostaglandins. This was statistically significant (P=0.0004). Forty-nine patients in the 360° group were not on prostaglandins with a success rate of 32 (65.31%) vs. 8 (38.10%) of the 21 patients in the 180° group who were not on prostaglandins. This was statistically significant (P=0.0350).

Eighteen patients in the 360° group had received prior ALT with a success rate of 9 (50.00%) vs. 11 (25.58%) of the 43 of the patients in the 180° group that had received prior ALT. This was statistically significant (P=0.0639). Eighty-eight patients in the 360° group had not received prior ALT with a success rate of 56 (63.64%) vs. 20 (30.77%) of the 65 the patients in the 180° group who had not received prior ALT. This was statistically significant (P<0.0001).

Table 7

Three month SLT success rates (>3mmHg) considering prostaglandin and prior ALT treatment

Factor		**360°**	**180°**	**Comment**
w/ Prostaglandins				
	Success	33 (55.93%)	23 (26.74%)	P=0.0004
w/o Prostaglandins				
	Success	32 (65.31%)	8 (38.10%)	P=0.0350
Subgroup analysis		P=0.3218	P=0.3039	
w/ALT				
	Success	9 (50.00%)	11 (25.58%)	P=0.0639
w/o ALT				
	Success	56 (63.64%)	20 (30.77%)	P<0.0001
Subgroup analysis		P=0.2791	P=0.5596	

Table 7. Three month success rates (>3mmHg) considering prostaglandin and prior ALT treatment. Subgroup analyses compare success rates of patients on and off prostaglandins or with and without prior ALT within treatment groups. Success rates were not significantly affected in either treatment group irrespective of prostaglandins or prior ALT. Abbreviations: SLT, selective laser trabeculoplasty, ALT, argon laser trabeculoplasty.

Subgroup analyses were conducted in order to determine the affect of prostaglandin and ALT treatment on success rates for SLT within each of the treatment arms. In the 360° group patients on prostaglandins had a success rate of 55.93% versus a rate of 65.31% for those patients not receiving prostaglandins. This was not a statistically significant difference (P=0.3218). In the 180° group patients on prostaglandins had a success rate of 26.74% versus a rate of 38.10% for those patients not receiving prostaglandins. This was not a statistically significant difference (P=0.3039). In the 360° group patients who had received prior ALT had

a success rate of 50.00% versus a rate of 63.64% for those patients who had not. This was not a statistically significant difference (P=0.2791). In the 180° group patients who had received prior ALT had a success rate of 25.58% versus a rate of 74.42% for those patients who had not. This was not a statistically significant difference (P=0.5596).

CONCLUSIONS

Selective laser trabeculoplasty (SLT) is a relatively new treatment technique and the optimal amount of power to be deliver and extent of trabecular meshwork to be treated are as yet undetermined. In order to further establish the optimal protocol for treatment of glaucoma with SLT we conducted a retrospective chart review of 216 patients. Of these 216 subjects 108 received 100 spots over 180° while the other 108 received 100 spots over 360°. Our results were similar to the findings of another study conducted by Rinke et al. (66) which found a trend towards 360° being more efficacious than 180°. In that study the 180° degree group had a 1.7 mmHg (8.3%) drop in IOP compared with the 1.49 mmHg (8.0%) IOP reduction in our study. In the 360° group there was a 4.5 mmHg (20.7%) drop in IOP in the Rinke et al. study while there was a 3.49 mmHg (18%) reduction in our study. While the trend towards 360° being more efficacious did not reach statistical significance in the Rinke et al. study, it did in ours. On the contrary to the Rinke study, another study by Nagar et al. (65) found that 360° and 180° of SLT were equally effective. Despite this, this study still showed the significance that different degrees of SLT application can make as they found that both 180° and 360° were more effective than 90°. A study by Chen et al. (55) showed that 90° and 180° of SLT had equivalent efficacies contradicting the significance of degree SLT treated found in the above mentioned studies.

The exact mechanism by which SLT acts is unknown. All existing hypotheses that attempt to describe this mechanism at least partially rely on the biological response to the induced expression of cytokines after SLT. These mechanisms are the increased permeability

of the endothelial cells in the TM and Schlemm's canal (20), remodeling of the extracellular matrix of the TM and repopulation of TM endothelial cells (5). All of these mechanisms influence each other and the induction of cytokine expression plays a potential role in modulating all of them. A potentially confounding variable in our study was the fact that the 180° group received prednisolone post-operatively. Steroids act by inhibiting phospholipase A2 from producing arachidonic acid. This is the main substrate for both the cyclooxygenase and lipooxygenase pathways which are responsible for generating inflammatory cytokines thought to be responsible for the biological response to SLT that lowers IOP. Due to the administration of steroids, the 180° group's response to therapy may have been reduced. The apparent difference in the efficacy between the two groups may, to a certain extent, reflect this difference in post-operative treatment rather than the fundamental efficacy of the two treatment protocols.

Another variable that may have affected the outcome between the two groups was the density of the energy applied to the TM. The 180° group had 100 spots applied over one half of the TM with a mean total energy of 107.4 mJ. This was nearly a three fold higher energy density than that used in the study conducted by Kramer et al. (2) which described the histological changes due to SLT application. In that study 50 spots were applied over 180° with a total energy of about 40 mJ. The 360° group, on the other hand, received a mean total of 45.703 mJ per 180° of TM, which was comparable to the energy delivered in the Kramer paper. In the Kramer study post-treatment scanning electron microscopy showed minimal mechanical disruption of the collagen scaffolding and trabecular beams with no evidence of crater formation or coagulative damage in the TM. Transmission electron microscopy found

that pigmented TM cells were selectively damaged and killed while leaving adjacent non-pigmented TM cells unharmed. While the lack of structural damage to the TM and selective damaging of pigmented TM cells can be assumed for the 360° group due to similar SLT protocols, this may not have been the case for the 180° group. This may account for the poorer response of patients in the 180° treatment protocol.

There are other baseline factors that have been documented to affect the outcome of SLT. One of these factors is prostaglandin treatment prior to SLT, which has been shown to cause higher failure rate of treatment. This was reported in a paper by Song et al. although the difference in outcomes between those treated and those untreated was not statistically significant. In the present study we found a significant inverse relationship between prostaglandin treatment and magnitude of IOP reduction. Despite this, prostaglandin treatment did not significantly affect SLT outcomes between the two groups according to the two success criteria. Furthermore, it did not affect the frequency of SLT success within both treatment groups during subgroup analyses. There were a greater number of patients in the 180° group that were on prostaglandins prior to SLT application. While this difference existed as a potential confounding factor it was not shown to affect the overall outcome when considered in the regression analysis. Baseline IOP and pseudophakic status are two further factors that has been shown to affect outcome of SLT (45,50,68,69). There were not statistically significant differences in the baseline IOP or frequency of pseudophakia between the two groups so any effect these factors may have had on the outcomes should have been equivalent for the two groups.

The limits of this study include the fact that it was conducted retrospectively, had a brief follow-up period, was conducted by two different surgeons and the increased spot density in the 180° group. There were also differences in the amount of patients on prostaglandins, with prior ALT, type of glaucoma, gender and ages varied between the two groups and total energy was greater in the 180° group. These factors were all considered when conducting the regression analyses and were not found to have a significant effect on outcomes.

In addition to the application of steroids administered post-operatively in one group and not the other discussed above, medication regimens in general were managed post-operatively at the discretion of the performing surgeon. This leaves the possibility that the change in IOP may not have only been effected by application of SLT. This was unlikely to have affected the outcome greatly considering that both groups had a statistically equivalent decrease in the number of medication they were taking post operatively. Another limitation is the fact that patients that required an additional application of SLT during the 3 month follow-up period were not included in analyses. This precludes the ability to evaluate rates outright treatment failure between the two groups.

The present study suggests that that 360° of SLT is more effective at lowering IOP after a three month follow-up period. This adds to the body of evidence also suggesting that greater degrees of SLT treatment are more efficacious. Further, prospective studies need to be conducted in order to elucidate what the optimal degree of treatment is.

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