Avoiding Drops in Glaucoma: SLT and Injectable Glaucoma Medications

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Ben Gaddie's Financial Disclosures

- Consultant/Honoraria in last 12 months:
  - Allergan
  - Novartis
  - Aerie
  - Bausch and Lomb
  - Sun Pharma
  - Carl Zeiss Meditech

Indications and Usage

- Durysta™ (Bimatoprost Implant) for Intracameral Administration for the Reduction of Intraocular Pressure in Patients with Open Angle Glaucoma or Ocular Hypertension

1. DURYSTA™ [package insert]. Irvine, CA: Allergan USA, Inc., March 2020.

Bimatoprost Implant: Sustained-Release, Biodegradable

Drug delivery platform: Can be modified to provide different release profiles[1]

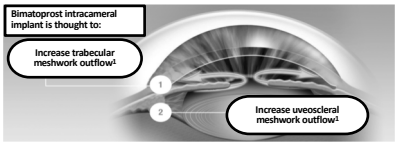
Biodegradable Polymers[2]

- **Ophthalmic drug delivery system for a single intracameral administration of a biodegradable implant**
- **Bimatoprost implant should not be readministered to an eye that received a prior bimatoprost implant**
- **Intracameral implant containing 10 mcg in the drug delivery system**

1. Lewis R, et al. *Am J Ophthalmol* 2017;175:137-147. 2. Lee, et al. *Pharm Res.* 2010. 27:2043-2053. 3. DURYSTA™ [package insert]. Irvine, CA: Allergan USA, Inc., March 2020.

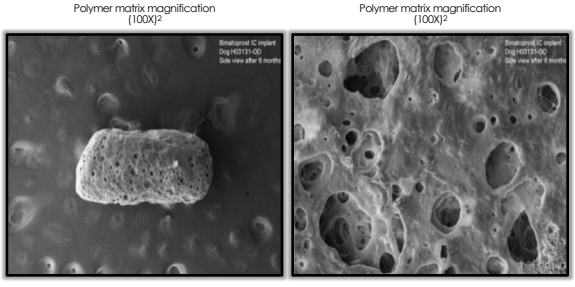
Bimatoprost Implant: Mechanism of Action

- Bimatoprost, a prostaglandin analog, is a synthetic structural analog of prostaglandin with ocular hypotensive activity
- Bimatoprost is believed to lower IOP in humans by increasing outflow of aqueous humor through both the trabecular meshwork (conventional) and uveoscleral routes (unconventional)
  - Elevated IOP presents a major risk factor for glaucomatous visual field loss. The higher the level of IOP, the greater the likelihood of optic nerve damage and visual field loss



1. DURYSTA™ [package insert]. Irvine, CA: Allergan USA, Inc., March 2020.

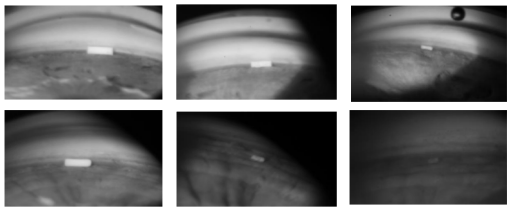
Polymer matrix-based implants biodegrade into lactic acid and glycolic acid.[1]



1. DURYSTA™ Prescribing Information; **2.** Medeiros *et al*, *Ophthalmology*. 2020

Biodegradation Of Implant over two years

Week 2 p injection | Year 1 p injection | Year 2 p injection



Bimatoprost Implant

Efficacy Results from Phase 3 FDA Clinical Trials
ARTEMIS I AND II

ARTEMIS

Study Background

Design	Two multicenter, randomized, parallel-group, patient and efficacy evaluator masked active controlled 20- month studies including eight month follow-up conducted in patients with OAG or OHT
Treatments	Twice daily topical timolol 0.5% or bimatoprost implant
Outcomes	**Co- Primary Endpoint:** • Mean IOP by Treatment Group • Treatment Difference in Mean IOP

IOP = intraocular pressure; OAG = open angle glaucoma; OHT = ocular hypertension

1. DURYSTA™ [package insert]. Irvine, CA: Allergan USA, Inc., March 2020. 2. U.S. National Library of Medicine ClinicalTrials.gov. Retrieved from website: www.ClinicalTrials.gov. ClinicalTrials.gov Identifiers: NCT02247804, NCT02250651 Accessed 11/1/20

Enrollment Criteria For Artemis Phase III Trials

Inclusion Criteria

- Adults with OAG or OHT requiring IOP-lowering treatment
- Iridocorneal angle: Shaffer grade ≥ 3
- Peripheral anterior chamber depth: Van Herick grade ≥ one-half corneal thickness
- Postwashout baseline IOP
  - Hour 0: 22 to 32 mm Hg
  - Hour 2: 19 to 32 mm Hg
- Central corneal endothelial cell density ≥ 1800 cells/mm

Exclusion Criteria

- History of narrow angle
- Nonresponsive to topical beta-blocker and/or topical prostamides, prostaglandins, or prostaglandin analog (PGA) therapy
- History or evidence of complicated cataract surgery or phakic intraocular lens (IOL) insertion
- Contraindications to beta-blocker therapy

1. Medeiros et al, *Ophthalmology*. 2020

DURYSTA (n = 374)

- 0 screening medications
- 1 screening medication
- 2 screening medications
- 3 screening medications
- ≥ 4 screening medications

26.1% on ≥ 2 medications at screening

4.3%

Timolol 0.5% BID (n = 374)

- 0 screening medications
- 1 screening medication
- 2 screening medications
- 3 screening medications
- ≥ 4 screening medications

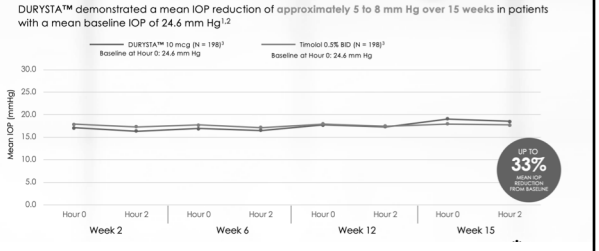
23.3% on ≥ 2 medications at screening

4.9%

Additionally, of 374 DURYSTA™ patients and 374 timolol patients, 7% and 6%, respectively, had prior selective laser trabeculoplasty (SLT).

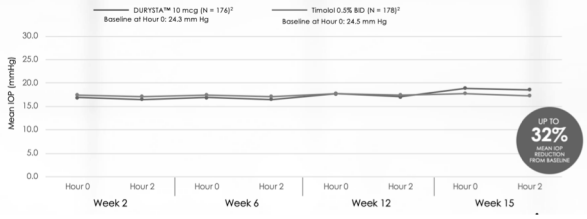
Artemis I Results

DURYSTA™ demonstrated a mean IOP reduction of approximately 5 to 8 mm Hg over 15 weeks in patients with a mean baseline IOP of 24.6 mm Hg[1,2]



Artemis II Results

DURYSTA™ demonstrated a mean IOP reduction of approximately 5 to 8 mm Hg over 15 weeks in patients with a mean baseline IOP of 24.3 mm Hg[1,2]



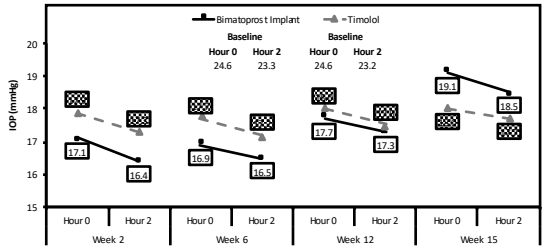
Most Common Adverse Events Reported in > 5% of Patients: Number (%) of Patients Overall[1]

Most Common Ocular Adverse Events	DURYSTA™ (n = 372)	Timolol 0.5% BID (n = 370)
Conjunctival hyperemia	102 (27.4)	62 (16.8)
Foreign body sensation in eyes	38 (10.2)	13 (3.5)
Eye pain	36 (9.7)	17 (4.6)
Photophobia	32 (8.6)	4 (1.1)
Conjunctival hemorrhage	29 (7.8)	24 (6.5)
Dry eye	27 (7.3)	16 (4.3)
Eye irritation	26 (7.0)	28 (7.6)
Intraocular pressure increased	25 (6.7)	10 (2.7)
Corneal endothelial cell loss	20 (5.4)	1 (0.3)
Vision blurred	19 (5.1)	11 (3.0)
Iritis	19 (5.1)	1 (0.3)
Most Common Nonocular Adverse Reaction	**DURYSTA™ (n = 372)**	**Timolol 0.5% BID (n = 370)**
Headache	19 (5.1)	12 (3.2)

1. Medeiros et al. *Ophthalmology*.

Mean IOP by Treatment Group and Treatment Difference in Mean IOP

Primary Endpoint



Bimatoprost Implant vs. Timolol (95% CI)

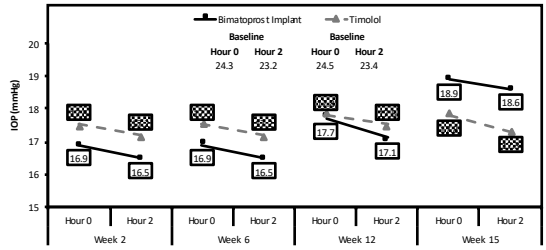
Hour 0	-0.8 (-1.47, -0.14)	-0.8 (-1.47, -0.21)	-0.3 (-1.09, 0.43)	1.1 (0.22, 1.89)
Hour 2	-0.9 (-1.50, -0.31)	-0.7 (-1.27, -0.04)	-0.2 (-0.90, 0.46)	0.9 (0.10, 1.64)

1. DURYSTA™ [package insert]. Irvine, CA: Allergan USA, Inc., March 2020.

ARTEMIS Study 1

Mean IOP by Treatment Group and Treatment Difference in Mean IOP

Primary Endpoint



Bimatoprost Implant vs. Timolol (95% CI)

Hour 0	-0.6 (-1.30, 0.13)	-0.6 (-1.35, 0.17)	-0.1 (-0.88, 0.72)	1.0 (0.15, 1.94)
Hour 2	-0.7 (-1.38, -0.05)	-0.6 (-1.36, 0.06)	-0.3 (-1.11, 0.42)	1.2 (0.35, 2.06)

1. DURYSTA™ [package insert]. Irvine, CA: Allergan USA, Inc., March 2020.

ARTEMIS Study 2

Contraindications

- **Contraindications:**
  - Active or suspected ocular or periocular infections
  - Corneal endothelial cell dystrophy (e.g. Fuch's Dystrophy)
  - Prior corneal transplantation or endothelial cell transplants (e.g., Descemet's Stripping Automated Endothelial Keratoplasy [DSAEK])
  - Absent or ruptured posterior lens capsule, due to the risk of implant migration into the posterior segment
  - Hypersensitivity to bimatoprost or any other components of the product

1. DURYSTA™ [package insert]. Irvine, CA: Allergan USA, Inc., March 2020.

Warnings and Precautions

- **Warnings and Precautions:**
  - **Corneal adverse reactions:** The presence of bimatoprost implants has been associated with corneal adverse reactions and increased risk of corneal endothelial cell loss. Administration of bimatoprost implant should be limited to a single implant per eye without retreatment. Caution should be used when prescribing bimatoprost implant in patients with limited corneal endothelial cell reserve.
  - **Iridocorneal angle:** Bimatoprost implant should be used with caution in patients with narrow iridocorneal angles (Shaffer grade < 3) or anatomical obstruction (e.g. scarring) that may prohibit settling in the inferior angle.
  - **Macular edema:** Macular edema, including cystoid macular edema, has been reported during treatment with ophthalmic bimatoprost, including bimatoprost implant. Bimatoprost implant should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

1. DURYSTA™ [package insert]. Irvine, CA: Allergan USA, Inc., March 2020.

- **Warnings and Precautions (Continued):**
  - **Intraocular inflammation:** Prostaglandin analogs, including bimatoprost implant, have been reported to cause intraocular inflammation. Bimatoprost implant should be used with caution in patients with active intraocular inflammation (e.g., uveitis) because the inflammation may be exacerbated.
  - **Pigmentation:** Ophthalmic bimatoprost, including bimatoprost implant, has been reported to cause changes to pigmented tissues, such as increased pigmentation of the iris. Pigmentation of the iris is likely to be permanent. Patients who receive treatment should be informed of the possibility of increased pigmentation. While treatment with bimatoprost implant can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.
  - **Endophthalmitis:** Intraocular surgical procedures and injections have been associated with endophthalmitis. Proper aseptic technique must always be used with administering bimatoprost implant, and patients should be monitored following the administration.

1. DURYSTA™ [package insert]. Irvine, CA: Allergan USA, Inc., March 2020.

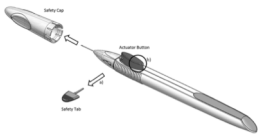
Adverse Reactions

- In controlled studies, the most common ocular adverse reaction reported by 27% of patients was conjunctival hyperemia.
- Other common adverse reactions reported in 5-10% of patients were foreign body sensation, eye pain, photophobia, conjunctival hemorrhage, dry eye, eye irritation, intraocular pressure increased, corneal endothelial cell loss, vision blurred, iritis, and headache.

1. DURYSTA™ [package insert]. Irvine, CA: Allergan USA, Inc., March 2020.

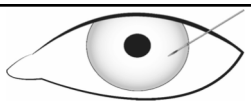
Administration

- Perform a detailed visual inspection of the applicator, including noting that the actuator button is not depressed, and the safety tab is in place.
- Carefully remove the plastic safety cap taking care to avoid contacting the needle tip.
- Inspect the needle tip for damage under magnification prior to use; the implant retention plug may be visible in the bevel and should not be removed.



Prior to use, remove the safety tab by pulling it out perpendicular to the long axis of the applicator.
Do not twist or bend the tab.

1. DURYSTA™ [package insert]. Irvine, CA: Allergan USA, Inc., March 2020.



- Stabilize the eye as the needle is advanced through the cornea
- Enter the anterior chamber with the needle bevel visible through clear cornea. Enter parallel to the iris plane, adjacent to the limbus through the clear cornea in the superotemporal quadrant
- The needle should be inserted approximately two bevel lengths with the bevel completely within the anterior chamber; avoid positioning the needle bevel directly over the pupil. Ensure the needle is not bent before depressing the actuator button
- Depress the back half of the actuator button firmly until an audible and/or palpable click is noted

1. DURYSTA™ [package insert]. Irvine, CA: Allergan USA, Inc., March 2020.

Administration (Continued)

- Following the release of the implant, remove the needle via the same track in which it was inserted and tamponade the opening. The implant should not be left in the corneal injection track.
- Check for injection site leaks; make sure that it is self sealing and the anterior chamber is formed.
- After injection, **do not** recap the needle. Dispose of the used applicator in a sharps disposal container in accordance with local requirements.
- Instruct the patient to remain upright for at least one hour after the procedure so the implant can settle.
- Some degree of eye redness and discomfort is expected following administration. However, it is recommended to instruct patients that if the eye becomes progressively red, sensitive to light, painful, or develops a change in vision, they should immediately contact the physician.

1. DURYSTA™ [package insert]. Irvine, CA: Allergan USA, Inc., March 2020.

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Enter the anterior chamber with the needle bevel visible through clear cornea. Enter parallel to the iris plane, adjacent to the limbus through clear cornea in the superotemporal quadrant.

Insert the needle approximately 2 bevel lengths, ensuring the bevel is completely within the anterior chamber; avoid positioning the needle bevel directly over the pupil.

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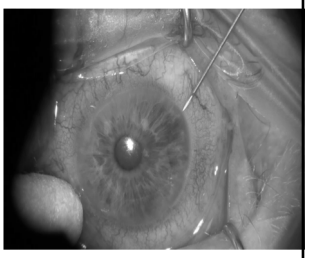
Release the implant by depressing the back half of the actuator button firmly until an audible and/or palpable click is noted.



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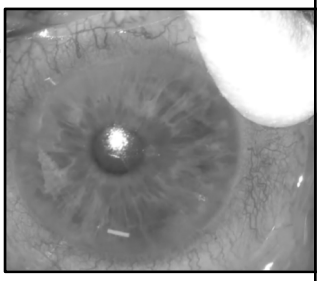
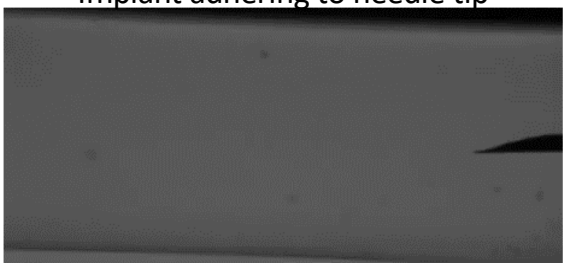


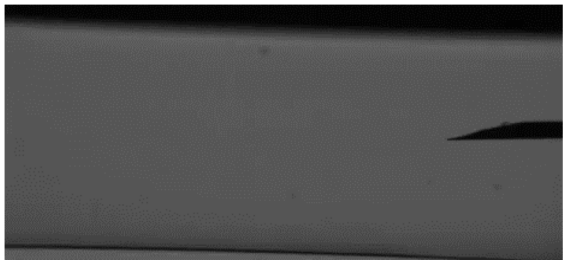
Troubleshooting Injection Issues:

Implant adhering to needle tip



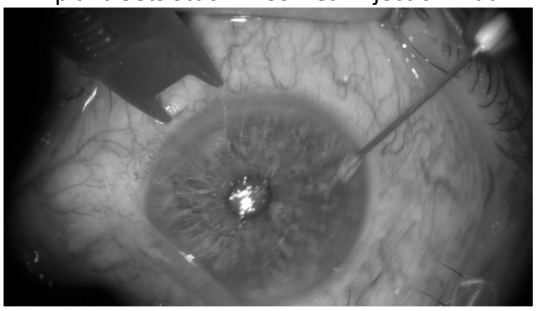
Troubleshooting Injection Issues:

Implant Floating in Anterior Chamber



Troubleshooting Injection Issues:

Implant Gets Stuck in Corneal Injection Track



SLT

Introduction

- In most developed countries (including USA) the standard first-line treatment for OAG and OHT is IOP lowering eye drops
  - Requires multiple office visits for monitoring and treatment adjustments or additions
  - Long term use of single or multiple topical medications with many ocular and systemic side effects
    - Can be a large factor in compliance, adherence and future surgical effectiveness[1,2]

1. Kirwan JF et al. Beta blockers for glaucoma and excess risk of airways obstruction: population based cohort study. BMJ. 2002;325:1396-1397.
2. Broadway DC et al. Adverse effects of topical antiglaucoma mediaction: II. The outcome of filtration surgery. Arch Opthalmol. 1994:112;1446-1454.

Introduction

- SLT reduces IOP by increasing trabecular outflow with a single, painless outpatient procedure with good safety profile and limited recovery time
- Approved by the FDA in 2001
- IOP lowering effect comparable to medication without medication associated side effects
- While not permanent, it is repeatable
- Still not routinely offered as first line treatment

Introduction

- Glaucoma has an adverse effect on Health Related Quality of Life due to[3,4]
  - Progressive loss of field of vision
  - Inconvenience of eye drops
  - Side effects of eye drops
  - Cost of mediations

3. Medeiros FA et al. Longitudinal changes in quality of life and rates of progressive visual field loss in glaucoma patients. Ophthalmology. 2015;122:293-301
4. Nordmann JP et al. Vision related quality of life and topical glaucoma treatment side effects. Health Qual Life Outcomes. 2003;1:75.

-Why?

The Kentucky Institute of Medicine projected that eyecare needs in the Commonwealth will increase by 80 % by 2020

Laser Trabeculoplasty

Argon Laser Trabeculoplasty
- Hot Laser: 600 mW for 0.1 sec forming blanching of tissue at site of photocoagulation
- Creates scarred, nonfunctional tissue

Selective Laser Trabeculoplasty
- Cold Laser: frequency-doubled Q-switched Nd:YAG laser emitting at 532 nm.
- Permits selective targeting of pigmented trabecular meshwork (TM) cells without causing structural or coagulative damage to the TM

LT Indications

- Uncontrolled open angle glaucomas
  - Failed medical treatment
  - Non-compliant patients
    - Keeping appointments
  - Primary Therapy?
- Pseudophakia
- Financial Considerations

- Timing is controversial
  - AGIS study: Caucasian vs African American
  - …long term visual function outcomes are better for the ATT sequence in black patients and better for the TAT sequence in white patients…

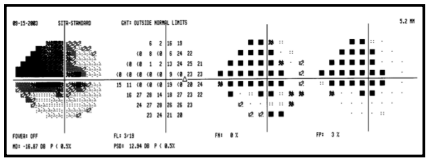
8/19/21 The Advanced Glaucoma Intervention Study (AGIS): 13. Comparison of treatment outcomes within race: 10- year results. Ophthalmology. 01/04/04; 111(4): 651-64. 35

LT Contraindications

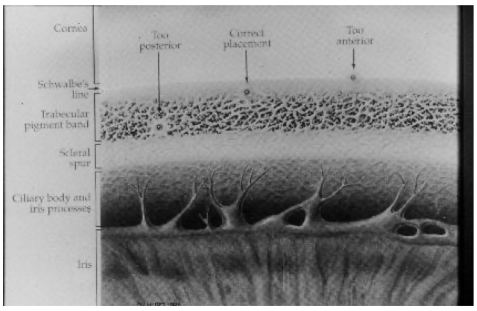
- Angle Closure/ Narrow Angle
- Uveitic Glaucoma or Ocular Inflammation
- Congenital Glaucoma
- Neovascular glaucoma
- Angle Recession (relative)
- Glaucoma Suspect (relative)
- Emergency IOP reduction needed
- Prior complications
- Greater than 30 IOPs (relative) – 6-10mm drop expected (AGIS)
- Under 40 yrs old, except pigmentary glaucoma. (AGIS)

8/19/21 The Advanced Glaucoma Intervention Study (AGIS): 11. Risk Factors for failure of trabeculectomy and laser trabeculoplasty. Am J Ophthalmol. 10/01/02; 134(4): 481-98. 36

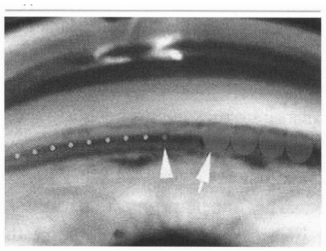
- **Fixation threatening VF loss warrants extra caution due to increased risk of central VF loss if post-op IOP spike**



ALT



Gonioscopy view of ALT/SLT



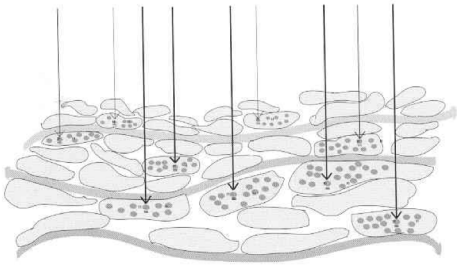
ALT (small dots) → photocoagulation; SLT (large dots) → biochemical response w/o thermal damage

Karmel, 2002

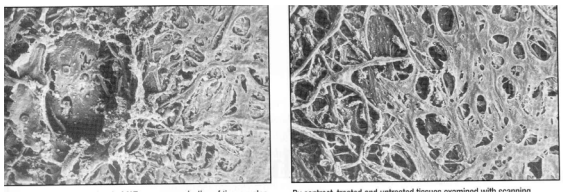
Selective Laser Trabeculoplasty (SLT)

- 400 um spot size
- 3.0 nsec duration compared to 0.1 msec ALT
- Necrosis-induced phagocytosis of debris at the spot of the burn
- No visible tissue response on TM during procedure
- Destroys melanosomes of pigmented TM cells
- Sparing adjacent non-pigmented cells and tissues

SLT: Selectively targets pigmented TM cells



ALT vs. SLT

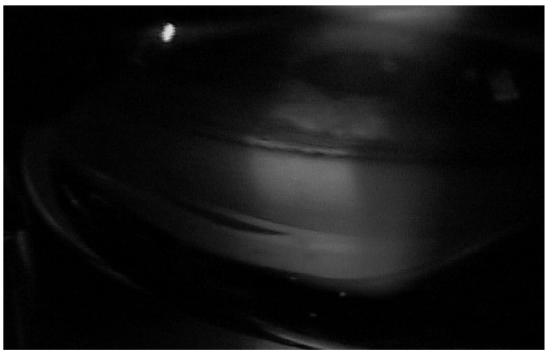


High energy level -> vaporizes tissue water → forms TM crater

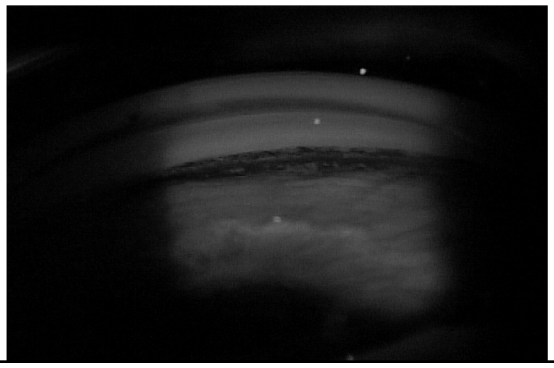
SLT: Treated/Untreated TM looks similar

Alvarado, 2002

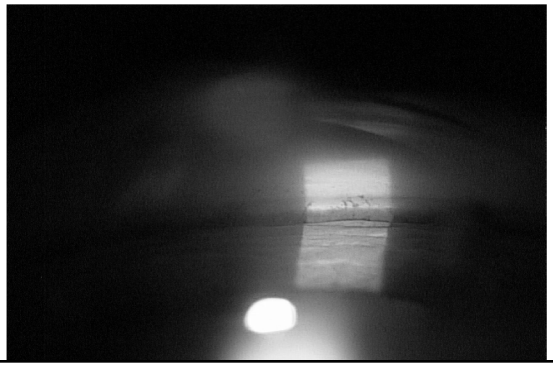
Superior Angle

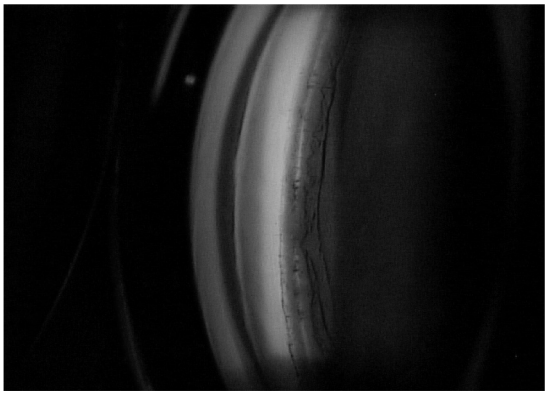


Inferior Angle

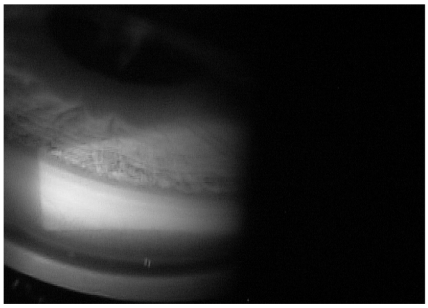


Ciliary Processes





Lightly Colored TM
Full CB



SLT General Considerations

- -Energy levels. Champagne bubbles . 8 1.0 mj.
- -Target selections. 400 micron. Spot size. Paint entire mesh work
- -Placement of lens. Quicker with assistance less bubbles
- -Treatment regimen: 180 degrees per session.

Pre-Op

- Basic exam components
  - VA, IOP, etc.
- Gonioscopy
  - Assess angle structure
  - Assess pigmentation
- 1 gt Iopidine or Alphagan
- Pilo 1% if need to pull iris out of angle to better visualize TM for treatment

SLT Procedure

- Will use lens to treat angle
  - Ritch Lens
  - Latina Lens
- Don't want to use a lens with a magnification button or can alter the beam diameter and energy

Latina SLT Gonio Lens

Multi Mirror

Procedure Technique

- Insert gonio lens (cushioning solution)
- Visualize angle
- Establish a system when performing these procedures and always do it the same (i.e. start at 6 and rotate clockwise)
- Before rotation lens identify a landmark

Procedure Technique

- Recommended initial power setting
  0.8 – 1.0 mj (won't need to go more than1.1 or 1.2 – go up in very small increments if needed)
- Desired tissue response will be subtle to see – a slight change in the surface of the TM is adequate treatment
- A small amount of bubble every few pulses appropriate

Procedure Technique

- Place approximately 100 treatment spots per 360°
- About a spot size between each treatment pulse
- Most people are currently treating 360° of one eye for first procedure
- 180° considered to be "partial" tx
- 180° + 180° = "complete"tx
- 360° + 180° = "re-treatment"

Procedure Technique

- If patient had PDS – you may want to only treat 180° of one eye initially
- Have seen cases of IOP increase in PDS patients due to excess pigment = extra inflammatory response
- Some are treating only 180° then wait for to see what response is obtained
- Rule of thumb is more pigment use less energy still applies with SLT

Post-Op

- Check IOP 30 – 45 minutes after procedure
- If any increase second drop of Iopidine or Alphagan
- Acular/Voltaren qid x four – seven days
- RTC one week – some are not having patient return at one week

Continued SLT Considerations

- Final treatment discussion:
- What to expect:
- Long term effectiveness:
- Multiple use discussion on exit:
- First line treatment?
- Medication compliance?
- Medication cost?
- Pigmentation decrease energy
- Use of gonioscopy increases SLT skill

Early Clinical Trials SLT

- Latina et al., 1998 Ophthalmol
- 70% response rate
- Avg decrease in IOP= 23.5% or5.8 mmHg
- Works well in previous ALT patients without causing IOP spikes

Procedure Billing

- 65855 – SLT/ALT code
- 10 day global period
- National average for reimbursement is approximately $316 per eye
- Kentucky allowable is $288.09

Background of SLT vs. Drops

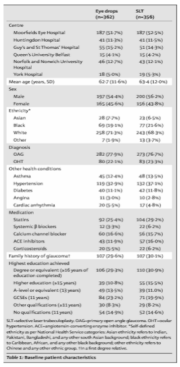
- A Cochrane systematic review in 2007 pointed to the need for research comparing SLT to medications via cost and efficacy
- 2 Meta-analyses were published in 2015 showing 360 degree SLT gives a similar IOP reduction to either PGA mono or combo therapy
- The time threshold at which SLT becomes cost effective against drops is estimated to be 1-3 years depending on cost of medications
- SLT is predicted to by cost effective when REPEATED once within 3 years compared to drops

Selective Laser Trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma

- United Kingdom study set in 6 hospitals
  - Recruited patients from 2012-2014
  - Observer masked
  - Randomized
  - Treatment naïve patients/newly diagnosed OAG
    - No previous IOP lowering drops, laser or surgery

LIGHT Study Design

- 718 patients entered the study (1235 eyes)
- Patients randomized on a 1:1 basis to either:
  - SLT (356 patients, 613 eyes)
  - Drops (362 patients, 622 eyes)



	Eye drops (n=362)	SLT (n=356)
Centre		
Moorfields Eye Hospital	187 (51·7%)	187 (52·5%)
Huntingdon Hospital	45 (13·3%)	45 (15·5%)
Guy's and St Thomas' Hospital	51 (15·2%)	13 (14·3%)
Queen's University Belfast	15 (4·1%)	15 (4·7%)
Norfolk and Norwich University Hospital	46 (12·7%)	43 (12·1%)
York Hospital	18 (5·0%)	19 (5·3%)
Mean age (years, SD)	62·7 (11·6%)	63·4 (12·0%)
Sex		
Male	197 (54·4%)	200 (56·2%)
Female	165 (45·6%)	156 (43·8%)
Ethnicity*		
Asian	28 (7·7%)	23 (6·5%)
Black	69 (19·1%)	77 (21·6%)
White	258 (71·3%)	243 (68·3%)
Other	7 (1·9%)	13 (3·7%)
Diagnosis		
OAG	282 (77·9%)	273 (76·7%)
OHT	80 (22·1%)	83 (23·3%)
Other health conditions		
Asthma	41 (11·4%)	48 (13·5%)
Hypertension	103 (28·5%)	111 (31·2%)
Diabetes	40 (11·1%)	43 (11·8%)
Angina	11 (3·0%)	10 (2·8%)
Cardiac arrhythmia	20 (5·5%)	17 (4·8%)
Medication		
Statins	92 (25·4%)	104 (29·2%)
Systemic β blockers	12 (3·3%)	10 (2·8%)
Calcium channel blocker	60 (16·6%)	58 (16·7%)
ACE inhibitors	43 (11·9%)	57 (16·0%)
Corticosteroids	20 (5·5%)	22 (6·2%)
Family history of glaucoma†	107 (29·6%)	107 (30·1%)
Highest education achieved		
Degree or equivalent (≥18 years of education completed)	106 (29·3%)	110 (30·9%)
Higher education (≥21 years)	39 (10·8%)	55 (15·5%)
A-level or equivalent (13 years)	69 (19·1%)	39 (11·0%)
GCSEs (15 years)	84 (23·2%)	75 (19·9%)
Other qualifications (≥15 years)	30 (8·3%)	29 (8·2%)
No qualifications (15 years)	14 (3·9%)	12 (3·4%)

SLT=selective laser trabeculoplasty. OAG=primary open angle glaucoma. OHT=ocular hypertension. ACE=angiotensin-converting-enzyme inhibitor. *Self-defined ethnicity as per National Health Service categories. Asian ethnicity refers to Indian, Pakistani, Bangladeshi, and any other Asian background. Black ethnicity refers to Caribbean, African, and any other black background. other ethnicity refers to Chinese and any other ethnic group. †≥ a first degree relative.

Table 1: Baseline patient characteristics

	Number of eyes with data (patients)	Eye drops (n=622 eyes; 362 patients)	SLT (n=613 eyes; 356 patients)
Diagnosis	1235 (718)	..	..
Ocular hypertension	..	185 (29·7%)	195 (31·8%)
Mild OAG	..	325 (52·3%)	311 (50·7%)
Moderate OAG	..	77 (12·4%)	67 (10·9%)
Severe OAG	..	35 (5·6%)	40 (6·5%)
Refractive error (spherical D)	1225 (713)	-0·2 (2·7)	-0·3 (3·2)
Visual acuity	1235 (718)	0·1 (0·1)	0·1 (0·2)
Visual field mean deviation (dB)	1233 (717)	-3·0 (3·6)	-3·0 (3·4)
HRT rim area (mm²)	1128 (656)	1·1 (0·4)	1·2 (0·4)
Intraocular pressure (mm Hg)	1233 (717)	24·4 (5·0)	24·5 (5·2)
CCT (μm)	1229 (715)	551·6 (36·2)	550·7 (38·1)
Pseudo-exfoliation	1233 (717)	12 (1·9%)	5 (0·8%)
Pseudophakia	1233 (717)	33 (5·3%)	39 (6·4%)

Data are n (%) or mean (SD). SLT=selective laser trabeculoplasty. OAG=primary open angle glaucoma. HRT=Heidelberg retina tomograph. CCT=central corneal thickness.

Table 2: Baseline ocular characteristics

Entrance Criteria

- For OAG
  - MD not worse than -12dB in the better eye
  - MD not worse than -15dB in the worse eye
- Visual acuity of 6/36 or better in treated eyes
- NO previous intraocular surgery
  - Except uncomplicated phacoemulsification at least 1 year prior to randomization into the trial
- Other exclusions:
  - Contraindication to SLT
  - Unable to use eye drops
  - Symptomatic cataract
  - Active treatment for some other type of ocular condition

OAG Disease Definition for LIGHT Study

- Used NICE thresholds for disease definitions and treatment initiation[5]
- Used real time web-based clinical decision support software
  - ONH analysis by HRT
  - HFA VF 24-2 + GPA
  - IOP measurements
- Disease category and stage were defined at baseline using preset objective severity criteria from the Canadian Target IOP Workshop[6]

5. National Institute of Health and Clinical Excellence. DoH; 2010. NICE: Guidance on Glaucoma: Diagnosis and management of chronic open angle glaucoma and ocular hypertension.
6. Damji KF et al. Target IOP Workshop participants; Canadian perspectives in glaucoma management: Setting target intraocular pressure range. Can J Ophthalmol. 2003; 38:189-197

Target IOP's in the LIGHT Study

- Based on Canadian Target IOP workshop
  - Disease stratification Mild, Moderate, or Severe
- Target IOP determined by both a % from a single untreated baseline measurement and an absolute threshold
  - Either 20 or 30% based on patient's clinical characteristics

Progression or Deterioration of Glaucoma During LIGHT Study

- Looking for progression of glaucoma OR conversion of OHT to OAG during the study
  - Impact on treatment escalations
- Decisions derived from the decision support software
  - Primarily based on HVF and HRT data
  - Verified by a consultant ophthalmologist for progression
  - Decide if it is "likely progression" or "possible progression"

Treatment Escalations in the LIGHT Study

- Based on guidelines from multiple international glaucoma and eyecare societies including AAO
- Treatment escalated IF:
  - There is strong evidence of progression irrespective of IOP level
  - IOP above target by more than 4 mmHg at a single visit
  - IOP above target by less than 4 mmHg and less strong evidence of progression…(possible progression)
- Additional 20% IOP reduction was then the goal if treatment escalated

SLT Laser Standardization

- Protocol defined settings and endpoints
  - 360 degree treatment
  - 100 non-overlapping spots
    - Approximately 25 per quadrant
  - Power could range from 0.3-1.4 mJ
- One re-treatment with SLT was allowed if IOP reduction was obtained with the first SLT
  - If there was and AE (IOP spike) then repeat was precluded
- After that the next escalation was medical therapy (drops)

Topical Medication Algorithm

- Drug classes for 1st, 2nd, and 3d line treatment were determined by the NICE guidelines[5]
- First line-PGA's
- Second line- Beta Blockers
- Third line- TCAI or Alpha Agonist
- Fixed combinations were allowed
- MMT=Clinician judged max most intensive combination of medicines that could be tolerated

5. National Institute of Health and Clinical Excellence. DoH; 2010. NICE: Guidance on Glaucoma: Diagnosis and management of chronic open angle glaucoma and ocular hypertension.

Outcome Measures

- Primary outcome
  - Health-related quality of life (HRQoL) at 3 years
    - Assessed by the EQ-5D
    - Recently this measure has come under scrutiny as to its ability to find differences in HRQoL in a short time frame like this study (3 years)
    - Glaucoma is largely asymptomatic even at levels sufficient to make driving unsafe
    - In this study, baseline HRQoL were above average
    - Unlikely that EQ-5D is sufficient tool to see meaningful data

Secondary Outcomes

- Cost and Cost effectiveness
- Glaucoma disease specific HRQoL
- Clinical effectiveness of SLT vs. Drops
- Safety of SLT vs. Drops

Results

- Overall 509 (95%) of 536 SLT treated eyes were at target IOP @ 3 years
- Target IOP achieved without medication in 419 (78.2%) of 536 eyes treated in SLT arm
  - 321 eyes (76.6%) required only one SLT session

Results

- 499 (93.1%) of the 526 eyes treated medically were at target IOP @ 3 years
  - 346 (64.6%) were using a single medication
- At 3 years:
  - 93.0% of visits were at target IOP for SLT group
  - 91.3% of visits were at target IOP for med group

Treatment Escalations and Progression of Disease During Study

- More treatment escalations occurred in the SLT group (348 eyes) than the Medication group (299 eyes)
- Progression
  - 36 eyes in the Medication group showed algorithm-confirmed progression
    - 3 eyes converted from OHT to OAG
    - 33 eyes with OAG progressed
  - 23 eyes in the SLT group
    - 2 eyes converted from OHT to OAG
    - 21 eyes with OAG progressed
- 11 eyes (1.8%) in the Medication group required incisional glaucoma surgery
  - NO EYES IN SLT GROUP REQUIRED INCISIONAL SURGERY

Adverse Events

- SLT Group
  - 6 eyes had an IOP rise of 5mm Hg or more on day of treatment
    - Only 1 eye required treatment
  - 122 eyes (34.4%) had transient discomfort, blurred vision or photophobia not requiring treatment
- Medication Group
  - 150 eyes had aesthetic side effects or allergic reactions

Cost of Therapy

- Eye drops were approximately double the cost effect of SLT
- Difficult to extrapolate to US market but general financial math should apply
- Eventual ophthalmic surgery (trab, tube, cataract etc) over the 3 years was significantly less in the SLT group compared to the Medication group

Primary Outcome Measure

- Primary outcome
  - Health-related quality of life (HRQoL) at 3 years
    - Assessed by the EQ-5D
- Small trend towards better HRQoL for SLT group vs. Medication group but not statistically significant
  - Recently this measure has come under scrutiny as to its ability to find differences in HRQoL in a short time frame like this study (3 years)
  - Glaucoma is largely asymptomatic even at levels sufficient to make driving unsafe
  - In this study, baseline HRQoL were above average
  - Unlikely that EQ-5D is sufficient tool to see meaningful data

Secondary Outcome Measures

- Cost and Cost effectiveness
- Clinical effectiveness of SLT vs. Drops
- Safety of SLT vs. Drops

Cost and Cost Effectiveness

- SLT as first line resulted in a significant cost savings relative to surgery and medication
  - Approximately 451 dollars/pounds savings in provider related visit costs per patient
  - For every patient given SLT in lieu of drops, the cost savings are greater than the cost of SLT for **2 additional patients!**
  - This is also equal to the cost of five additional office visits

Clinical effectiveness of SLT vs. Drops

- Rate of Disease Progression
  - In the Medication group 36 patients (5.8%) had disease progression
  - In the SLT group 23 patients (3.8%) had disease progression
    - 74% remained drop free at 3 years

Clinical effectiveness of SLT vs. Drops

- IOP Control
  - SLT first approach provided better IOP control over 3 years with more visits at target IOP compared to drops
    - Less intense drop treatment than Medication group
    - NO glaucoma surgeries required compared to Medication group
  - Could be due to adherence with SLT vs. Drops

Clinical effectiveness of SLT vs. Drops

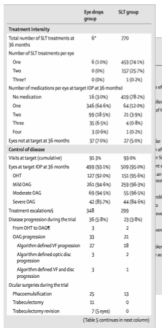
- IOP Control
  - SLT provides better diurnal IOP stability[6]
    - Could be due to continuous effect on TM versus episodic administration of medication
  - Primary SLT afforded drop free control of IOP for 3 years in 74.2% of patients
    - This is much higher than in previous studies with less stringent success criteria
    - Prior treatment and more severe disease likely reduce the effect of SLT in those patients[7]
    - Likely the reason for such a robust response in treatment naïve patients in this study

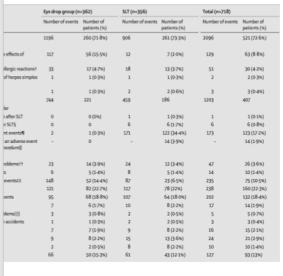
6. Greenidge KC et al. Effect of argon laser trabeculoplasty on the glaucomatous diurnal curve. Ophthalmology. 1983;90:800-804
7. Nagar M et al. A randomized, prospective study comparing selective laser trabeculoplasty with latanoprost for the control of intraocular pressure in ocular hypertension and open angle glaucoma. Br J Ophthalmol. 2005:89:1413-1417.

Safety of SLT vs. Drops

- This study showed a greater safety profile of SLT than previously reported
  - No systemic side effects reported
  - Only 1 eye had an IOP spike
    - Compared to previously reported rates of 28.8%[8]
    - 2-week IOP checks did not change management for any patient and appears to be unnecessary
      - Avoidance of this could save more $ to the system
  - Lower rate of cataract surgery in SLT arm which supports the existing evidence of drops increasing incidence of cataract and surgery[9]

8. Wong et al. Systematic review and meta-analysis on the efficacy of selective laser trabeculoplasty in open-angle glaucoma. Surv Opthalmol. 2015;60:36-50.
9. Heijl A et al. Reduction of intraocular pressure and glaucoma progression; results from the Early Manifest Glaucoma Trial. Arch Opthalmol. 2002;120:1268-1279





Conclusions

- Selective laser trabeculoplasty provides superior IOP stability to drops, at a lower cost AND
  - 74% or ¾ of patients are successfully controlled without drops for at least 3 years after a single treatment

Conclusions

- Selective laser trabeculoplasty as an initial treatment for glaucoma is associated with the following:
  - Lower cost
  - Good clinical outcomes
    - 2-week follow up not necessary
  - Lower symptom scores
  - Drop-freedom for most patients
- SLT should be offered as an alternative to IOP lowering drops as initial therapy on a more widespread basis