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Selective Laser Trabeculoplasty

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1. Introduction

Selective laser trabeculoplasty (SLT) is a relatively recent modality for treating patients with open-angle glaucoma and ocular hypertension. Similarly to argon laser trabeculoplasty, SLT uses laser energy to target the trabecular meshwork and lower intraocular pressure by increasing aqueous outflow. However, although argon laser trabeculoplasty has been used successfully for several years to treat open-angle glaucoma, it has been shown to cause collateral thermal damage to the trabecular meshwork (Kramer & Noecker, 2001). This often results in scarring and synechiae formation, which compromise the possibility of further re-treatment. SLT uses a low-energy pulse (0.8 mJ to 1.2 mJ) and short pulse duration (approximately 3 nsec) in order to selectively target trabecular pigmented cells and reduce energy dissipation to the surrounding tissue. It was first reported in 1995 when Latina and Park irradiated a culture of pigmented and non-pigmented trabecular meshwork cells with different types of laser sources and analyzed their effect by electron microscopy (Latina & Park, 1995). They showed that selective cytotoxicity on pigmented trabecular meshwork cells could be achieved with pulse durations of 10 nsec and irradiance between 20 mJ/cm^2 and 1000 mJ/cm^2 for the 532 nm, frequency-doubled Q-switched Nd:YAG laser. Fracture of melanin granules and rupture of lysosomal membranes in the pigmented trabecular meshwork cells and absence of ultrastructural damage in neighboring non-pigmented cells were revealed.

2. Mechanism of action

SLT technique employes frequency-doubled Q-switched Nd:YAG laser with a 532 nm wavelength emission. The pulse duration of 3 nsec, with an energy level of 0.6-1.0 mJ, grants a selective photothermolysis of the pigmented trabecular meshwork cells, sparing the surrounding non-pigmented cells. Morphologic changes induced by argon laser trabeculoplasty and SLT in cadaver eyes have been studied by Kramer and Noecker, with scanning and transmission electron microscopy (Kramer & Noecker, 2001). They found that argon laser trabeculoplasty lesions appear as ablation craters approximately 70 μm in diameter, with peri-lesional coagulative damage. The detachment of trabecular endothelial cells from the trabecular beams was also observed. Electron microscopy showed intact intracellular chromophore granules. The SLT morphologic effects appeared to be less

dramatic than argon laser trabeculoplasty. The beams of the trabecular meshwork were intact except rare crack-like defects between preserved beams. No coagulative damage or trabecular endothelial cells detachment was visible. Electron microscopy showed that many pigmented trabecular cells contained fragmented intracytoplasmic choromophore granules. Differences in the observed tissue effects between argon laser trabeculoplasty and SLT can be partly explained by differences in the energy delivered by the two techniques. The energy irradiance of a typical argon laser trabeculoplasty pulse of 0.1 second duration, 50-µm spot diameter and 800 mW power is approximately 4 million mJ/cm², whereas that of a SLT pulse of 0.8 mJ and 400-µm spot diameter is about 600 mJ/cm². The typical SLT irradiation delivers light energy in very short nanosecond pulses. Therefore, energy is deposited in the primary absorption sites so rapidly that it doesn't reach the thermal relaxation time of the trabecular meshwork pigmented tissue. This results in a extremely fast temperature rise which causes the vaporization of water around melanosomes with the formation of microbubbles. Alvarado et al. proposed a possible explanation of SLT efficacy in reducing intraocular pression (Alvarado et al., 2005). The authors demonstrated the ability of nanosecond laser irradiation (similar to SLT) of trabecular meshwork cells to increase four-fold the permeability of the Schlemm's canal endothelial cells. This phenomenon seems to be mediated by cytokines secreted by the irradiated trabecular meshwork cells. It's been shown that adding cytokines like IL-8, IL-1α, IL-1β and TNF-α to Schlemm's canal endothelial cells, even in absence of irradiated trabecular meshwork cells, still increases cell permeability. Another study reported a 4- to 5- fold increase in monocyte presence in the trabecular meshwork after SLT treatment, enhancing both the outflow facility and the conductivity of Schlemm's canal endothelial cells in vitro (Alvarado, Katz, Trivedi, & Shifera, 2010). Despite the above-mentioned evidences, the exact mechanism of SLT efficacy in lowering intraocular pressure in vivo remains unclear, thus requiring further investigations.

3. Indications

Any form of glaucoma having an intact trabecular meshwork and Schlemm's canal with an altered outflow capability is a potential candidate for SLT. Thus, indications for SLT include primary open angle glaucoma, secondary glaucoma such as pseudoexfoliation glaucoma and pigmentary glaucoma. Secondary inflammatory glaucomas may be controindicated due to a chance of post-treatment anterior chamber reaction. Any angle-closure glaucoma is not a good candidate for SLT.

4. Treatment

4.1 Treatment parameters

The settings for SLT are fixed except for the power. Spot size is 400 µm and the pulse duration is 3 nsec. The starting power depends on the degree of angle pigmentation. In a normally pigmented eye a 0.7-0.8 mJ power is generally sufficient. Highly pigmented eyes may require less energy (0.4-0.6 mJ) while for less pigmented ones powers up to 1.0 may be needed. The delivered energy has then to be adjusted increasing or decreasing the power level by 0.1 mJ until a threshold energy is reached. This endpoint consists in cavitation microbubbles formation that can be seen in the aqueous humor next to the trabecular

meshwork (champagne bubbles). Treatment should then be delivered 0.1 mJ below the threshold energy. The power level may be modified during the procedure if there is a significant variation in trabecular meshwork pigmentation.

4.2 Treatment technique

The treatment technique is similar to argon laser trabeculoplasty (Latina et al., 1998). Pretreatment with an alpha-agonist can be used to prevent early post-operative intraocular pressure spikes . After topical anesthesia, a Goldmann three-mirror lens or Latina SLT lens is used to focus a low-power laser aiming beam on the pigmented trabecular meshwork (Barkana and Belkin, 2007) . As coupling agent, methylcellulose or artificial tear gel are commonly used. Pilocarpine eye drops may be necessary in cases of narrow angle due to its ability to pull the peripheral iris away from the angle, improving the visualization of the trabecular meshwork. The size of the treatment spot is much larger than the one used in argon laser trabeculoplasty (typically a 50 µm spot) and covers entirely the antero-posterior width of the trabecular meshwork (Barkana and Belkin, 2007) .

4.3 How much angle should be treated?

Approximately 50 non-overlapping, confluent spots are applied to 180° of the angle circumference, or 100 spots to the full angle circumference. Some ophthalmologists prefer the 180° procedure according to the argon laser trabeculoplasty experiences, which showed a lower post-treatment intraocular pressure spike incidence. Nonetheless others go for a more extended procedure, treating 360° in a single session, considering SLT a safer procedure than argon laser trabeculoplasty. A study from Nagar et al did not show a significant increase of post-treatment intraocular pressure spike after full circumference angle treatment (Nagar, Ogunyomade, O'Brart, Howes, & Marshall, 2005). However, the authors reported a correlation between the angular extension treatment and its intraocular pressure lowering effect. This prospective, randomized clinical trial was conducted to compare 90°, 180°, and 360° SLT with latanoprost 0.005% for the control of intraocular pressure in ocular hypertension and open angle glaucoma. Thirty-nine eyes were randomized to receive latanoprost. Thirty-five eyes were randomized to the 90° SLT group, 49 eyes to 180° SLT group, and 44 eyes to the 360° SLT group. The mean follow up was 10.3 months. Spikes of intraocular pressure at 1 hour (5 mmHg or more) were seen in three eyes (9%) after 90° SLT, eight eyes (16%) after 180° SLT, and 12 eyes (27%) after 360° SLT. Mean intraocular pressure at 1 hour was significantly higher with 360° compared to 90° SLT treatments ($p<0.05$). In the 90° SLT group 12 eyes (34%) achieved a >20% intraocular pressure reduction. Whereas the same goal was obtained in the 65% and 82% in the 180° and 360° groups, respectively. In a retrospective consecutive chart review, Shibata et al. evaluated the efficacy of 180° and 360° SLT in the adjunctive treatment of medically treated open angle glaucoma. After an average follow-up of 19.5 months (180° group) and 17.9 months (360° group), they found that the 360° SLT showed a statistically higher intraocular pressure reduction as compared to the 180° SLT group. Moreover, a Kaplan-Meier survival analysis showed higher success rate after 360° SLT than after 180° SLT (Shibata et al., 2010)

4.4 Post-treatment medications

After the procedure, patients usually continue to take their preoperative glaucoma medications until the intraocular pressure is re-evaluated. Non-steroidal anti-inflammatory

eye drops are recommended for the post-treatment management. However, this last measure presents some controversial aspects. As mentioned above, the post-operative inflammation with its characteristic cytokine expression profile may play a pivotal role in the intraocular pressure-lowering effect of SLT via the enhancement of Schlemm's endothelial cells permeability (Alvarado et al., 2005; Alvarado, Iguchi, Martinez, Trivedi, & Shifera, 2010).

5. Efficacy

The first pilot study evaluating the intraocular pressure lowering effect of SLT was conducted in 1998 (Latina et al., 1998). Fifty-three eyes with uncontrolled open angle glaucoma despite intraocular pressure-lowering medications or previous argon laser trabeculoplasty treatment, received 180° SLT and continued their pretreatment medical therapy. The patients were followed up for 26 weeks and a mean intraocular pressure reduction of 18.7% (4.6 mmHg) was reported. Lanzetta et al showed a higher efficacy with a IOP reduction of 40% by treating with 360° SLT (Lanzetta et al., 1999) Some randomized, controlled clinical trials compared SLT to argon laser trabeculoplasty and to medical therapy. Table 1 summarizes the efficacy results of controlled and uncontrolled studies.

5.1 SLT *vs* argon laser trabeculoplasty

SLT seems to be a valuable alternative to argon laser trabeculoplasty showing analogue efficacy, but being theoretically safer in terms of trabecular meshwork damages. There are several evidences supporting the SLT effectiveness through its comparison with argon laser trabeculoplasty.

In a randomized clinical trial, Damji et al. compared argon laser trabeculoplasty and SLT capacity to lower intraocular pressure in eyes affected by open angle glaucoma with a 1 year follow up. They enrolled 176 eyes of 152 patients randomly assigning 89 eyes to 180° SLT (baseline intraocular pressure was 23,84 mmHg) and 87 to 180° argon laser trabeculoplasty (baseline intraocular pressure was 23.48 mmHg). Their study showed a non-significant difference between the two treatments arms. In the SLT group intraocular pressure was reduced by 5.86 mmHg, and in the argon laser trabeculoplasty group it was lowered by 6.04 mmHg ($p=0.846$). No significant differences in IOP were also noticed during all the follow up time points preceding the 12 months. In the same study SLT was an effective option for pseudoexfoliation glaucoma too: twenty-three eyes in the argon laser trabeculoplasty group and 16 in the SLT group were affected by pseudoexfoliation glaucoma and the mean intraocular pressure reduction in the two subgroups was 5.4 mmHg and 5.7 mmHg respectively. The percentage of eyes reaching an intraocular pressure reduction ≥ 20 % at 12 months was 59.7 % in the SLT group and 60.3 % in the argon laser trabeculoplasty group confirming non significant differences in the two arms (Damji et al., 2006).

Long-term efficacy was evaluated in a study by Juzych et al. They showed that argon laser trabeculoplasty and SLT have similar efficacy in reducing intraocular pressure at 5 years. One-hundred-ninety-five eyes with uncontrolled open angle glaucoma on maximally tolerated medications and no previous glaucoma surgery or iridectomy were studied. Forty-one eyes were treated once by 180° SLT, the remaining by 180° argon laser trabeculoplasty. Twenty-eight patients in the SLT group and 128 in the argon laser trabeculoplasty group had never been laser treated before entering the study. At the end of the 5 years follow up, 20 SLT and 40 argon laser trabeculoplasty patients were available for

Author	*SLT protocol*	*Population*	*Follow-up*	*Baseline IOP mm Hg*	*IOP reduction Mm Hg (%)*	*Treatment success criteria*	*Success %*	*Comments*
(Latina et al., 1998)	Nasal 180° SLT	53 eyes on MTMT or previous ALT	26 weeks (only 44 eyes)	24.6	4.6 (18%)	IOP reduction ≥ 3 mmHg	73%	Results were similar in both previously ALT treated and MTMT
(Lanzetta, Menchini, & Virgili, 1999)	360° SLT	8 eyes of 6 patients with POAG, some on MTMT	6 weeks	26.6 ± 7	10.6 ± 5.2 (40%)	NA	NA	
(Kajiya, Hayakawa, & Sawaguchi, 2000)	180° SLT	17 eyes of 10 patients with POAG, 1 eye with PEXG	6 months	22.8	6.7 (29%)	NA	NA	
(Chen et al., 2004)	180° SLT 90° SLT	2 groups of 32 patients with OHTN or OAG, some with previous ALT	7 months	26.1 ± 1.7	6.16 (24%) in responders 7.01 (28%) in responders	IOP controlled without retreatment or surgery at 7 months	59% 53%	Significant correlation between IOP reduction and TM pigmentation.
(Gracner, 2001)	180° SLT	50 eyes with OAG	6 months	22.5	5.06 ± 2.37 (22.5%)	IOP reduction ≥ 3 mmHg	88%	
(Hodge et al., 2005)	180° SLT	72 OAG on MTMT, some with previous ALT	12 months	23.8 ± 4.9	5.8	IOP reduction of ≥ 20% after 1 year	60%	IOP reduction significantly related to higher baseline IOP, but not to all other factors examined
(Damji, Shah, Rock, Bains, & Hodge, 1999)	180° SLT 180° ALT	2 groups of eyes with OAG	6 months	22.8 ± 3.0 22.5 ± 3.6	4.8 ± 3.4 (21%) 4.7 ± 3.3 (21%)	NA	NA	Similar IOP reduction by SLT and ALT
(Damji et al., 2006)	180° SLT	2 groups of eyes with OAG	12 months	23.8 ± 4.9	6.1 ± 5.9 (27%)	IOP reduction ≥ 20%	59.7 %	Similar IOP reduction by SLT and ALT.
(Martinez-de-la-Casa et al., 2004)	180° SLT 180° ALT	2 groups of 20 eyes with POAG no previous ALT	6 months	24 ± 4.7 23.6 ± 3.8	5.4 (23%)	IOP reduction ≥ 3 mmHg	80% 85%	Similar IOP reducton by SLT and ALT troughout the study
(Juzych et al., 2004)	180° SLT 180° ALT	OAG on MTMT, 41 treated with SLT, 154 with ALT	32.5 ± 15.9 months	23.9 ± 2.6 24.3 ± 4.1	18%, 23% and 27% in successful cases at 1, 3, 5 yrs 18%, 21% and 23.5% for successful cases at 1, 3, 5 yrs	IOP reduction ≥ 3 mm Hg without additional medication or surgery	68%, 46% and 32% at 1, 3 and 5 yrs 54%, 30% and 31% at 1, 3 and 5 yrs	Success rates similar between ALT and SLT, between patients with or without prior ALT
(Melamed et al., 2003)	Nasal 180° SLT	45 eyes of 31 patients with OAG or OHTN, 37 newly diagnosed or after washout	Range 3 - 24 months	25.5 ± 2.5	7.7 ± 3.5 (30%) at last follow up	IOP reduction ≥ 20% IOP controlled without topical medication at last follow-up	96% 93%	

Author	*SLT protocol*	*Population*	*Follow-up*	*Baseline IOP mm Hg*	*IOP reduction Mm Hg (%)*	*Treatment success criteria*	*Success %*	*Comments*
(Lai, Chua, Tham, & Lam, 2004)	360° SLT	29 chinese patients with POAG	5 years (82.8% completed follow-up)	26.2 ± 4.2	8.6 ± 6.7	IOP reduction ≥ 21% without medications IOP reduction ≥ 21% on medications	72% 83%	Similar IOP reduction by SLT and medications
(Gracner, 2002)	Inferior 180° SLT	10 patients with PEXG	12 ± 5.5 months	23.6 ± 5.7	6.0 ± 3.3	IOP reductions ≥ 20% and no progressive VF or ON changes after 1 year	70%	Results not statistically different between eyes with POAG and PEXG
		10 patients with POAG	13.5 ± 4.3 months	22.8 ± 2.4	6.5 ± 2.8		80%	
(Song et al., 2005)	90% had 180° SLT	94 patients with OAG	10.5 months	17.6	2.1	IOP reduction > 3 mmHg	32%	
(Francis, Ianchulev, Schofield, & Minckler, 2005)	180° SLT	66 patients with medically controlled POAG or PEXG	12 months (91% completed follow-up)			Ability to decrease medications while maintaining target IOP	87% discontinued a mean of 2.0 medications at 6 months and 1.5 at 12 months	
(Nagar et al., 2005)	Xalatan	167 patients with OHT or OAG newly diagnosed or medically controlled after washout	10.3 months	29.3		IOP reduction ≥ 20% IOP reduction ≥ 30% with no additional medications	90% 78%	
	90° SLT					IOP reduction ≥ 20% IOP reduction ≥ 30% with no additional medications	34% 11%	
	180° SLT					IOP reduction ≥ 20% IOP reduction ≥ 30% with no additional medications	65% 48%	
	360° SLT					IOP reduction ≥ 20% IOP reduction ≥ 30% with no additional medications	82% 59%	
(Cvenkel, 2004)	inferior 180° SLT	44 eyes of 31 patients with medically controlled OAG	25.57 (range 22--34)	25.6 (range 22--34)	4.8 mm Hg (18.6%) at 6 months 4.4 mm Hg (17.1%) at 12 months	IOP reduction ≥ 3 mm Hg	66% at 3 months 79% at 6 months	

Author	*SLT protocol*	*Population*	*Follow-up*	*Baseline IOP mm Hg*	*IOP reduction Mm Hg (%)*	*Treatment success criteria*	*Success %*	*Comments*
							63% at 3 months	
(Kim & Moon, 2000)	Temporal or nasal 180° SLT	16 eyes (13 patients) with POAG	12 months (15 eyes)	244	4.93 mm Hg (20.2%)	IOP reduction ≥ 3 mm Hg	81% of eyes	
(Johnson, Katz, & Rhee, 2006)	360° SLT	132 eyes (95 patients) with OAG	3 months	20.9	3.74 ± 4.58 mm Hg (12.4%)	IOP reduction ≥ 30% IOP reduction 21%-30%	24% 43%	
(McIlraith et al., 2006)	Latanoprost (26 eyes) inferior 180° SLT (74 eyes)	100 eyes with newly diagnosed early OAG and OHT	12 months	24.6 26.0	7.7 mm Hg (30.6%) 8.3 mm Hg (31%)	IOP reduction ≥ 30% IOP reduction ≥ 30%	43% 55%	No significant difference in IOP reduction between SLT and latanoprost
(Zaninetti & Ravinet, 2008)	180° or 360° SLT	36 eyes of 26 patients (only 36 completed 24 mos f-up) with OAG (either OHT, POAG,PEXG or PG) among them 8 naïve eyes	2 yrs (36 eyes)	19.2± 4.7	3.3 mmHg (17%)	≥3 mmHg IOP decrease ≥20% IOP decrease	48% 41%	
(Birt, 2007)	inferior 180° SLT after receiving 360° ALT (27 eyes) inferior 180° SLT only (30 eyes) inferior 180°ALT only (39 eyes)	96 eyes affected by OAG (POAG , PEXG or PG)	1 yr	21.5 mmHg ALT+SLT 22.9 mmHg SLT 22.0 mmHg ALT	4.8 mmHg (19.3%) ALT+SLT 5.8 mmHg (23%) SLT 5.6 mmHg (24%) ALT			
(Alvarado et al., 2005)	IOP assesment in the same 24 eyes in three moments: on PGA before SLT (PGA-IOP) then off PGA before SLT (BASELINE-IOP) then after SLT (SLT-IOP)	24 eyes	90 days	15.9 mmHg (PGA-IOP) 21.5 mmHg (BASELINE-IOP)	6.6 mmHg difference between SLT-IOP and BASELINE-IOP 1 mmHg difference between SLT-IOP and PGA-IOP			PGA and SLT showed same ability in decreasing IOP

Author	*SLT protocol*	*Population*	*Follow-up*	*Baseline IOP mm Hg*	*IOP reduction Mm Hg (%)*	*Treatment success criteria*	*Success %*	*Comments*
(Shazly et al., 2010)	Nasal 180° SLT	19 eyes with POAG 8 eyes with PEXG	27.1 months in POAG group (3 withdrawals by month 30) 20.4 months (4 withdrawals by month 30)	23.3 23.6	5.7 5.5	Success if not return to baseline IOP values and/or not need for any further glaucoma-treatment either medical, laser or surgical	77% at 30 to 42 months 74% at 30 to 32 months 75% remain off medication for 2.5 yrs after SLT (either POAG or PEXG)	
(Cellini et al., 2008)	inferior 180° SLT	15 eyes with uncontrolled PEXG	10 days and 30 days	25.8	7.7 0.4 (return to baseline IOP so trabeculectomy was needed)	20% IOP decrease or visual field stabilization after SLT	0%	SLT is not able to lower IOP in uncontrolled PEX G due to it's inefficacy in reducing the MMP-2 / TIMP-2 ratio.
(Hong et al., 2009)	All eyes underwent 360° SLT twice due to loss of IOP control at 6 or more months after SLT1	44 eyes with POAG or PEX or PG	8 months	20.1 before SLT1 19.5 before SLT2	4 after SLT1 2.9 after SLT2	Success if peak IOP reduction ≥ 20%	50% after SLT1 43% after SLT2	A second 360° SLT may be helpful when the first alone has failed in controlling IOP.
(El Mallah et al., 2010)	4 eyes 180° SLT 27 eyes 360° SLT	31 eyes with normal tension glaucoma (NTG)	12 months extended, if necessary, until 3 post SLT IOP measures were obtained	14.3	2.1	NA	NA	Intervisit IOP variation was also reduced by SLT.

SLT: selective laser trabeculoplasty; MTMT: maximally tolerated medical therapy;ALT: argon laser trabeculoplasty; IOP: intraocular pressure; POAG: primary open angle glaucoma; PEXG: pseudoexfoliation glaucoma; OHT: ocular hypertension; OAG: open angle glaucoma; PG: pigmentary glaucoma; PGA: prostagandin analogue; NTG: normal tension glaucoma;

Table 1. Summary of SLT efficacy studies in peer-reviewed journals

evaluation and intraocular pressure reduction did not significantly differ being 27.1 ± 21.4 % in the SLT group and 23.5 ± 25.2 % in the argon laser trabeculoplasty group (p=0.75). In the SLT group IOP reduction was 18.1 ± 10.2 % and 23.4 ± 13.2 % at 1 and 3 years, respectively. In the argon laser trabeculoplasty group IOP reduction was 18.1 ± 18.9 % at 1 year and 20.8 ± 15.6 % at 3 years. Both the 1 year (p=0.99) and the 3 years (p=0.56) intraocular pressure percentage reduction were non significantly different. Another success criterion was considered an intraocular pressure reduction ≥ 20%. This was observed in 58% at 1 year, 38% at 3 years and 31% at 5 year in the SLT group and 46%, 23%, 13% in the argon laser trabeculoplasty group at the same follow up times. All the mentioned results were achieved with no need of further laser irradiation, medications or surgical treatments and demonstrated a substantially equal efficacy between argon laser trabeculoplasty and SLT.

5.2 SLT *vs* medical therapy

SLT may not only be an option for those patients not responding to medications, but it may also be considered a first line alternative as it far less demanding in terms of compliance.
In a prospective randomized 6-month follow-up study, Nagar et al. evaluated SLT and latanoprost on 40 eyes affected by either open angle glaucoma or ocular hypertension. Twenty eyes underwent SLT and 20 were treated with a latanoprost. Only 30 patients completed the follow up. Mean intraocular pressure reduction at 6 months was 6.2 mm Hg in the SLT eyes and 7.8 mm Hg in the latanoprost group. A 20% intraocular pressure reduction at was reached in 75% of eyes of the SLT group and 73% of the latanoprost group. Both SLT and latanoprost have been shown to significantly reduce IOP fluctuation. Success in fluctuation reduction was 50% after SLT and 83% in the latanoprost group. Forthy-one percent and 64% reduction in IOP fluctuation was achieved after treatment with SLT or latanoprost, respectively. (Nagar et al., 2009).
Alvarado et al. also provided evidences of a similar efficacy of prostaglandin analogue eye drops and SLT in reducing intraocular pressure. Non-significant differences in IOP were observed in 24 eyes sequentially exposed to the two treatments at different times and after a washout phase. Prostaglandin analogue and SLT reduced intraocular pressure by 5.58 mmHg (25.37%) and 6.6 mmHg (29.93%) from the baseline respectively (Alvarado et al., 2005).

5.3 Long-term follow-up

SLT long-term success versus argon-laser trabeculoplasty has been investigated by Damji et al (Damji et al., 2006). No statistical significant difference was found between patients randomized in the argon laser trabeculoplasty group and the patients randomized in the SLT group over 12 months. Juzych et al confirm these results over a 5-year follow-up period (Juzych et al., 2004). So, these data indicate that, despite the lack of a microscopically evident damage to the trabecular meshwork, SLT is at least as effective as argon-laser trabeculoplasty in reducing intraocular pressure in the long term.

6. Adverse events and safety profile

Most studies report a relatively lower side effects rate of SLT compared with argon-laser trabeculoplasty, which can be ascribed to significantly lower energies delivered to the ocular

tissues. The most common complications observed after SLT are post-operative intraocular pressure spikes, anterior chamber inflammation and ocular discomfort.

6.1 Intraocular pressure spikes

The overall incidence of intraocular pressure spikes following 360° SLT is expected to be lower than after ALT, ranging from 3 to 10%. Intraocular pressure should be measured 1 hour after the procedure. An intraocular pressure increase of more than 5 mmHg should be considered significant and treated with additional topical or oral glaucoma medications. In order to prevent the occurrence of this complication, some authors suggest pre-medication with alpha-agonist and pilocarpine drops. The occurrence of intraocular pressure spike in heavily pigmented angles seems to be more frequent. Lower SLT energy levels have been proposed for such patients by some authors (Harasymowycz et al., 2005). In some cases of pseudoexfoliation glaucoma there might be an increased risk of intraocular pressure spikes following SLT. Cellini et al. reported intraocular pressure spikes in 15 patients affected by pseudoexfoliative glaucoma. This failure was demonstrated to correlate with a decreased ratio between tissue inhibitor metalloproteinase and matrix metalloproteinases concentrations (TIMP-2/MMP-2) in the aqueous humor (Cellini, Leonetti, Strobbe, & Campos, 2008).

6.2 Anterior chamber inflammation

The inflammatory response triggered by SLT may be responsible for anterior chamber reaction. This complication, including cells, flares and conjunctival injection has been commonly reported in several studies, with an incidence up to 83% of the first report from Latina. However it was always a transient event with no sequelae. SLT-related hypema has been anecdotally reported (Rhee, Krad, & Pasquale, 2009; Shihadeh, Ritch, & Liebmann, 2006).

6.3 Ocular discomfort

During or after the procedure, ocular discomfort or even pain can occur. Latina et al. reported post SLT discomfort in 15% of the treated eyes. Pain scores after SLT where recorded by Martinez-de-la-Casa et al. and showed to be significantly lower than post-argon laser trabeculoplasty scores during the first 24 hours (Martinez-de-la-Casa et al., 2004). In a study comparing topical latanoprost to SLT, 39% of patients complained of ocular discomfort after the laser procedure, as compared to 0% of cases after topical medication (Nagar et al. 2005).

7. Specific cases

7.1 Pigmentary glaucoma

There is some evidence showing a correlation between the degree of angle pigmentation and the effectiveness of SLT (Chen, Golchin, & Blomdahl, 2004). A study by Melamed included 3 cases of pigmentary glaucoma; in these patients SLT produced an intraocular pressure reduction in 24% of eyes. (Melamed, Ben Simon, & Levkovitch-Verbin, 2003) Damji et al. obtained an intraocular pressure reduction of 5.6 mmHg in 5 pigmentary glaucoma patients treated with SLT after 12 months (Damji et al., 2006). On the contrary, Harasymowicz et al.

reported an intraocular pressure elevation in 3 patients included into the study and affected by pigmentary glaucoma (Harasymowycz et al., 2005).

7.2 Pseudoexfoliation glaucoma

SLT can be considered as a safe and effective method of therapy for pseudoexfoliation glaucoma similarly to other types of open angle glaucoma. In a small prospective trial, Gracner et al compared the results of 180° SLT treatment in patients with primary open angle glaucoma and patients with pseudoexfoliation glaucoma. After 18 months, there was a comparable IOP reduction between the 2 groups (Gracner, 2001). Shazly et al. confirmed these data in a study comparing the SLT results on 19 eyes with primary open-angle glaucoma and 18 eyes affected by pseudoexfoliation glaucoma (Shazly, Smith, & Latina, 2010). Previously, also Melamed and Chen et al had similar findings (Chen et al., 2004; Melamed et al., 2003).

7.3 Prior argon laser trabeculoplasty treatment

SLT represent a practicable option in eyes previously treated with argon-laser trabeculoplasty. Some studies suggest that SLT is not associated with unfavorable outcomes in eyes with prior argon-laser trabeculoplasty and that the intraocular pressure-lowering efficacy is comparable to laser-naïve eyes. Latina et al. reported an intraocular pressure reduction of 5 mmHg or more in 40% of eyes that had not undergone previuos trabeculoplasty and 57% in those with previous argon laser trabeculoplasty (Latina et al., 1998). Song et al. found no differences in the success rate between laser-naïve eyes and eyes previously treated with argon-laser trabeculoplasty (Song et al., 2005). Similarly, Birt did not find statistically significant differences in outcomes between patients previously treated with 360° argon-laser trabecuoplasty and laser-naïve eyes (Birt, 2007).

7.4 Primary angle closure with persistent intraocular pressure elevation after iridotomy

A report from Ho et al (Ho et al., 2009) showed that SLT might be an option for patients with primary angle closure glaucoma that underwent a successfully opening of the irido-trabecular angle with peripheral laser iridotomy and persistent intraocular pressure elevation (≥21 mmHg). Sixty patients were enrolled in the study and were treated with SLT if at least 90° of pigmented trabecular meshwork was visible. During a study period of 6 months, an intraocular pressure reduction of more than 20% was obtained in 54% of cases. No statistically significant correlation was found between the degree of angle treated and the amplitude of intraocular pressure lowering effect.

7.5 Normal tension glaucoma

El Mallah et al investigated SLT effectiveness on normal tension glaucoma. In their study they observed not only a post SLT reduction of the mean intraocular pressure, but also a narrowing of the intraocular pressure inter-visit variation. Both these values were significantly reduced. The mean intraocular pressure reduction was 2.1 mmHg. The intraocular pressure inter-visit variation was evaluated by considering the range and the standard deviation of multiple intraocular pressure measurements performed on each eye preceding and following SLT by approximately 12 months. Both these two parameters were

significantly diminished after SLT: by 4.5 and 1.9 mm Hg respectively. The authors stress the importance to record the mentioned intraocular pressure intervisit variation parameters in every patient undergoing SLT due to their correlation to the glaucoma progression (El Mallah, Walsh, Stinnett, & Asrani, 2010).

7.6 Steroid-induced ocular hypertension

SLT has been shown to effectively reduce intraocular pressure in patients with intravitreal and subtenon triamcinolone acetonide-induced intraocular pressure elevation (Baser & Seymenoglu, 2009; Pizzimenti, Nickerson, Pizzimenti, & Kasten-Aker, 2006; Rubin, Taglienti, Rothman, Marcus, & Serle, 2008; Yuki et al., 2010). However the role of SLT in post-steroid hypertension is still controversial due to the fact that it is non clear whether the lowering effect is more attributable to SLT or to the physiological drug wash out.

7.7 Pseudophakic glaucoma

SLT has been shown effective in pseudophakic glaucoma (Nagar, Shah, & Kapoor, 2010). Furthermore Werner et al. have not found any difference in SLT efficacy between phakic and pseudophakic eyes (Werner, Smith, & Doyle, 2007).

7.8 Glaucoma after penetrating keratoplasty

Nakakura et al. successfully treated with SLT a medication-resistant IOP elevation following penetrating keratoplasty. The decrease in IOP was stable at 6 months and no adverse effect or graft rejection was recorded (Nakakura, Imamura, & Nakamura, 2009).

8. Is SLT repeatable?

When patients treated with argon laser trabeculoplasty require a repeated treatment, this is usually limited by complications such as intraocular pressure spikes and sustained intraocular pressure elevation. SLT delivers less energy to the trabecular meshwork and is non-destructive in nature, for these reasons multiple treatments are possible. Repeat treatment with SLT has been found to be safe and may be beneficial in some patients. Hong et al, described the results obtained repeating SLT on eyes previously treated with 360° SLT that had lost its efficacy. They found that repeating SLT is effective in reducing intraocular pressure. The mean intraocular pressure reduction at 8 months after the first and second procedure did not significantly differ, being 4 mmHg and 2.9 mmHg, respectively (Hong et al., 2009).

9. Conclusions

SLT can be considered a valuable alternative to medical therapy in the management of open angle glaucoma. According to the most recent findings, SLT should not only applied when medical therapy fails but as a first-line treatment. SLT has been found to be equally efficacious as prostaglandin analogues in reducing intraocular pressure as a primary treatment option in open angle glaucoma and ocular hypertension (McIlraith, Strasfeld, Colev, & Hutnik, 2006) with a good safety profile. Furthermore, this treatment results in significant decrease in the amplitude of diurnal intraocular pressure fluctuation (Kothy, Toth, & Hollo, 2010) which is related to glaucoma damage progression. The application of

this therapeutic modality is supported by a lack of trabecular meshwork injury that allows re-treatments. Eliminating the need for topical medications, SLT can minimize patient noncompliance and result in appropriate intraocular pressure control. Thus, it can also be a good choice for patients who are allergic to all types of topical medications without interfering with the success of future surgery (Gavric, Gabric, Dekaris, Bohac, & Draca, 2010).

The efficacy results, the effect duration and the good safety profile, might set SLT treatment as "gold standard" first-line therapy for open angle glaucoma, in the near future.

A better comprehensive of SLT mechanism of action is needed, as well as the research for new laser sources to better target the trabecular meshwork cells, obtaining the desired effect with even less damage (Titanium Sapphire Trabeculoplasty: TiSalt 790nm, described by Goldenfeld and al.,2009).

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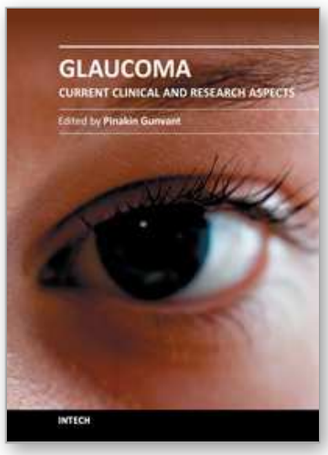

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This book summarizes current literature about research and clinical science in glaucoma and it is a synopsis and translation of the research conducted by individuals who are known in each of their respective areas. The book is divided into two broad sections: basic science and clinical science. The basic science section examines bench- and animal-modeling research in an attempt to understand the pathogenesis of glaucoma. The clinical science section addresses various diagnostic issues and the medical, laser and surgical techniques used in glaucoma management.

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