An Overview of Clinical Evidence for SLT

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SLT

* Unique Physical Properties
* Mechanism of Action
* Clinical Data (EBM,more than 6 years of experience)
* Safety and Efficacy
* Technique
* Question of Repeatability

**Use of SLT as Primary Rx

Background and Rationale for SLT

* Lasers have a long history of use in the management of glaucoma

* Argon laser trabeculoplasty (ALT) was initially utilized in patients who failed medical therapy

* Glaucoma Laser Trial (GLT) established efficacy of ALT in lowering IOP in primary open-angle glaucoma patients

Background and Rationale for SLT

* Limitations of ALT
* Post-treatment increase in IOP; PAS
* Limited efficacy of ALT re-treatment
* Coagulative damage to the trabecular meshwork; may limit efficacy of further non-surgical therapy
* Selective laser trabeculoplasty (SLT) developed as an alternative to ALT

Selective Laser Trabeculoplasty

A treatment for Open Angle Glaucoma

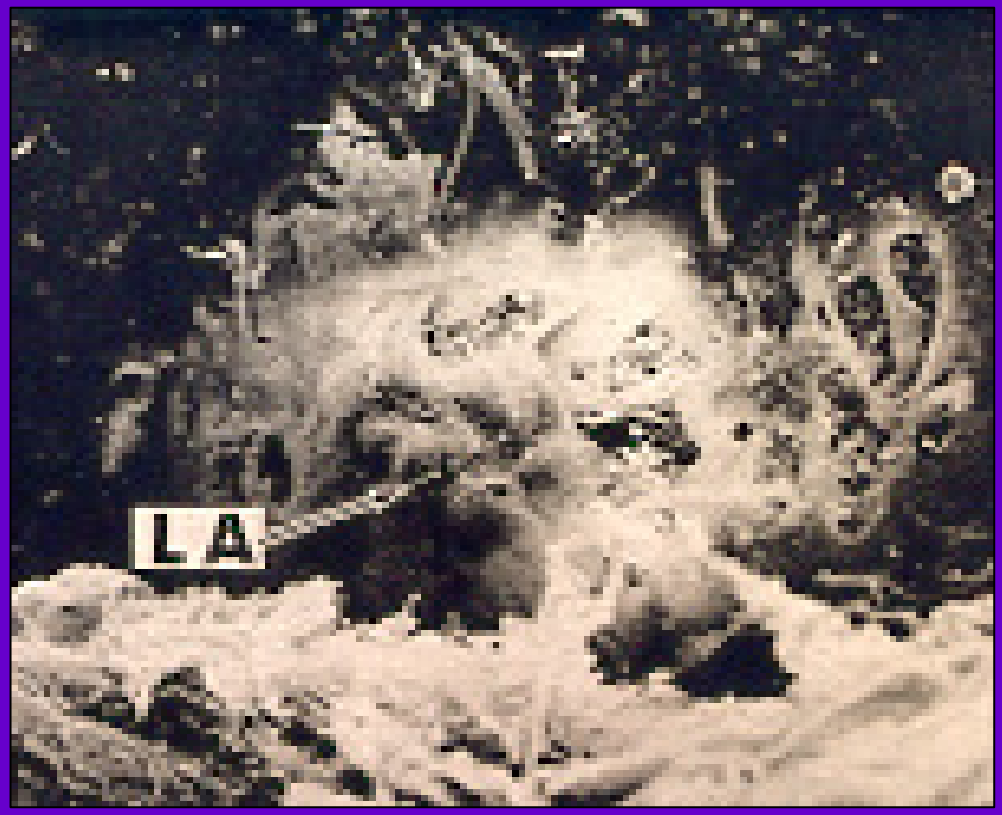
* Q-Switched frequency doubled (532 nm) Nd:YAG Laser

* Permits selective targeting of pigmented trabecular meshwork cells without causing structural or coagulative damage to the TM

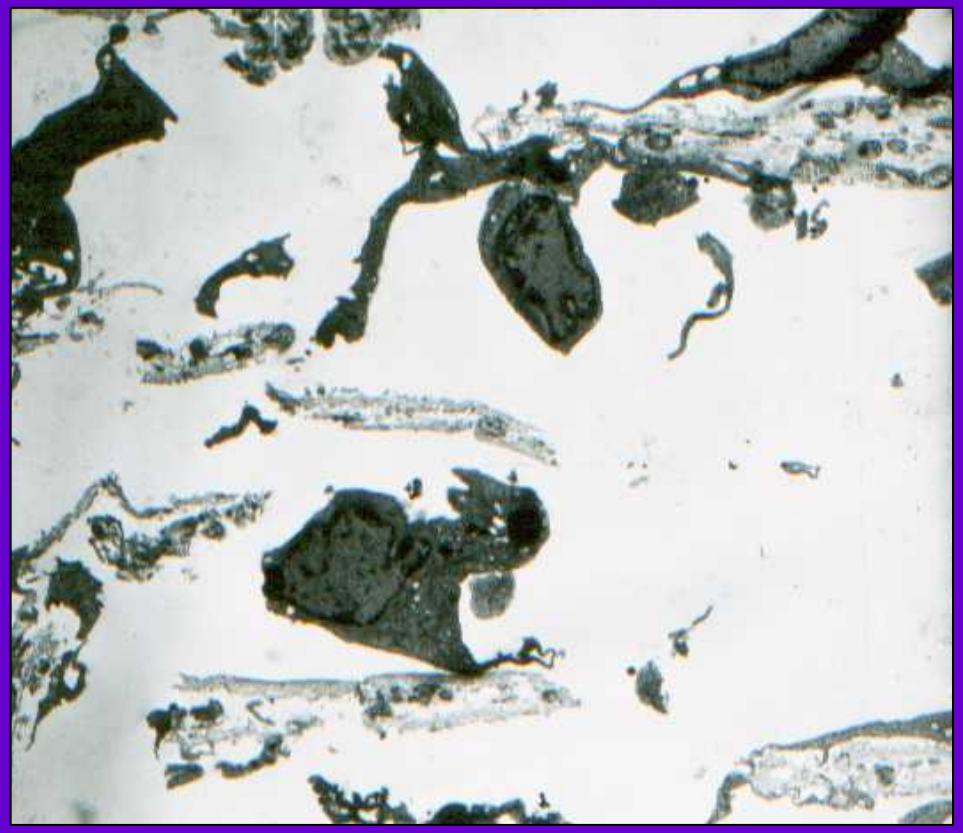
Trabecular Meshwork

* Cellular and Structural Components
* TM cells are phagocytic and contain variable amounts of melanin
* ALT induces focal scarring and coagulation damage with reduced flow through the lasered site

Argon Laser Coagulation of TM

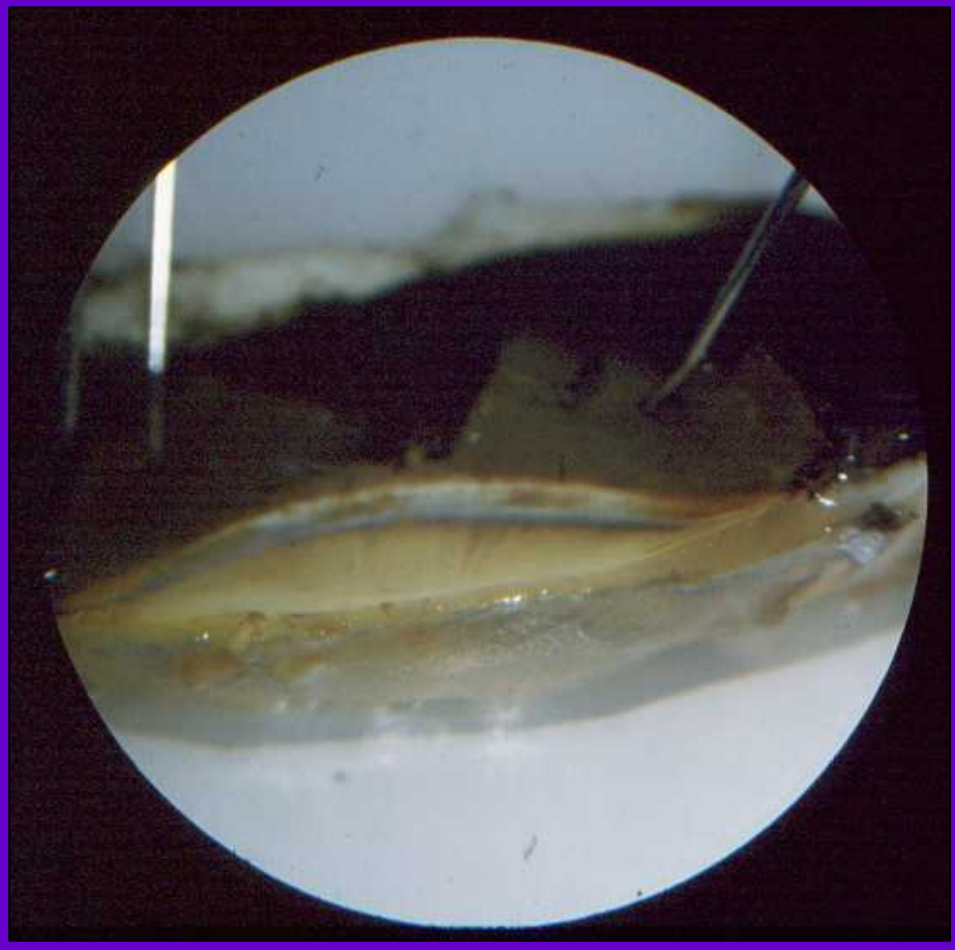


TEM 1 hr after ALT

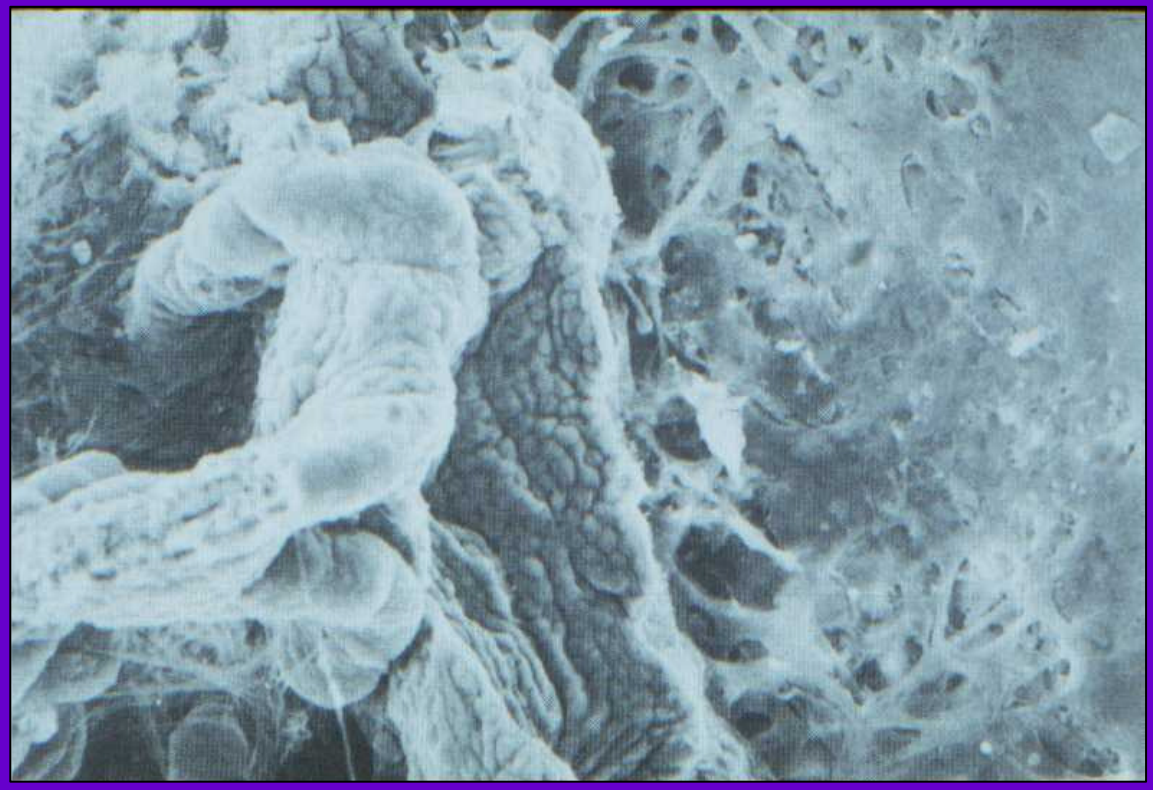


TEM – enhanced phagocytosis

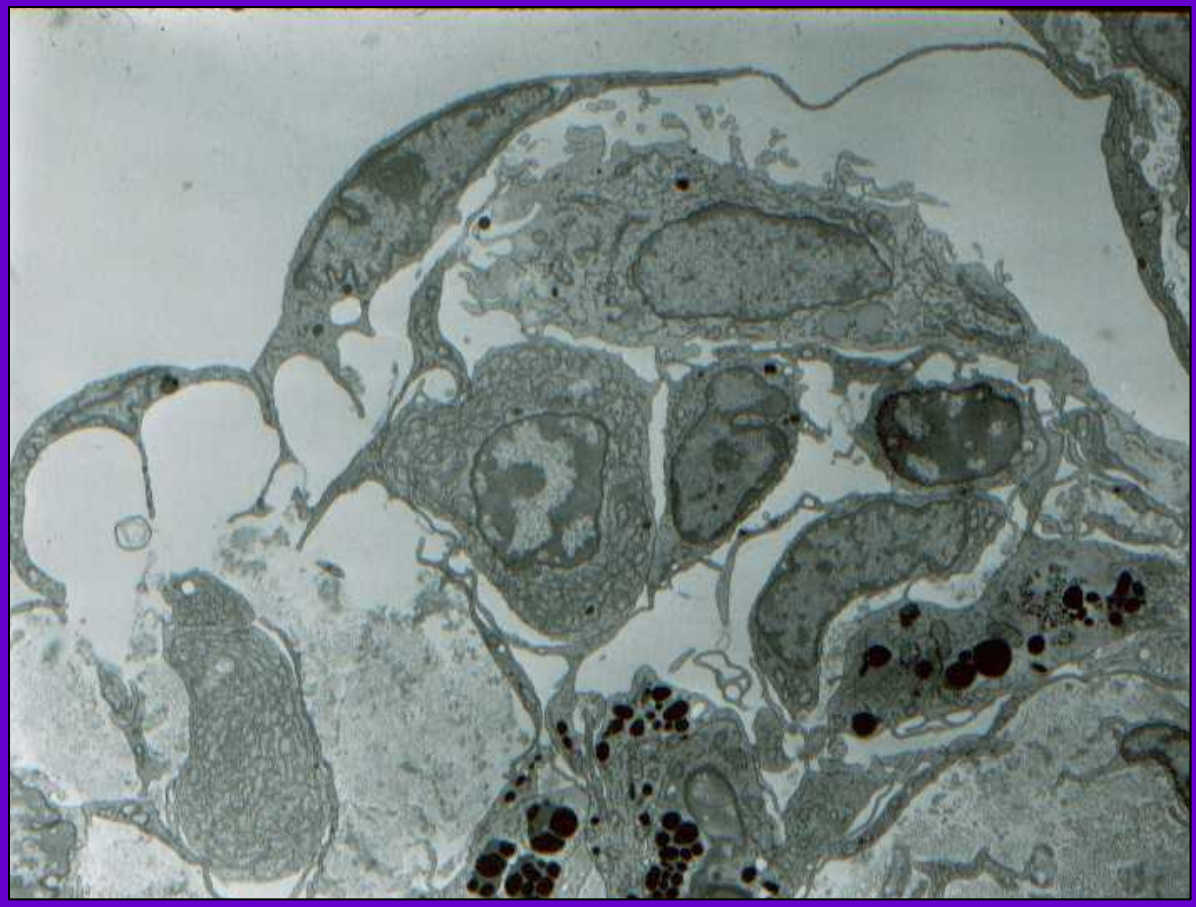
4 weeks after ALT (monkey)



SEM - 4 weeks after ALT

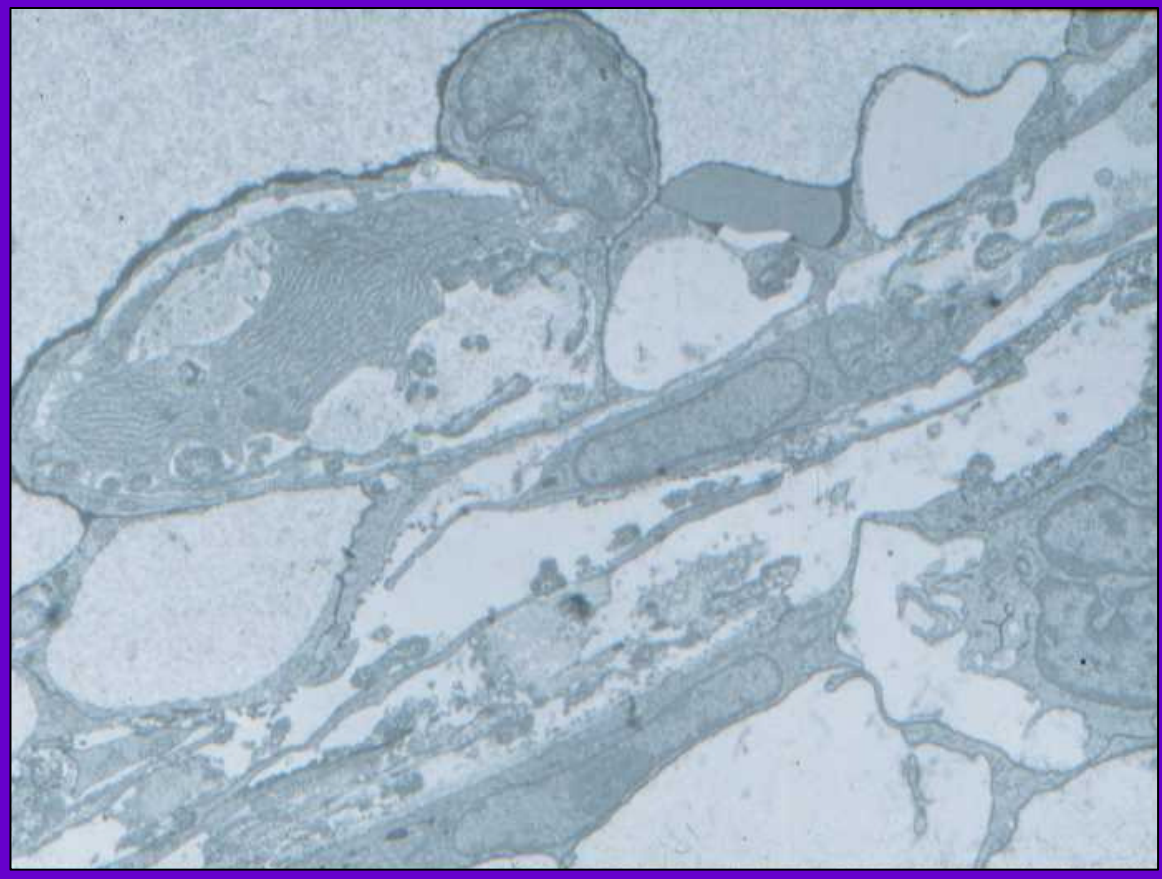


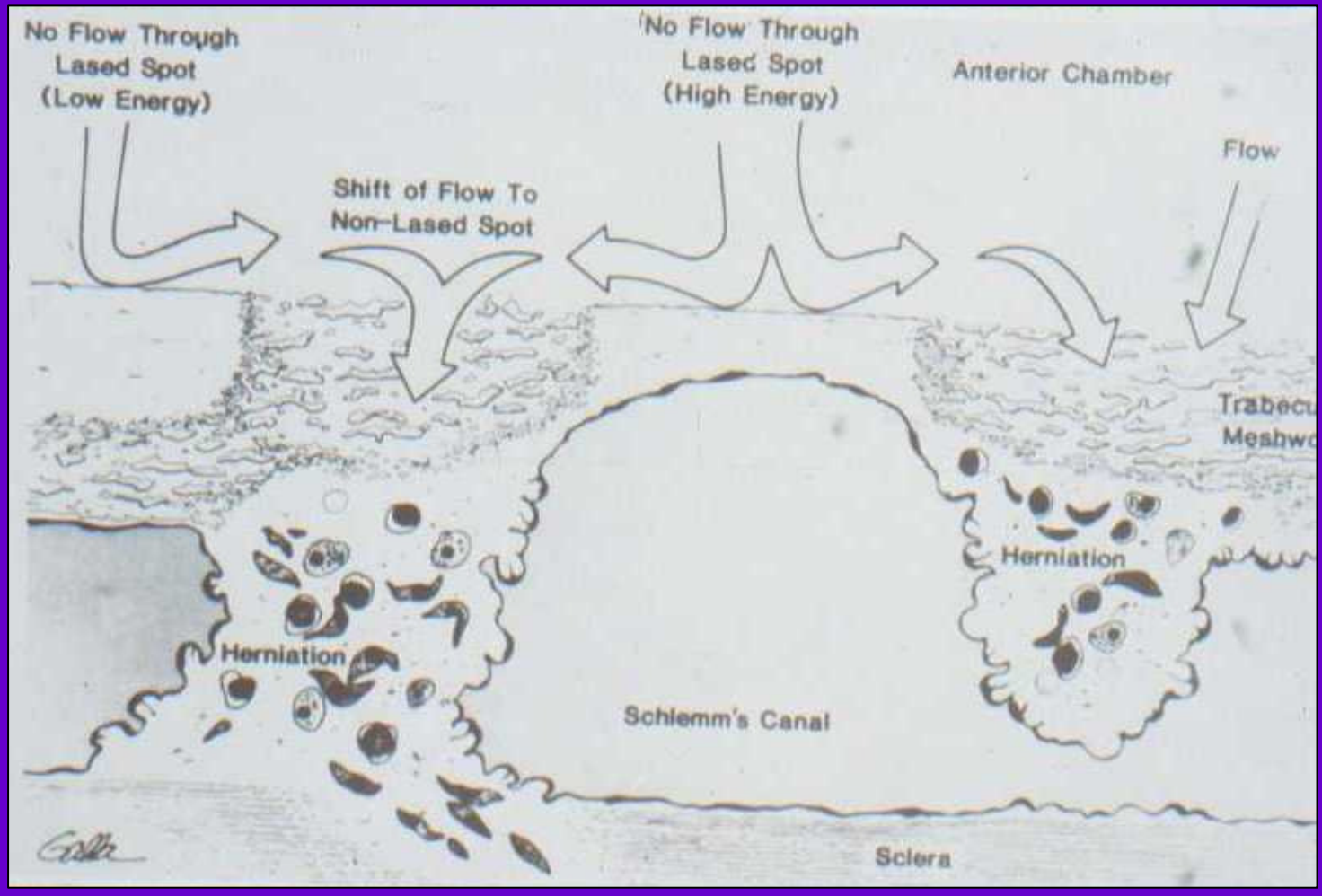
ALT – induced trabeculitis



ALT – scarred lasered region

ALT – non lasered region (ferritin)




No Flow Through
Lased Spot
(Low Energy)
No Flow Through
Lased Spot
(High Energy)
Anterior Chamber
Flow
Shift of Flow To
Non-Lased Spot
Herniation
Herniation
Schlemm's Canal
Sclera

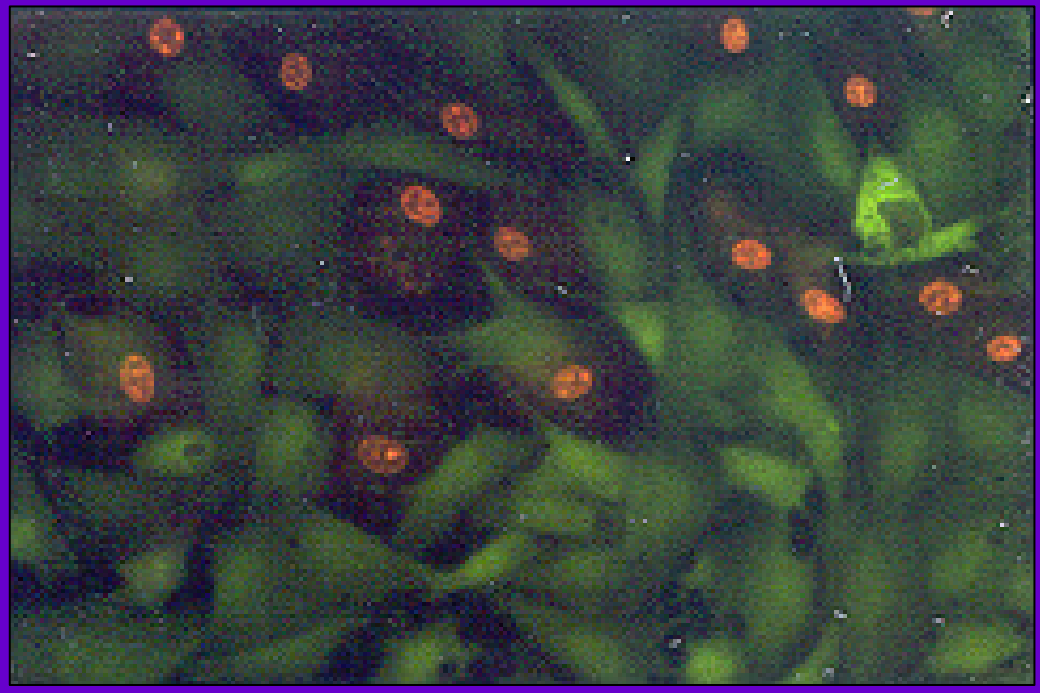
ALT - Biological effects

* Increased phagocytic activity of TM cells
* Induced “ trabeculitis “
* Shift of aqueous flow
* Up – regulation of mmp’s

However, You do not need the "Over-Kill" of ALT in order to induce biological enhancement of the TM…

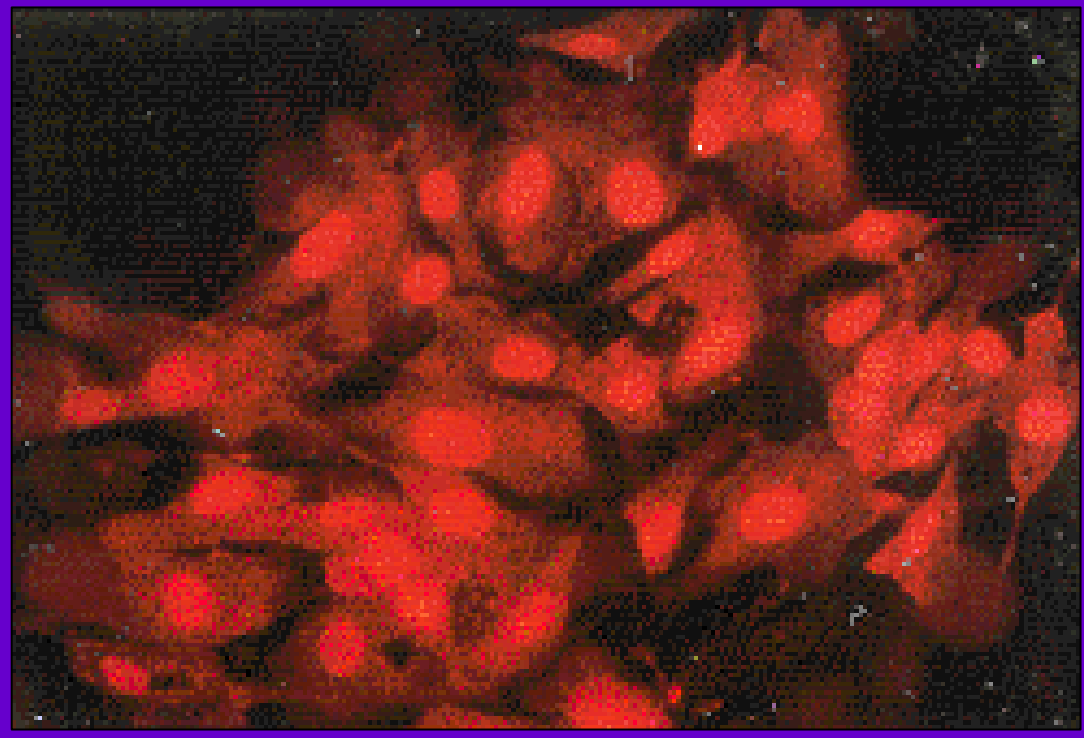
A more gentle Rx of Pigmented Cells alone will achieve similar effects !

TM Cells
532 Nd:YAG pulse - fluorescence



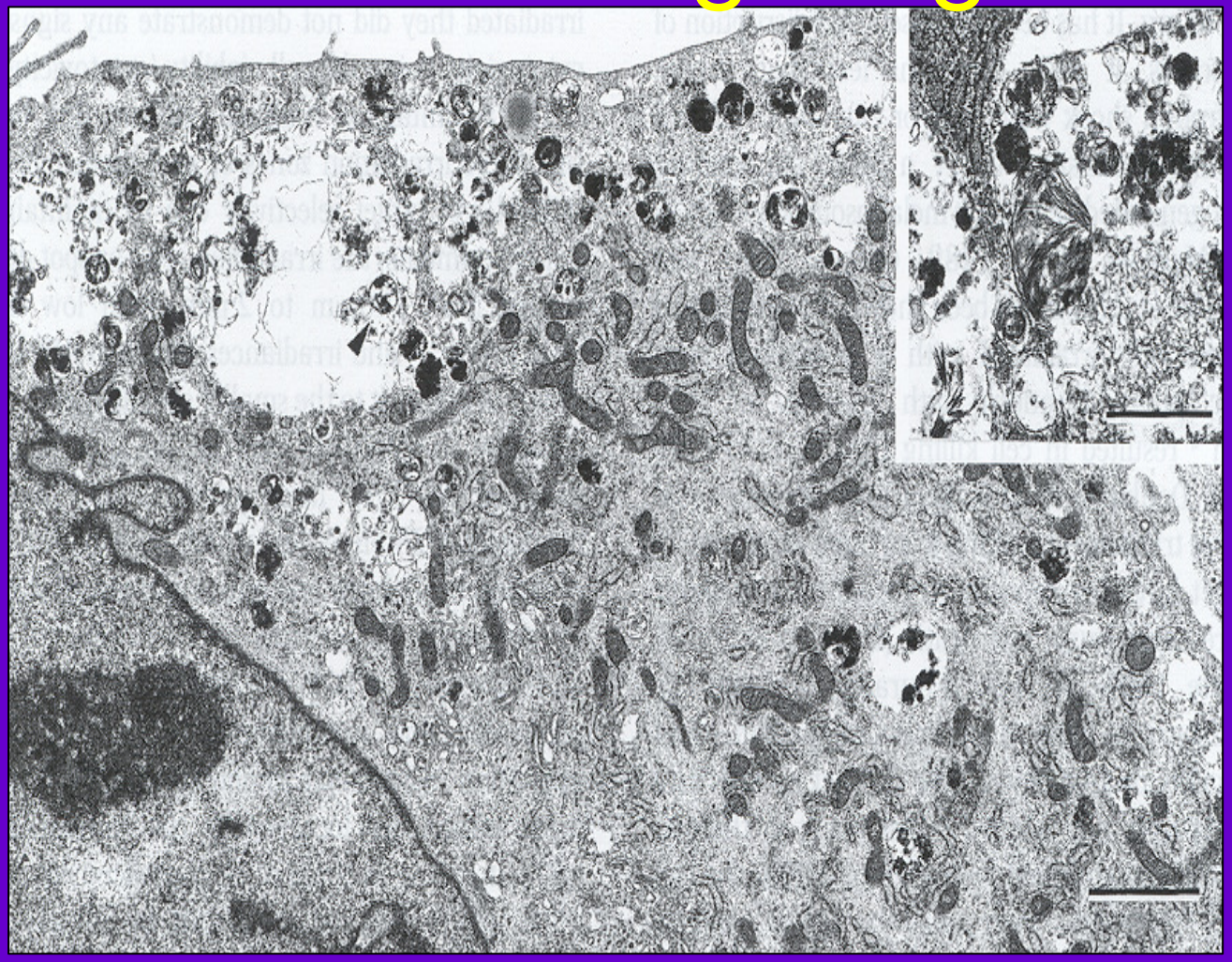
M. Latina, M.D

TM Cells
Argon Laser 0.1 sec pulse



M. Latina, M.D

SLT – intracellular pigment targeting



M. Latina, M.D

SLT
Selective Rx of Melanin – containing trabecular cells only.

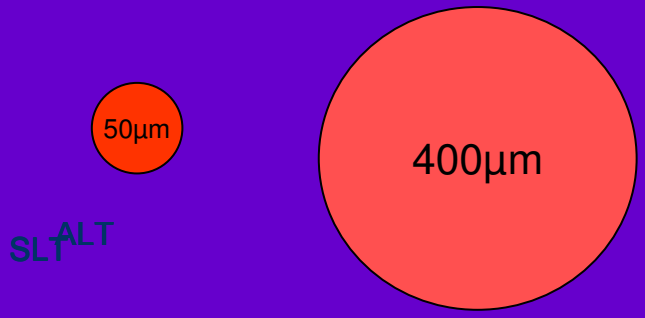
* No coagulative necrosis
* Induced synthesis of IL – 1 alpha and beta
* Recruitment of macrophages

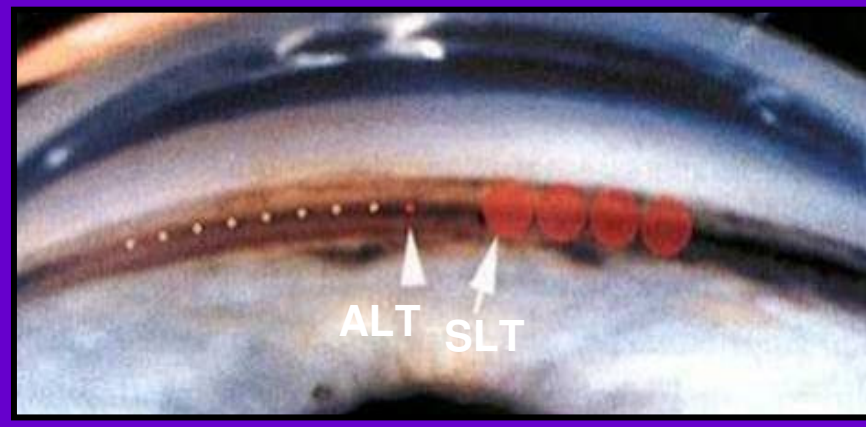
SLT – Biological and Physiological Studies (Alvarado, IGS, Athens, 2007)

* Aqueous Outflow is increased after SLT
* Laser Activated TM cells synthesize ligands which increase permeability of inner wall of SC
* Media conditioned by SLT increases SC cells permeability when added to naive control

SLT compared to ALT

Spot size comparison:



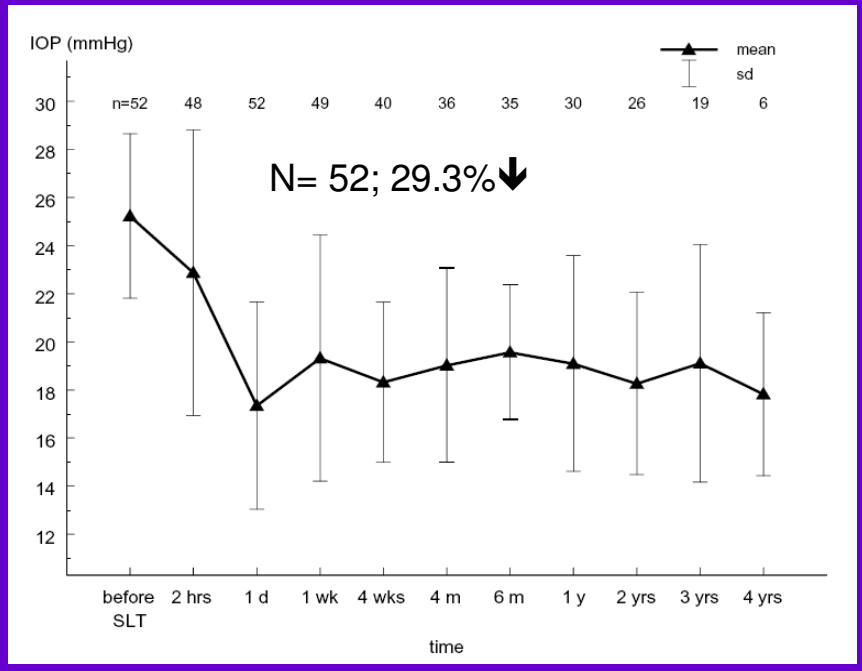


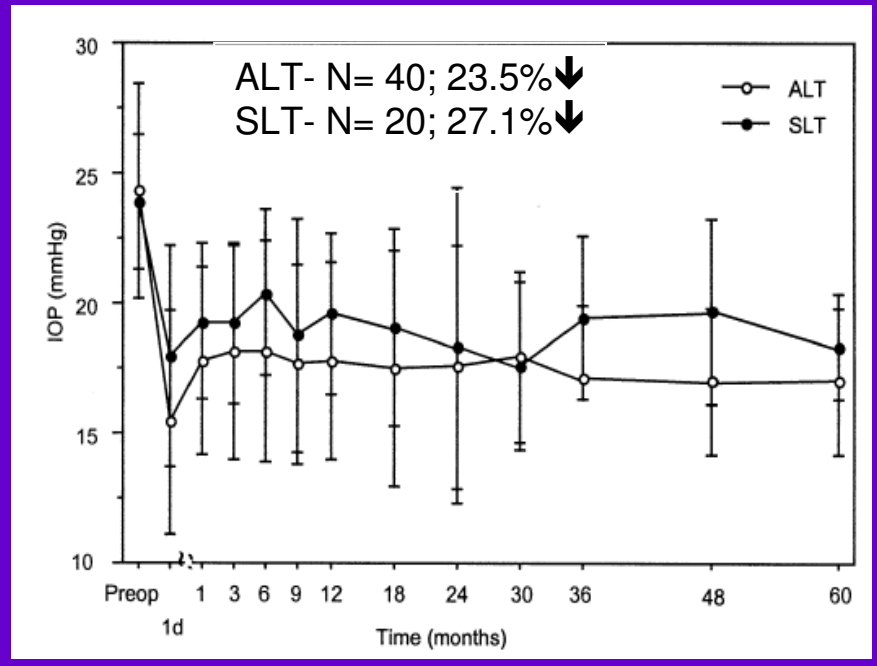
ALT		SLT
50 micron	SPOT SIZE	400 micron
500 – 1,000 mW	ENERGY OUTPUT	0.8 – 1.5 mJ
10 ms	PULSE DURATION	3 ns
60,000 mJ/cm^2	FLUENCE	600 mJ/cm^2

[6]Latina MA, Tumbocon JA. Selective Laser Trabeculoplasty: The Evolution of Laser Treatment for Open Angle Glaucoma

SLT- Longevity

SLT produces satisfactory IOP reduction that can last at least up to five years



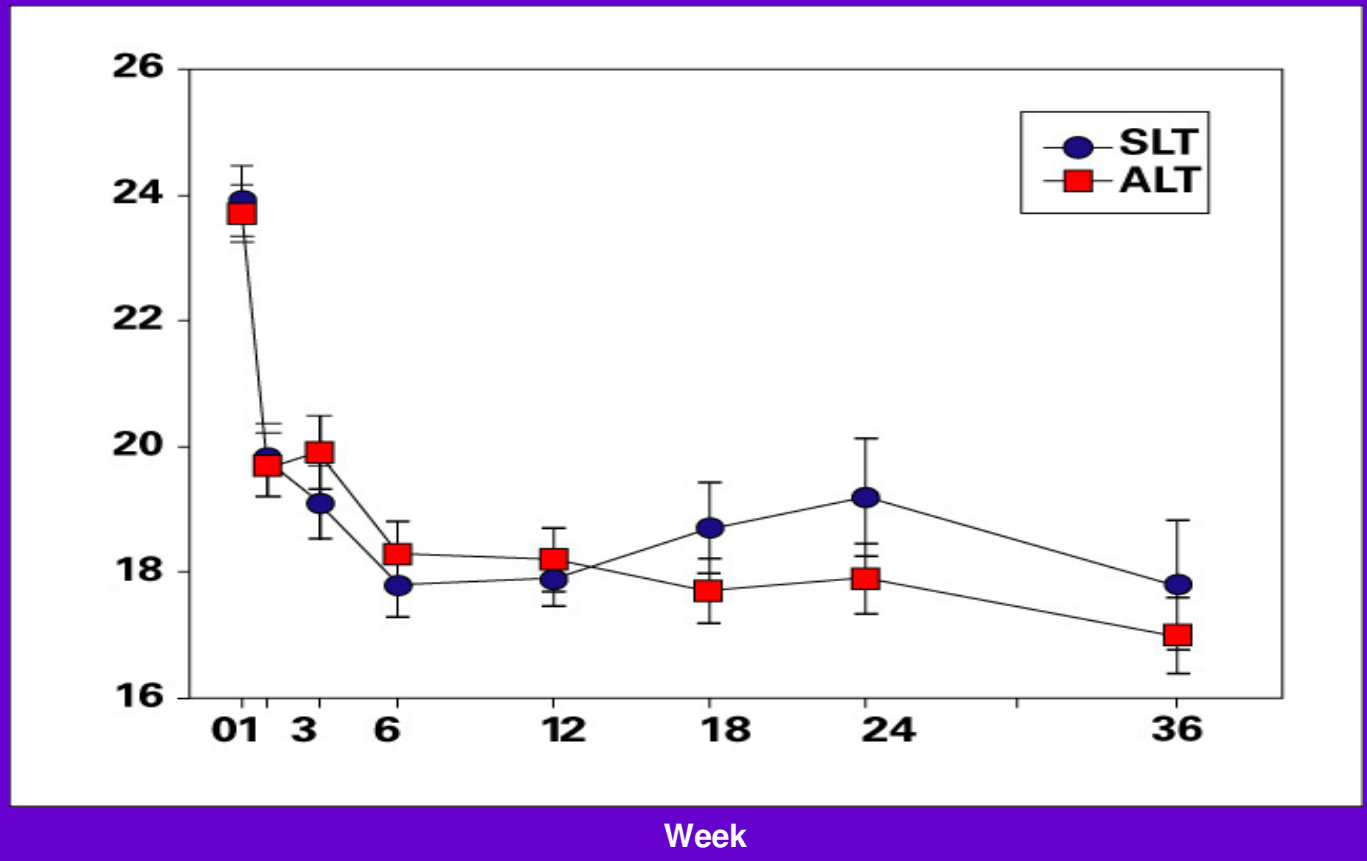


Weinand, EJO 2006;16:100-4

Juzych, Ophth. 2004;111:1853–59

Alternative to ALT

Clinical Trial Results Comparing IOP reduction between SLT and ALT[7]



[7]*Damji KF, Bovell AM, Hodge WG. Selective Laser Trabeculoplasty: A Review and Comparison to Argon Laser Trabeculoplasty. Ophthalmic Practice 2003;21:54-58*

SLT – Clinical Experience

Study	no. of patients		IOP reduction	FU time
Latina et a	120	MTMT+ s/p ALT	17.10%	26 w
Howes	107	MTMT	20%	11 m
Damji	118	MTMT	6.5 mmHg	24 m
Larsson	60	MTMT	6.2 mmHg(24%)	6 m

SLT – Other Studies

* 90 deg. is as effective as 180 deg. Rx (Chen et al. 2004)

* 5 year FU of Chinese patients – SLT is equal to medical Rx (Lai et al. , 2004)

* SLT as effective as ALT, but associated with less inflammation and better tolerated by patients (Martinez de la Casa et al. , 2004)

SLT
Factors influencing success:

Baseline IOP Only

The higher the IOP at treatment, the greater the reduction

Not related to:

- **Age**
- **Sex**
- **Race**
- **Family history**
- **Other glaucoma risk factors**
- **Type & severity of OAG**
- **Trabecular meshwork pigmentation (unlike ALT)**
- **Pseudoexfoliation**
- **Number of glaucoma medications (unlike ALT)**
- **Previous ALT (unlike ALT)**
- **SLT as primary therapy**
- **Systemic Hypertension**
- **Diabetes Mellitus**

Hodge 2005; Nagar 2005; Chen 2004

SLT – Clinical Experience

In all studies only minor complications reported such as:

* IOP spikes (in 3-11%)
* Limited AC reaction

No PAS formation!

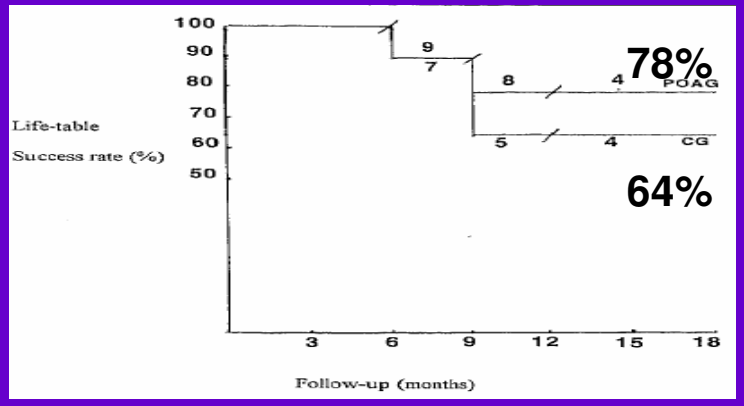
SLT

can be used to treat various forms of OAG

Table 3. IOP Decrease in Different Types of Glaucoma

Diagnosis	No. of Eyes	Preoperative IOP, mm Hg*	Final IOP, mm Hg*	% IOP Decrease	*P* Value†
POAG	29	25.5 ± 2.0	18.5 ± 2.8	27	<.001
OHT	6	25.5 ± 1.1	17.0 ± 2.6	31	<.001
PXFG	5	28.6 ± 3.2	16.8 ± 0.8	41	.001
PDG	3	26.0 ± 2.6	19.7 ± 2.3	24	NA‡
NTG	2	20.5 ± 0.7	14.5 ± 2.1	29	NA‡

Melamed Arch. Ophth. 2003;121:957



SLT for PXF & POAG – at 18 months no significant differences in:

- IOP reduction (31.4 vs. 35.1%↓)
- Success rate (≥20%↓)

Gračner EJO 2002;12:287

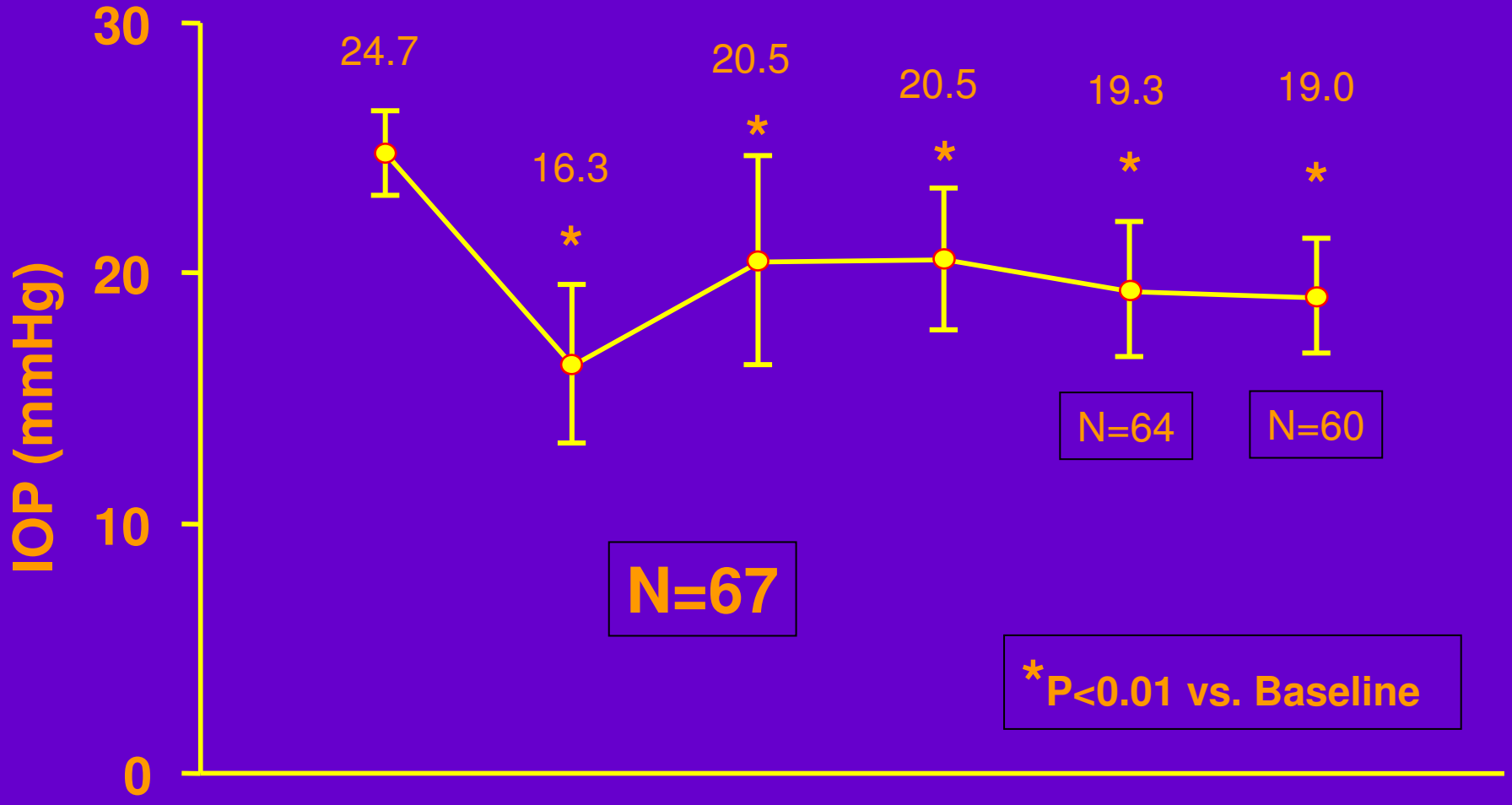
SLT
PDG & PXF

- The amount of TM pigmentation was not a significant predictor of success [Hodge 2005]
- No race differences, but four of the six eyes with PDG and PXF failed to respond [Nagar 2005]
- PDG & PXF – similar IOP reduction to POAG & OHT [Melamed 2003]
- No difference between results of PXF & PDG and other types, but TM pigmentation ➔ delayed IOP lowering [Chen 2004]

However – there are 6 case reports of paradoxical IOP rise [up to 20%] in heavily pigmented angles [Harasymowycz 2005; Van de Viere 2006]

SLT can be used regardless of angle pigmentation, but there may be more complications in eyes with heavily pigmented trabeculum

SLT-PACG Study



Time	Baseline	1 day	1 week	4 weeks	3 month	6 months
mmHg		- 8.4	- 4.3	- 4.2	- 5.5	- 6.7
		- 34.0 %	- 17.5%	-17.1%	- 22.1%	- 23.0

IOP

Barkana ARVO 2007

Repeatability of SLT

Additional IOP reduction after repeated SLT, but to a lesser extent than primary response (20 % vs. 30 %)

Nagar et al. , IGS – Athens, 2007

SLT – side effects

AC reaction common – always temporary

Table 1 Percentage of eyes with transient adverse events reported during the first week after treatment

Adverse event	Latanoprost	90° SLT	180° SLT	360° SLT
Discomfort/pain	0%	6%	20%	39%
Uveitis	0%	31%	41%	50%
IOP spike	0%	11%	16%	27%

Nagar BJO 2005

Also:
Short duration pressure spikes (~ 10%)
Six case reports of paradoxical IOP elevation

Neither significant nor long-term side effects

Why should we use SLT as a primary treatment in Glaucoma?...

Reasons:

* GLT study supports ALT as primary Rx
* SLT is effective in MTMT and even post ALT patients
* SLT is extremely safe
* SLT may be repeated more than twice
* Avoiding side effects and cost of chronic drug use

Selective Laser Trabeculoplasty (SLT) as Primary Treatment in Open Angle Glaucoma

Shlomo Melamed, Guy J. Ben Simon &
Hana Levkovitch-Verbin

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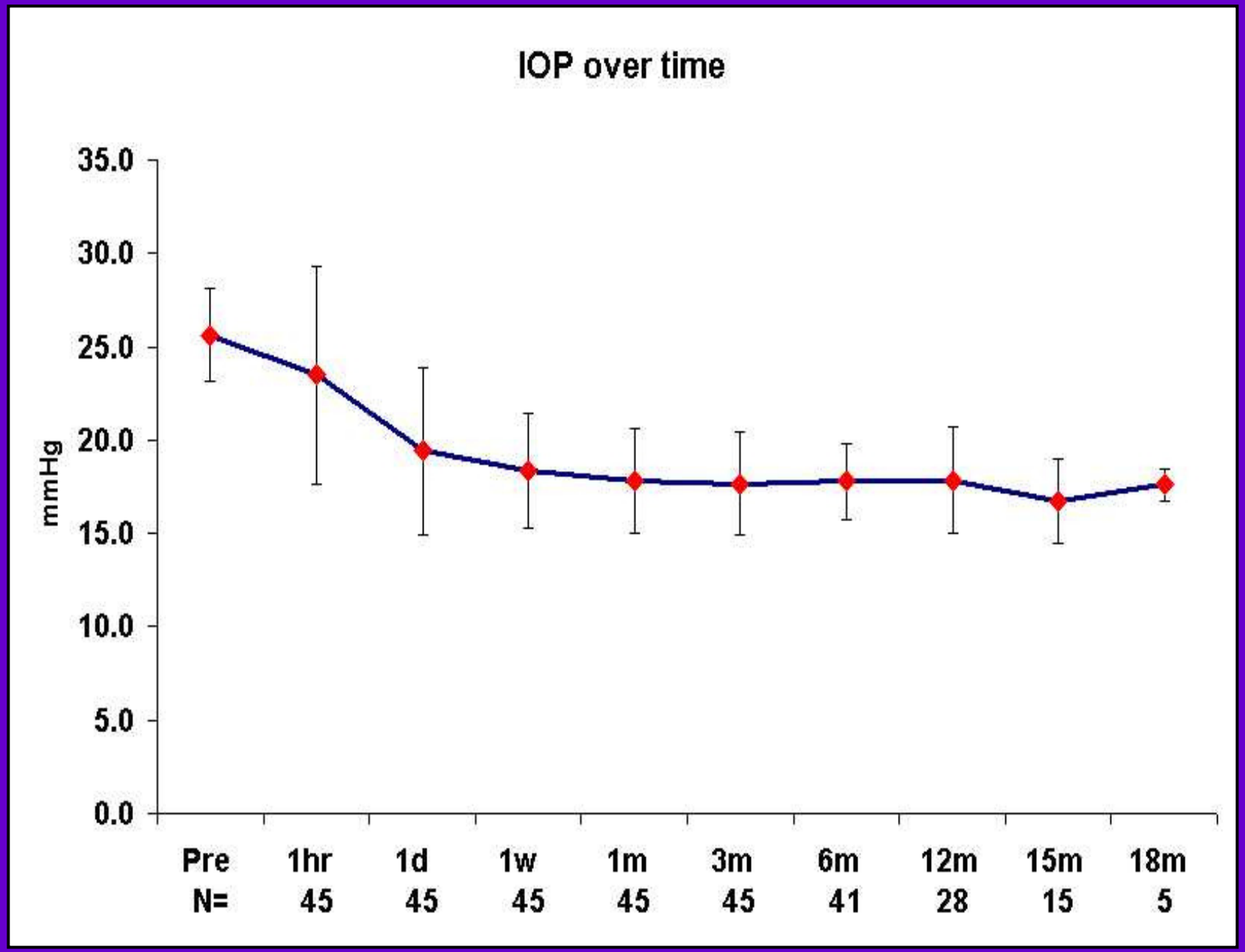
Goldschleger Eye Institute, ISRAEL


IOP over time
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
mmHg
Pre
1hr
1d
1w
1m
3m
6m
12m
15m
18m
N=
45
45
45
45
45
41
28
15
5

Extent of IOP reduction

IOP Reduction (mmHg from Baseline)	(N=45) n (%)
≤2	2 (4.4%)
>2 to 4	3 (6.7%)
≥5	40 (88.9%)

Interestingly…

IOP reduction over 5 mmHg within 1 hour was detected in 33% of eyes

Mechanism?…

* Mechanical effect of photodisruption
* Early recruitment of inflammatory mediators

SLT as initial and adjunctive study for OAG

McIlraith et al. , J Glaucoma , 2006

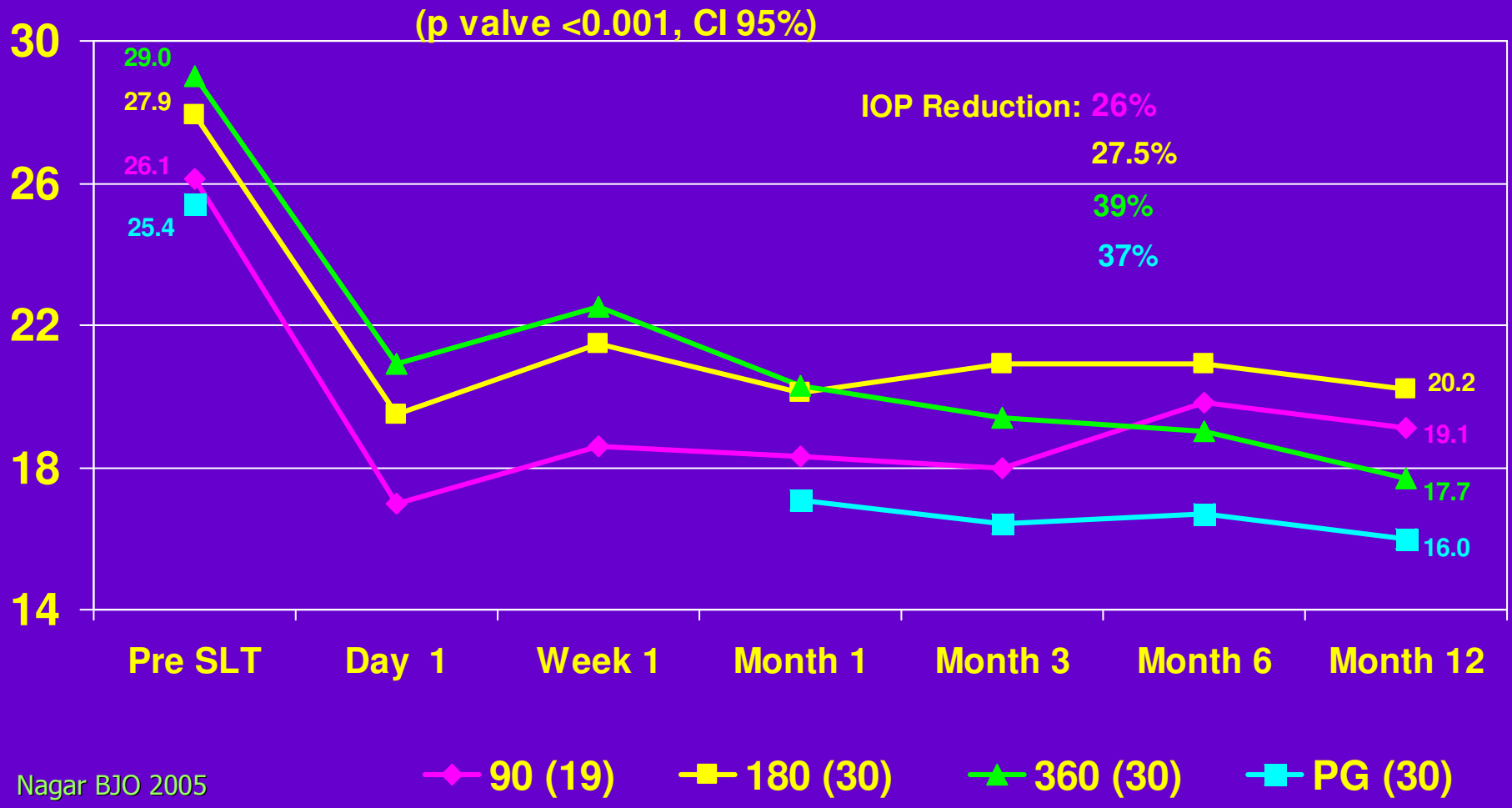
* Prospective, Multi-Center ,Non - Randomized Study
* Newly diagnosed OAG assigned to Primary SLT or Latanoprost
* Similar effect of SLT as Latanoprost
* 30% IOP reduction in both groups!!

A randomised, prospective study comparing SLT with latanoprost for the control of IOP in OHT and OAG

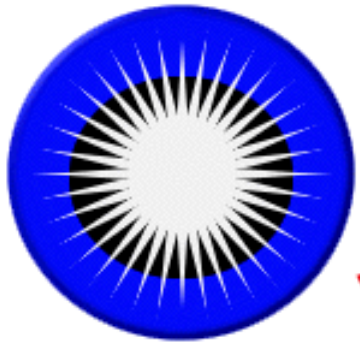
Nagar BJO 2005;89:1413

* N = 167 eyes
* Washout period = 5 weeks
* Baseline IOP = 29.3
* Latanoprost (39), SLT: 90 (35), 180 (49), 360 (44)
* Mean follow-up = 10.3 mo
* Success (20% IOP drop) = 80%

SLT: Dose Response



Nagar BJO 2005



SLT/MED

US/Canada Clinical Study

SLT/MED is a Prospective Randomized Controlled Clinical Trial comparing Selective Laser Trabeculoplasty Vs. Topical Medical Therapy as initial monotherapy

SLT/ Meds Primary Therapy

* Prospective, multicenter trial
* Randomized patients (not eyes)

Group 1: SLT 360/ SLT 180/ SLT 180

Group 2: Meds: current practice

Mean IOP changes and number of intervention steps

Variables	
Medicine Group	
IOP Change	7.6
Follow-up	10.7(±2.2)
No of Steps	1.3(±0.6)
SLT Group	
IOP Change	6.7
Follow-up	11.6(±2.7)
No of Steps	1.1(±0.4)
P for IOP changes:	***0.79***

Conclusions from interim results

* Comparable IOP reduction: SLT and medication (long term?)
* Safety, compliance, cost: SLT > meds
* Individual decision: mutually determined between physician and patient after informed consent

SLT
causes no permanent or serious side effects

Topical beta-blockers

are generally contraindicated in patients with compromised cardiovascular or pulmonary function

arrhythmias

bronchospasms

Vertigo

Depression

Impotence

Prostanoids

latanoprost – 23%

travoprost - 28%

All mild and transient, mainly

Conjunctival Hyperemia

Discomfort on instillation

Summary

* SLT is effective and very safe
* SLT should be offered as an initial treatment choice in certain POAG, OHT and PXG patients
* Repeatability of Rx is an advantage
* No major complications