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Purpose:

Aqueous outflow system configuration (OSC) determines aqueous flow and IOP, parameters that become abnormal in glaucoma¹. We describe a pilot study with an *ex vivo* system using visually guided positioning & real time observation of OSC changes (Δ s) in response to transcleral μ P laser (Iridex™) pulses.

Background:

Physical tissue responses are highly relevant because outflow system tissue configuration determines aqueous flow and IOP, parameters that become abnormal in glaucoma; pilocarpine provides an example.

Materials and Methods:

Methods: *M. fasc.* primates A (PrA) & B (PrB). PrA: microscope, video recordings, calibration micrometer, 1 mm thick radial limbal segments from 4 quadrants (Q), micromanipulator, single pulse of 810 nm μ P laser, duty cycle 31.3%. Paired parameters of stepwise power; range: 500-3000 mW, stepwise duration; range: 125-3,000 msec. Energy range: 0.08-2.35 Joules. (Clinically, Energy (CE) of ~1.59 J (Fig. 1) is applied per single location.) Video capture during pulse. PrA: Motion quantitated from still frames with ImageJ. PrB: H&E & trichrome in 4 Q after Rx with clinically used total energy.

Results:

See Videos: www.youtube.com/user/ibmurray
Results: PrA - Visible μ P effects confined to longitudinal ciliary muscle (CM) near sclera (Fig. 2). Contraction & relaxation was visible at ≥ 0.08 J in the IN & SN Q and at ≥ 0.16 J in the IT and ST Q. The CM facing the AC transiently moved inward & posteriorly at ≥ 0.75 Joules in all Q. A Δ in Schlemm's canal shape occurred when the scleral spur (SS), and trabecular meshwork (TM) moved posteriorly Fig. 3 & 4. (Videos www.youtube.com/user/ibmurray). CM bundles relaxed/recovered to near pre μ P configuration at low energies with a progressive reduction in the recovery response as energy increased (Fig. 5). CM bundles turned white at 2.35 J (~ 48% > than CE) with a lack of recoil/relaxation resulting in persistent Δ s in CB, SS & TM configuration. Ciliary epithelial damage was absent at clinical setting by direct observation (PrA & (Fig 1) & histology (Pr A & B, Fig.6,7)

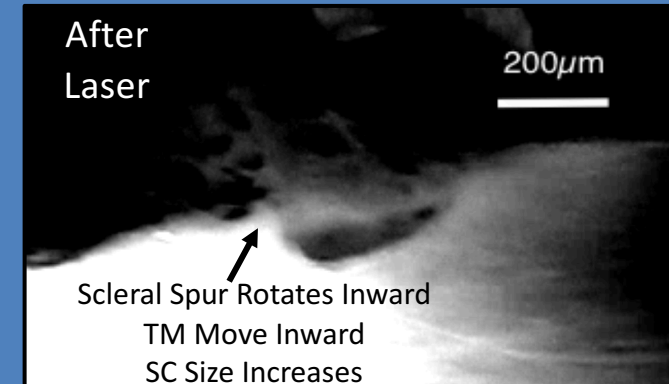
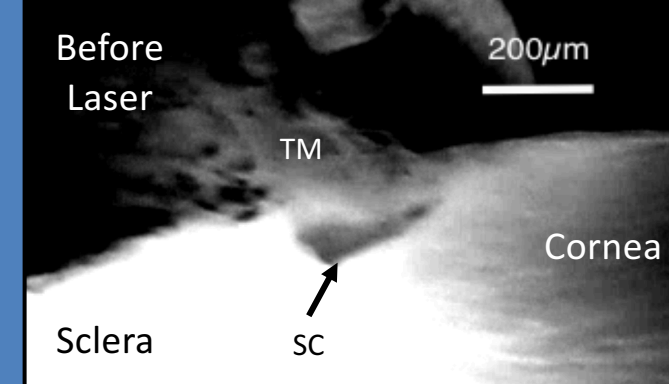
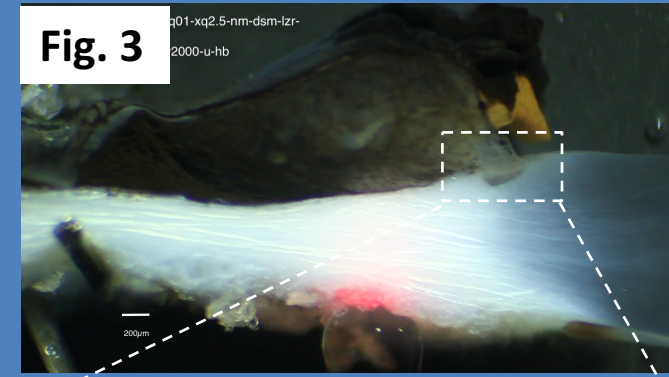
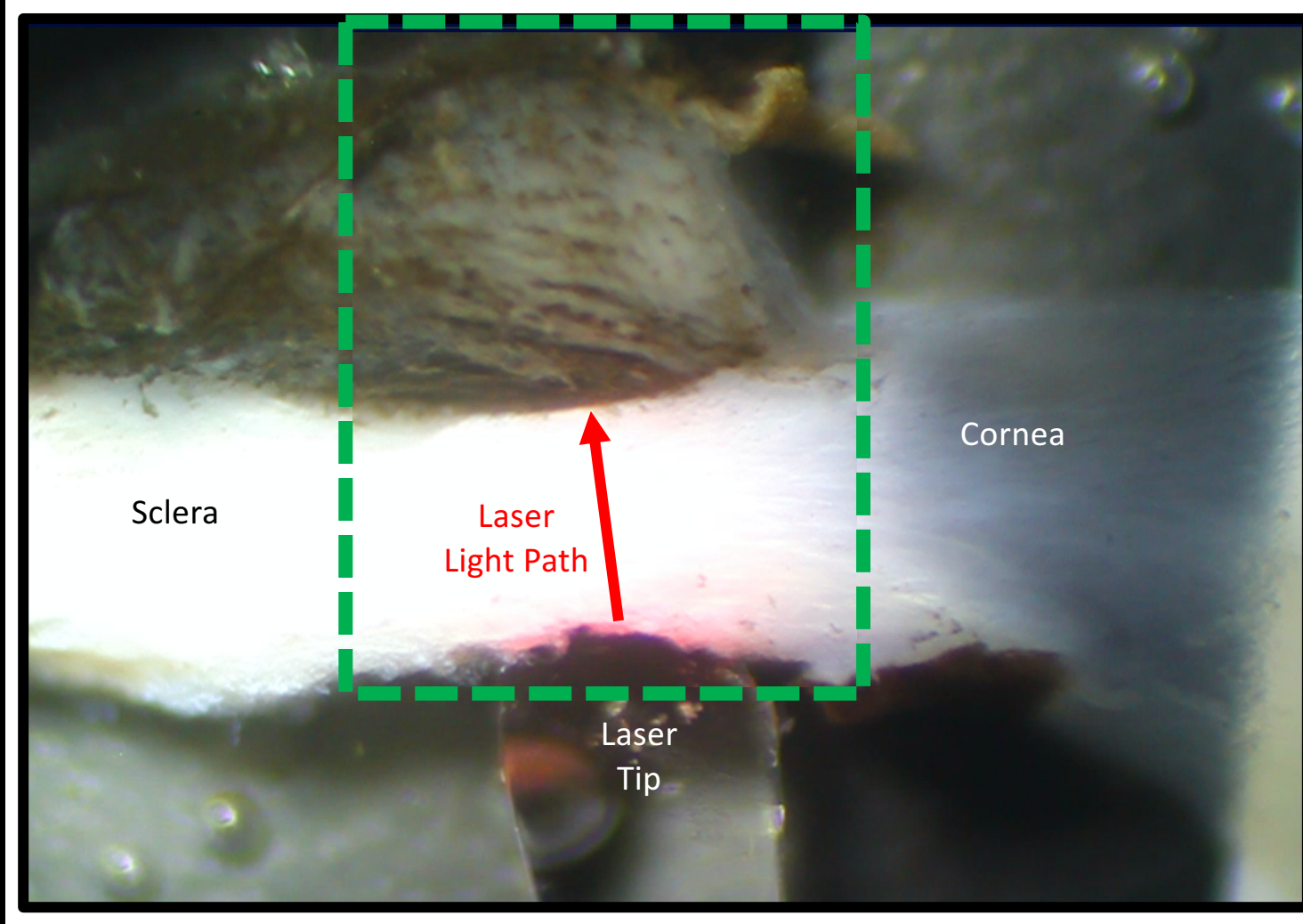
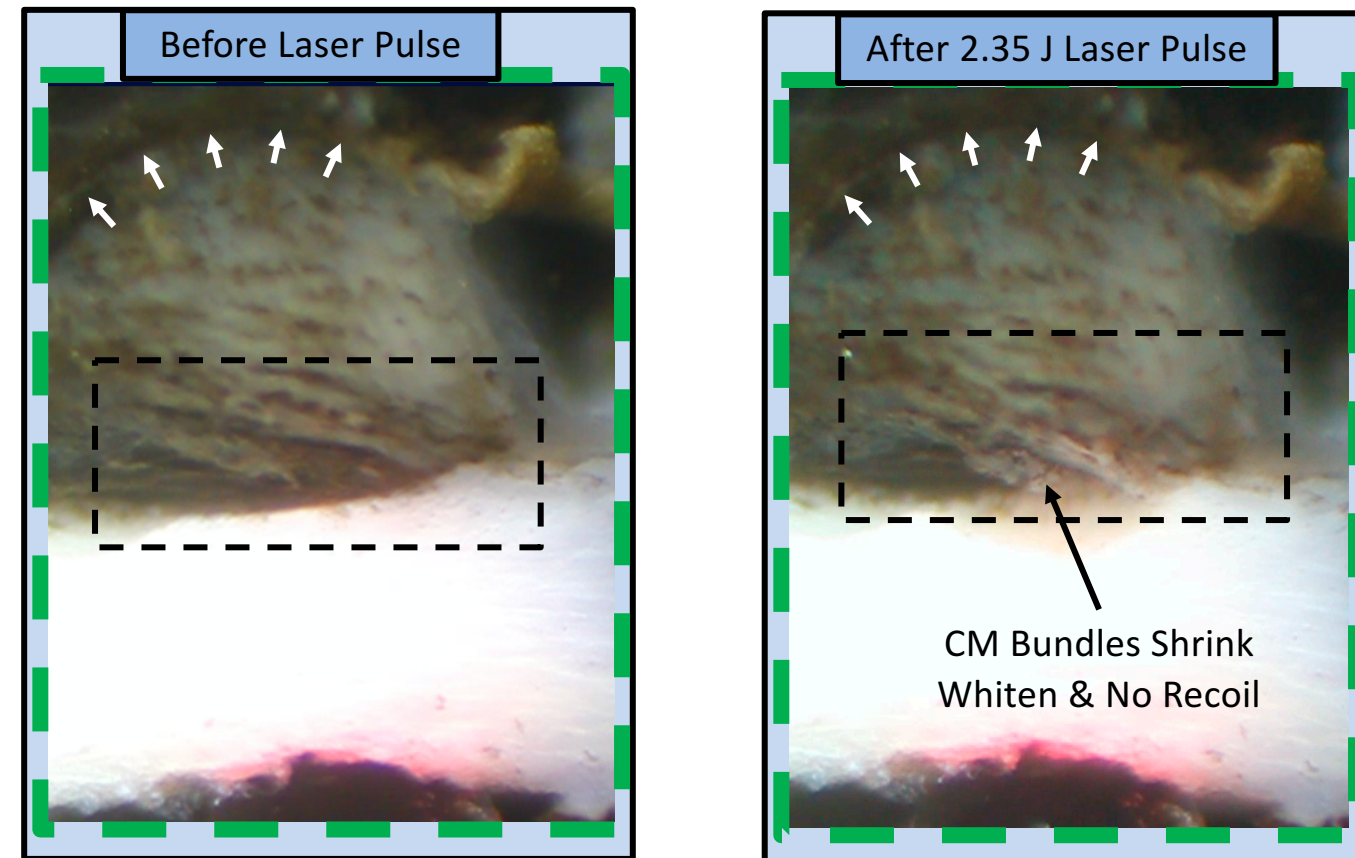
Video of Real Time Motion: Access by QR Code

Or: www.youtube.com/user/ibmurray



Micropulse Laser Effects on Ciliary Muscle & Scleral Spur

Fig. 2 No Evidence of Ciliary Epithelium Motion or Damage (White Arrows) ↑



Scleral Spur Rotates Inward
TM Move Inward
SC Size Increases

Fig. 4 Laser Energy vs. Tissue Responses

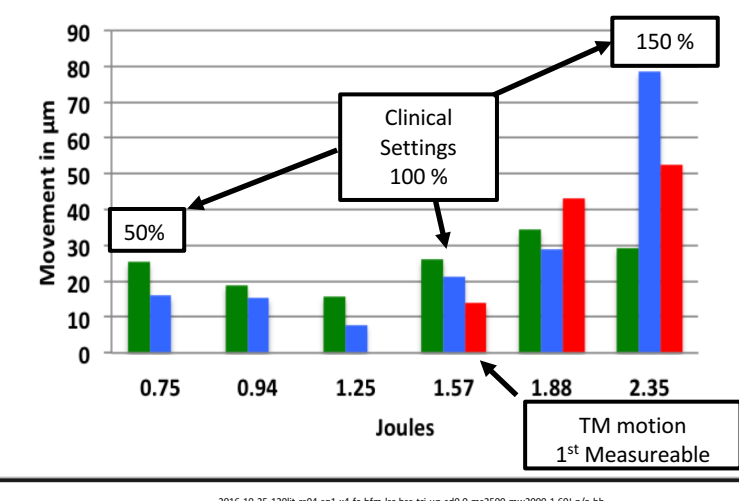


Fig. 5 Tissue Recovery after Responses

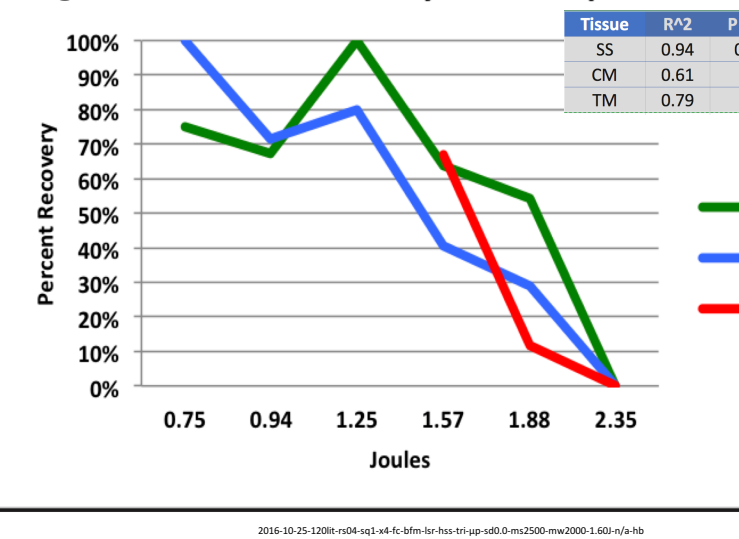
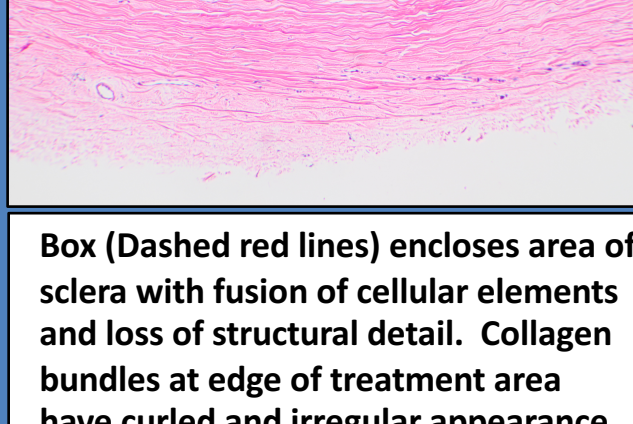
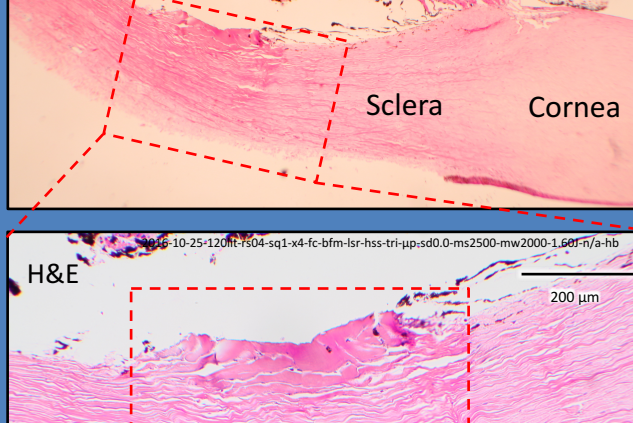
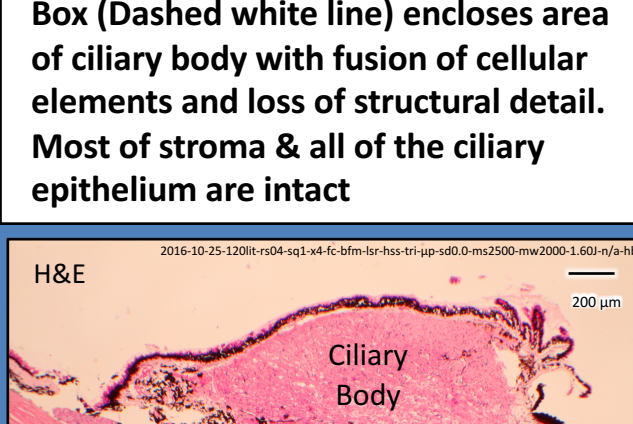
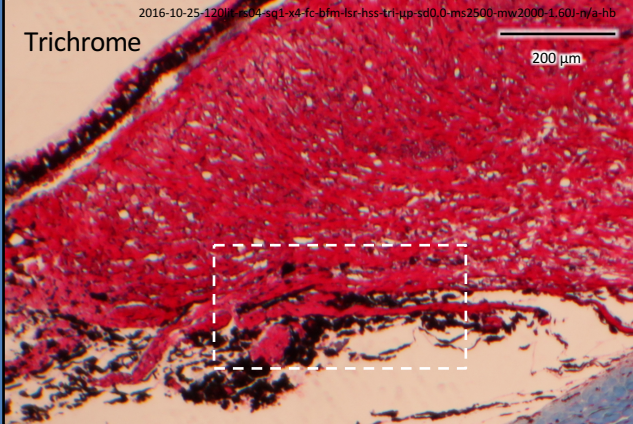
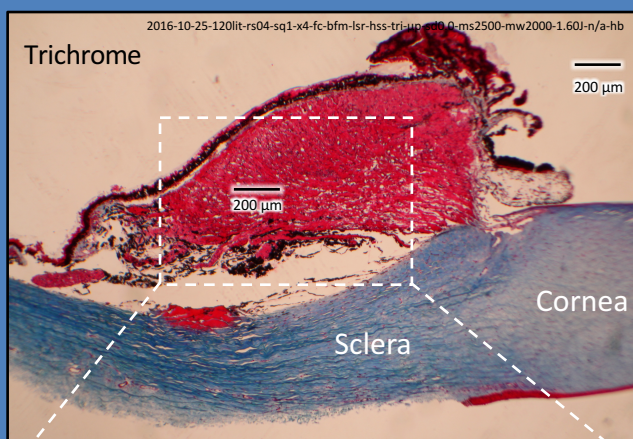


Fig. 6 Histology After Laser With Same Settings as in Fig. 1 = 2500 ms, 2000 mW 80 sec/5 clock hours



Box (Dashed white line) encloses area of ciliary body with fusion of cellular elements and loss of structural detail. Most of stroma & all of the ciliary epithelium are intact.

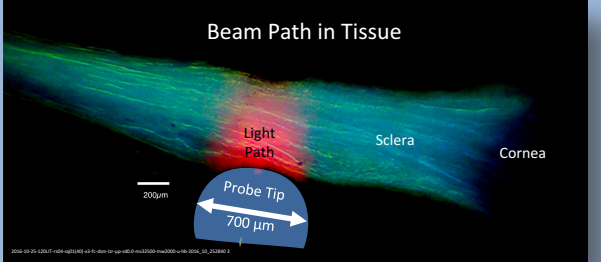
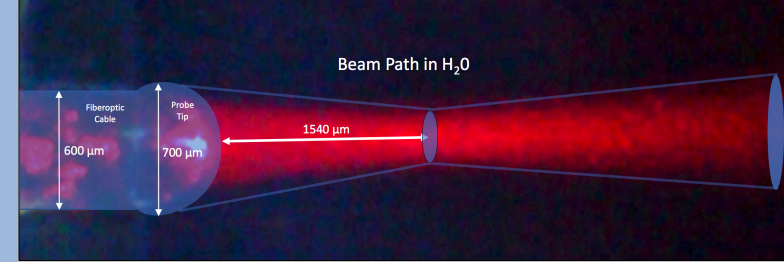
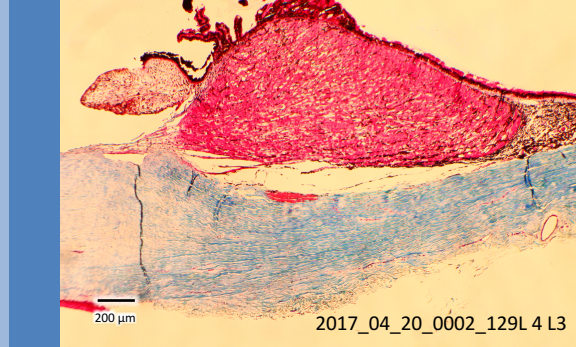
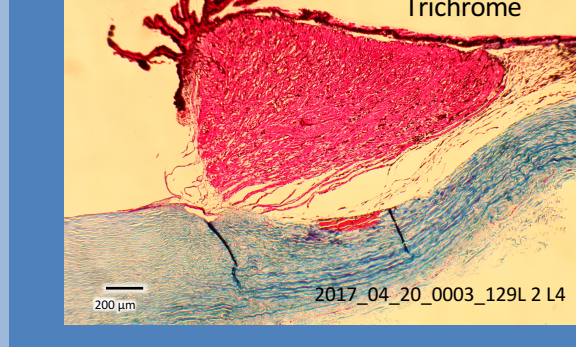
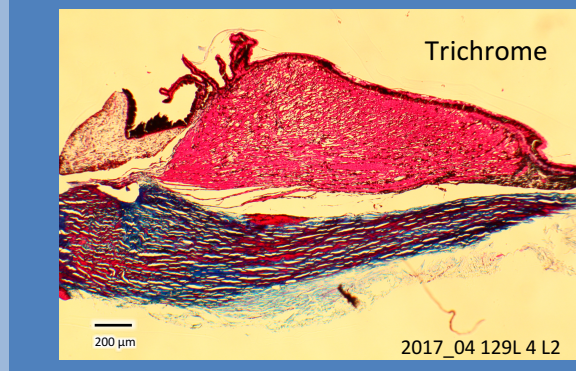


Fig. 7 Histology After Laser With Settings 50 % of Fig. 1 = 1250 ms, 2000 mw 40 sec/5 clock hours



Evidence of laser-induced tissue changes localized to inner sclera and outer ciliary body but most of stroma & all of ciliary epithelium intact.

Discussion:

Transcleral μ P laser induces contraction of the CM, a well-characterized muscle response to μ P lasers.^{1,2} CM shortening caused posterior and inward movement of the SS & TM to Δ aqueous outflow pathway shape. Clinically used μ P parameters are sufficient to induce OSC Δ s generally associated with improved aqueous flow.³⁻⁸ Our preparation permits systematic assessment of effects of probe location, power vs. duration relationships, total energy and focal depth. Studies to characterize optimized parameters may improve success rates and reduce morbidity.

Conclusions: Micropulse Laser Effects

- Ciliary Muscle Shortens
- Ciliary Muscle Face and Scleral Spur Move Inward and Posteriorly
- Trabecular Meshwork Moves Inward & Schlemm's Canal Enlarges
- Outflow System Effects Are Like Pilocarpine
- Inner Sclera & Ciliary Body (CB) Near Sclera Have Coagulative Changes
- Laser Changes Confined to Longitudinal Bundles of Ciliary Muscle
- No Direct Ciliary Epithelial Damage Apparent
- Our System Can Vary Laser Parameters to Determine Variables That Cause Pilocarpine-like Outflow System Relationship Changes

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References:

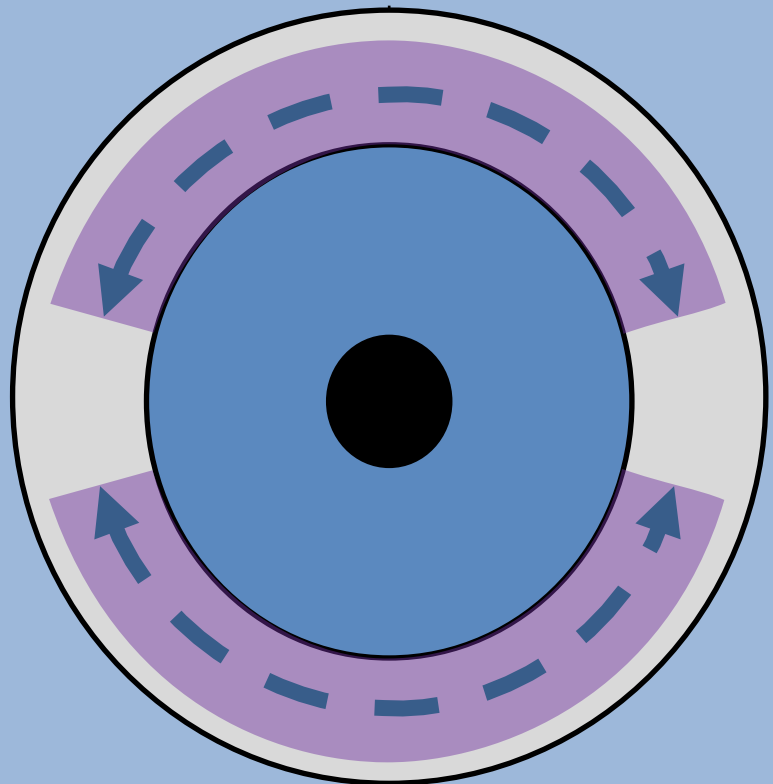
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Financial Disclosures
Healionics, Istar

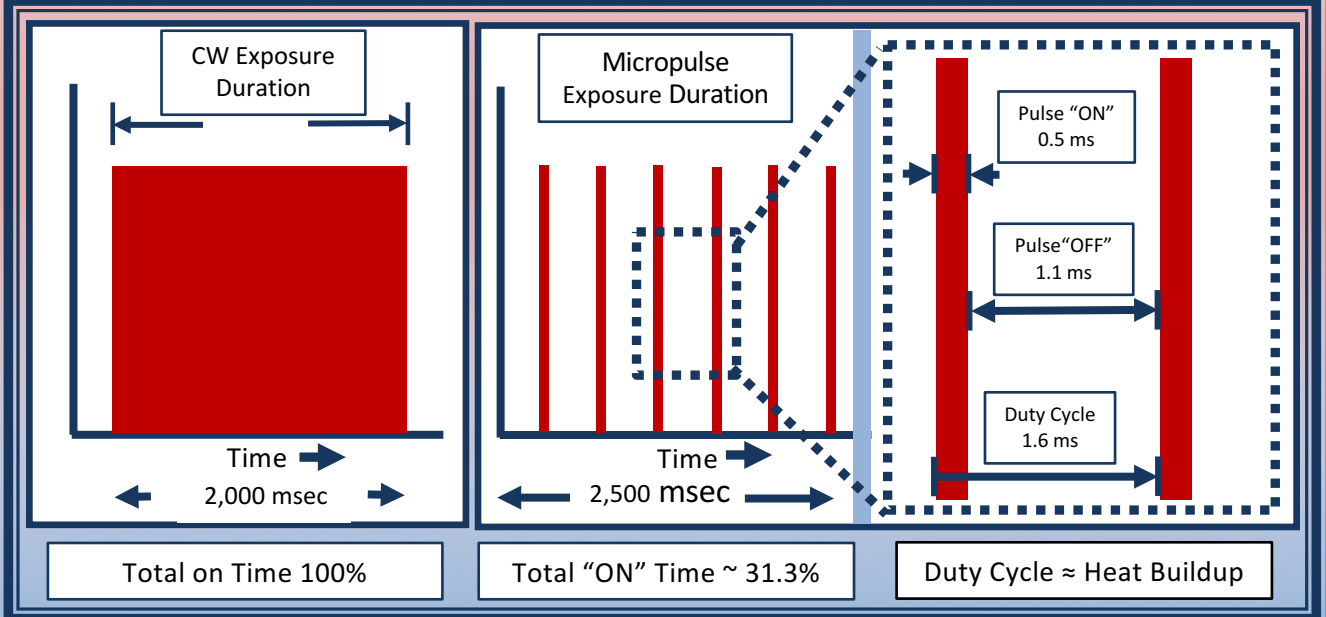
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Fig. 1 Single Probe Site Energy Calculation

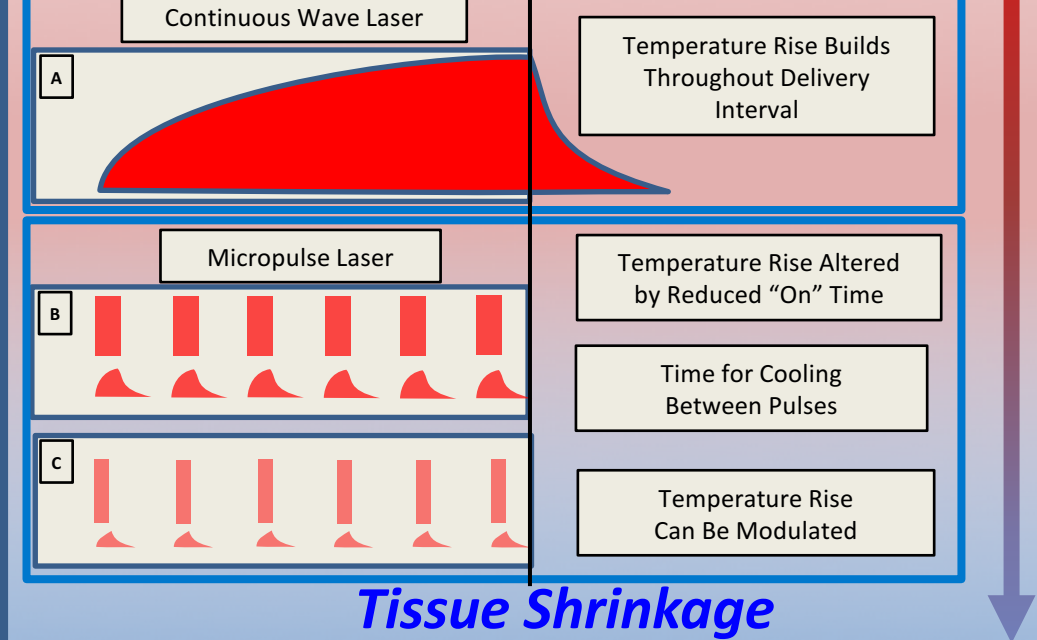
Parameter	Iridex Values	Comments
Circumference	52.9 mm	At Location Posterior to Limbus
Clock Hours Treated	10	Spare 3:00 and 9:00 LPC Nerves
Treatment Path Length	44.1 mm	Treatment Path Length
Probe Diameter	700 μ m	
Total Probe Locations	63	Assume contiguous probe sites
Duration	160 sec	80 Seconds each hemisphere
Milliwatts	2000	2W = 2000 mW
Joules Calculation	mW x ms = microjoules (10-6)	Calculation without Micropulse
Micropulse	31.3% Total "ON" Time	Multiply Joules by 31.3 %
Joules/Probe Location	1.59 J	
Total Joules	100.16 J	J = W X sec X Duty Cycle (31.3%)



Micropulse Use to Control Heat Damage



Coagulative Disruption



Tissue Shrinkage