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Microscope Real-time Video (MRTV), High- resolution OCT (HR-OCT) & Histopathology (HP) to Assess How Transcleral Micropulse Laser (TML) Affects the Sclera, Ciliary Body (CB), Muscle (CM), Secretory Epithelium (CBSE), Suprachoroidal Space (SCS) & Aqueous Outflow System

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Abstract Number: 2825

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DisclosureBlock: Murray A. Johnstone, None; Shaozhen SONG, None; Steven Padilla, None; Kimika Wen, None; Chen Xin, None; Joanne C. Wen, None; Elizabeth Martin, None; Ruikang K. Wang, None;

Purpose
Mechanisms of IOP reduction after TML remain unclear although TML is widely used in the management of glaucoma. We describe 3 imaging modalities to explore tissue changes induced by TML that may assist in understanding mechanisms of action & improving treatment parameters.

Methods
Immediately after removal of non-human primate eyes, radial sections of the limbus (2 mm wide) were maintained in a saline bath & a micropulse laser probe positioned so the beam path passed through sclera to CB. To simulate clinically relevant energies, Joules used in sections were 0.75 (n=2), 1.50 (n=2), & 2.5 (n=1). MRTV imaged throughout the pulse, HR-OCT before & after; HP followed after. Distance from scleral spur (SS) to probe before & after the laser was measured with ImageJ using MRTV images; paired t-tests were done with JMP.

Results
The MRTV beam path tracing focused in tissue at ~700 µm depth near the interface of sclera & longitudinal CM. MRTV showed that the internal scleral surface facing the CB in the path of the beam immediately underwent shrinkage. The adjacent CB longitudinal muscle also simultaneously shortened or contracted. Sclera & CM shrinkage resulted in local SCS enlargement. The scleral spur moved posteriorly by 27.0 ± 3.0, 107.6 ± 8.6 & 92.4 ± 12.3 µm at 0.75, 1.5 & 2.25 Joules respectively; final position in each differed significantly from baseline ($p < 0.0001$). The attached TM moved inward & posteriorly with Schlemm's canal (SC) enlargement. Histology & a newly developed platform for imaging the entire CB thickness with OCT confirmed the RTV findings. No CB secretory epithelium damage was identified with MRTV, HR-OCT or HP.

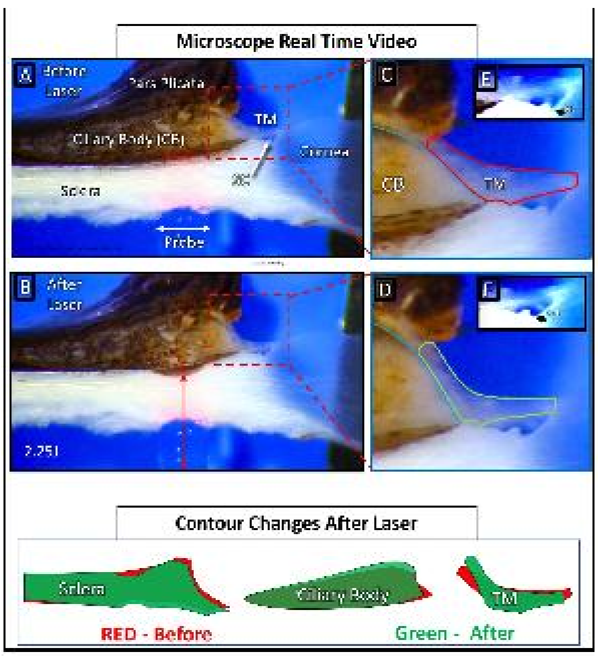
Conclusions
The TML caused a Δ in sclera thickness, shortening & local shrinkage of the longitudinal CM with

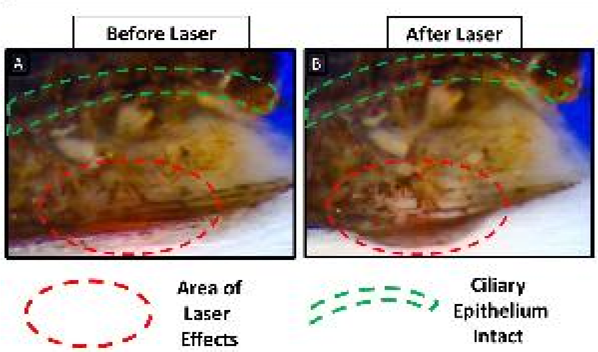
enlargement of the SCS. Inward & posterior movement of the SS & TM caused SC to enlarge. Absence of CBSE damage suggest SCS enlargement, a uveoscleral flow increase & conventional aqueous outflow pathway changes as mechanisms of action, rather than direct CBSE damage. Additional lab studies may assist in further characterizing mechanisms of action & provide insights related to appropriate treatment parameters.

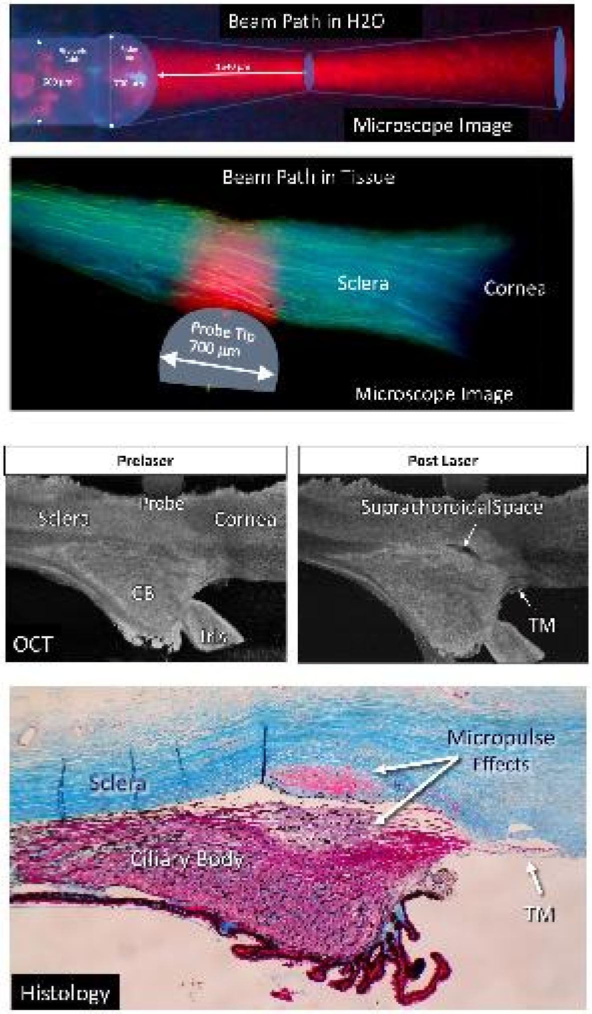
Layman Abstract (optional): Provide a 50-200 word description of your work that non-scientists can understand. Describe the big picture and the implications of your findings, not the study itself and the associated details.

The micropulse laser treats glaucoma by lowering intraocular pressure. Pressure can be reduced by either reducing secretion or increasing outflow of aqueous humor. The micropulse procedure is a transcleral procedure involving passage of laser energy through the sclera, the white surface coat of the eye. At the higher energy levels used before micropulse introduction, the mechanism of action was found to be damage to tissues that secrete aqueous thereby reducing aqueous inflow.

Our study uses three imaging modalities to explore the effects of the micropulse procedure. We find evidence that shrinkage of tissue causes a space to develop between the sclera and ciliary muscle inside the eye. An increase in this space is thought to provide a means of improving aqueous outflow by what is called the uveoscleral outflow pathway. We also find the technique increases tension on the ciliary muscle, causing effects like those of pilocarpine, a drug that improves conventional aqueous outflow. We do not identify damage to the tissue that secretes aqueous. A better understanding of the mechanism of action of the micropulse laser may provide insights that will lead to improved delivery parameters and new innovations in delivery systems.






Beam Path in H2O
Microscope Image
Beam Path in Tissue
Sclera
Cornea
Probe Tip
700 µm
Microscope Image
Prelaser
Sclera
Probe
Cornea
CB
Iris
OCT
Post Laser
SuprachoroidalSpace
TM
Micropulse
Effects
Sclera
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