SPECIALTY EYE INSTITUTE

Subthreshold Laser Treatment for Macular Edema

Carmelina M. Gordon M.D.

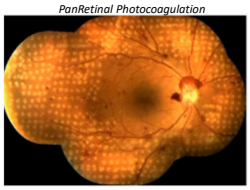
Subthreshold Laser Treatment

- Tissue sparing laser therapy or non-damaging retinal treatment
- 810 nm and 577 nm lasers
- Produce a therapeutic effect without inducing detectable retinal damage
- Effect has been shown in CSR, DME, RVO, Wet AMD and PDR

- Luttrull et al Subthreshold diode micropulse for treatment of CSDME. BJO 2005
- Larsen, et al Subthreshold micropulse diode lser treatment in DME BJO 2003
- Figeuira et al Prospective randomised controlled trial comparing sub-threshold micropulse diode laser and conventional green laser for CSDME. BJO 2009
- Lavinsky et al Randomized clinical trial evaluating mETDRS versus normal or high-density micropulse photocoagulation for DME. Invest Ophthlmol Vis Sci. 2011
- Vujosevic et al . Microperimetry and fundus autofluorescence in DME: subthreshold mocropulse laser versus mETDRS laser photocoagulation. Retina 2010
- Parodi et al. Subthreshold grid laser versus IVT Bevacizumab as second line therapy for macular edema secondary to BRVO after conventional grid laser. Graefe's archive 2015

Retinal Photocoagulation

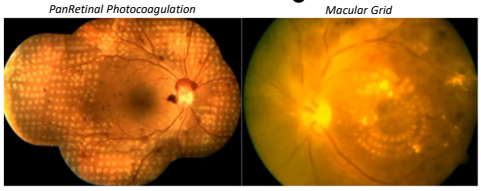
PanRetinal Photocoagulation



Proliferative Diabetic Retinopathy
Balancing supply and demand:
- Hypoxic retina cannot sustain full retinal metabolic demand. It secretes VEGF cytokines leading to neovascularization.
- Extensive destruction of photoreceptors in suppressing VEGF signaling and thus prevents angiogenesis.

Retinal Photocoagulation

PanRetinal Photocoagulation *Macular Grid*



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Macular Edema:
Macular grid reduces edema via unknown mechanism.

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PanRetinal Photocoagulation *Macular Grid*

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Macular Edema:
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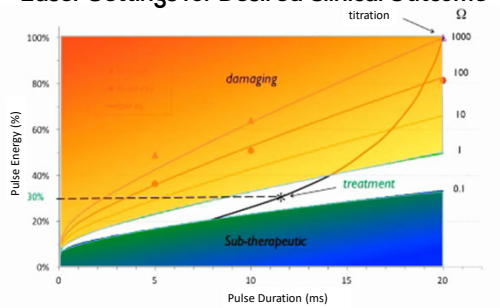
Hypothesis: Cells surviving the thermal stress activate repair pathways which help restoring normal function.

Subthreshold lasers available

- End Point Management
- Micropulse
- Selective RPE Treatment

EndPoint Management Algorithm: Laser Settings for Desired Clinical Outcome



Mechanism of action of Subthreshold Laser

- Expression of HSP 70 that suppresses the strong proangiogenic VEGF cytokine and upregulates PEDF which is antiangiogenic.

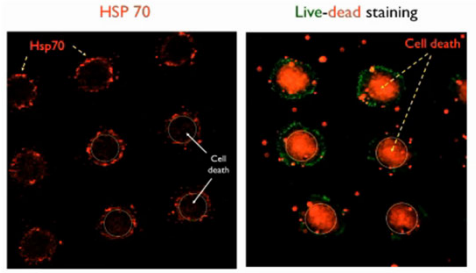
Li et al Cell Biochem and Biophysics 2015

- Expression of GFAP which restores function of the Muller cells

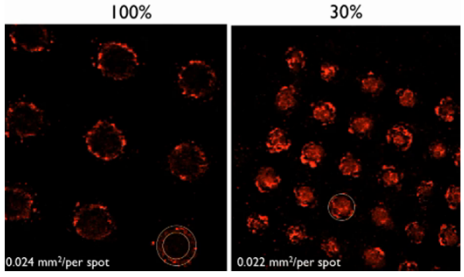
Midena et al Retina 2018

Barely-Visible Burns (100%)

RPE, 7 hours post-laser



Heat-shock Protein Expression HSP 70, 7 hours post-laser



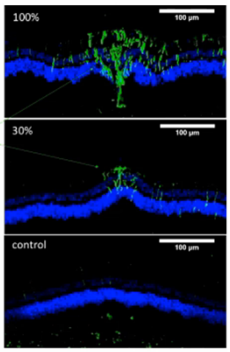
GFAP Expression at 1 Month

GFAP: Glial fibrillary acidic protein

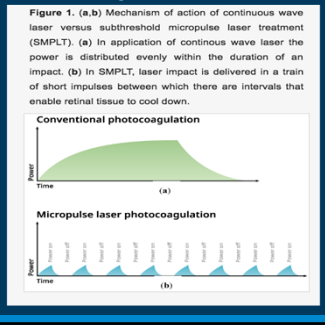
Activated Muller cells

Clinical cases

Control



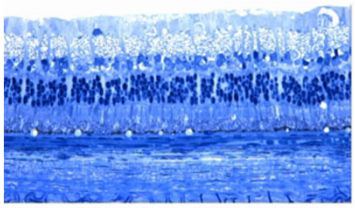
Micropulse Laser



SRT

Selective RPE Treatment (SRT)

t < 50 µs



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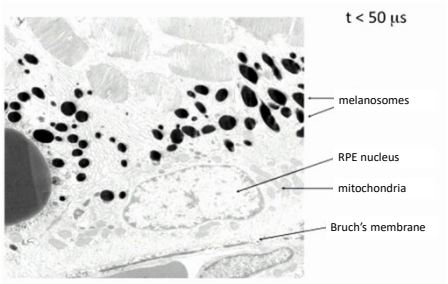
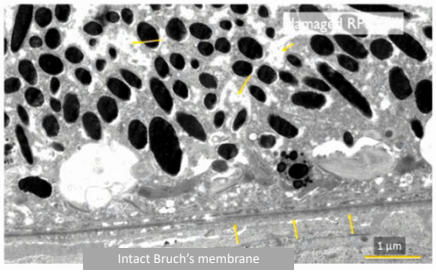


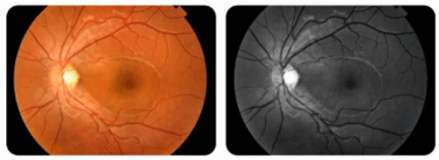
SRT

1 hour post laser
2W, 100 µm, 6m/s, 16 µs



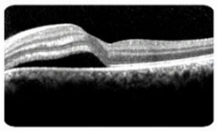
Clinical Cases

Central Serous ChorioRetinopathy



27 years old, military pilot
VA: 20/20 OD, 20/25 OS for 1 month

Patient denied the use of steroids or other medications, and decided to wait for spontaneous resolution.



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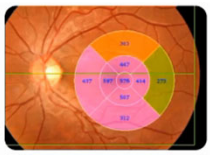
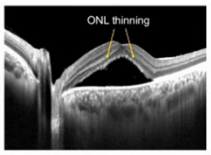
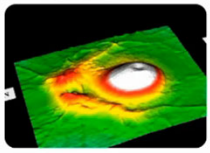




Returned after 3 months
VA 20/30



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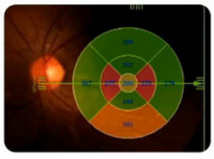
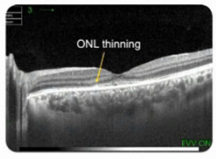
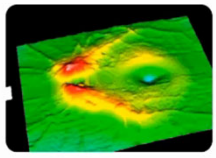




3 months after NRT:
VA 20/15



Slide 14

SS1 Stephanie Shackelford, 3/18/2019

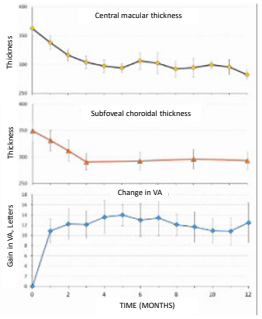
Clinical cases

Central Serous ChorioRetinopathy

21 eyes, 20 patients

Minimum duration prior to treatment: 4 months.

Average duration prior to treatment: 11 +/- 4 months.



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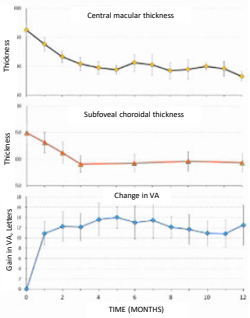
Treat-ments	1	2	3	4	Average
	16%	58%	16%	10%	**2.2**



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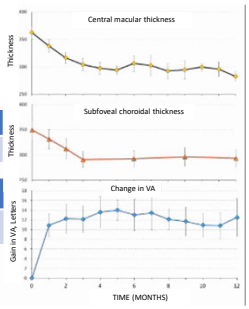
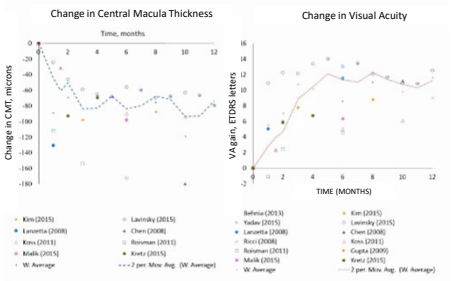
Fluid Resolution	Complete	Partial	Non-Responder
	81% (17/21)	19% (4/21)	0



Clinical cases

Non-damaging retinal laser therapy for CSCR: Overview of clinical studies

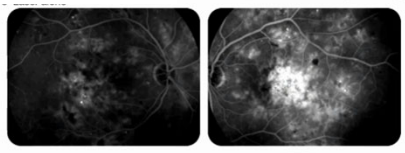


Clinical cases

Diabetic Macular Edema

21 patients treated to date.
Multiple Lucentis/Avastin/Eylea
Prior to subthreshold laser

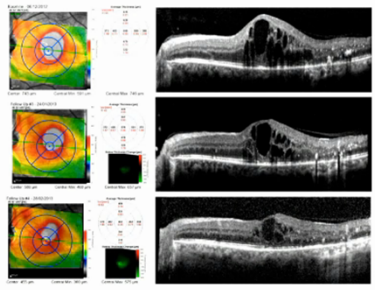
Retreat at 3 months if did not respond.
Retreat as needed if recurred (4-9 months)



- Visual acuity 20/80
- Severe nonproliferative diabetic retinopathy with macular edema

Clinical cases

Diabetic Macular Edema



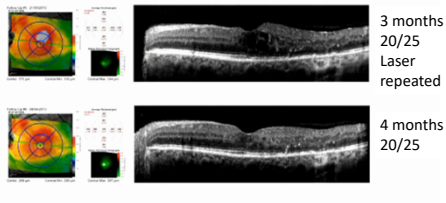
acute
20/80

1 month
20/60

2 months
20/60

Clinical cases

Diabetic Macular Edema



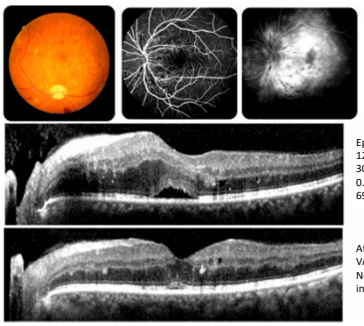
3 months
20/25
Laser repeated

4 months
20/25

Δ Central Macular Thickness = 699-397=302 um
Δ **VA: from 20/80 to 20/25**

Clinical cases

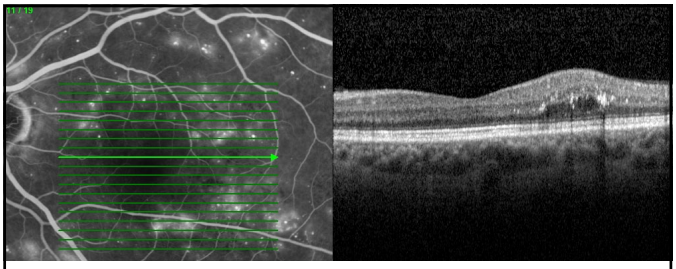
Diabetic Macular Edema



47 years old, female
Type 2 diabetes for 12 years
Diffuse DME
BCVA 20/80 OU

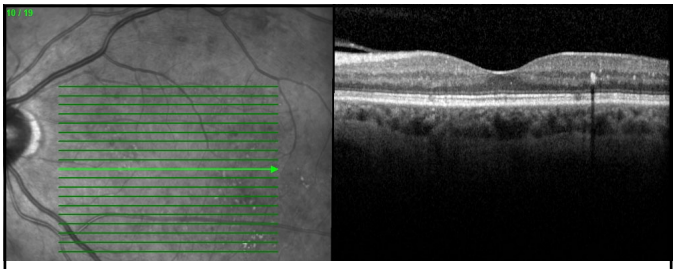
EpM,
120mW (100%)
30%, 200µm
0.25 D spacing
693 spots

After 6 months
VA 20/25
No Anti-VEGF injections



DME

- 46 year old female
- NPDR with DME
- Focal laser 9/14/18
- Vision 20/40

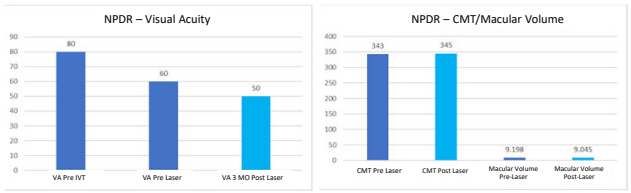


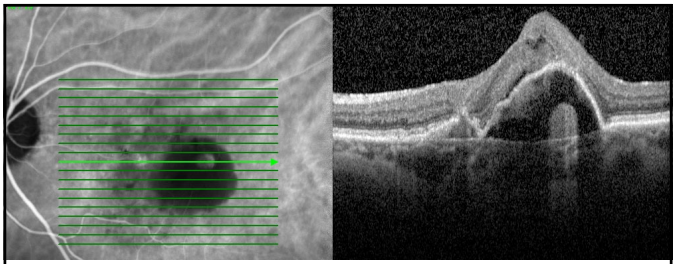
DME

- 3 months post laser
- Vision 20/30

NPDR

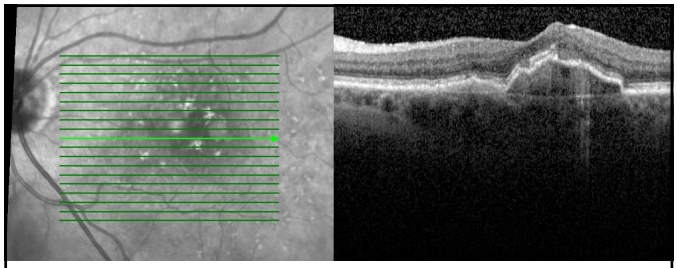
P=56





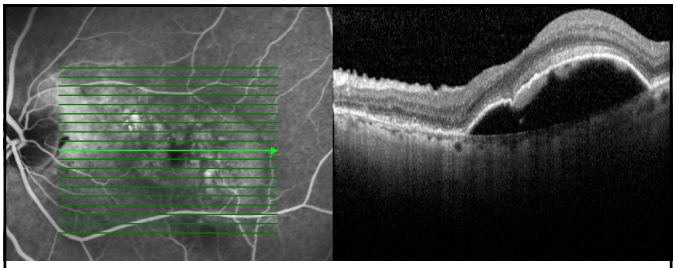
Wet AMD left eye

- 88 y/o female, had IVT Avastin x 13 since 7/7/16
- Laser done 10/5/18
- Vision 20/50



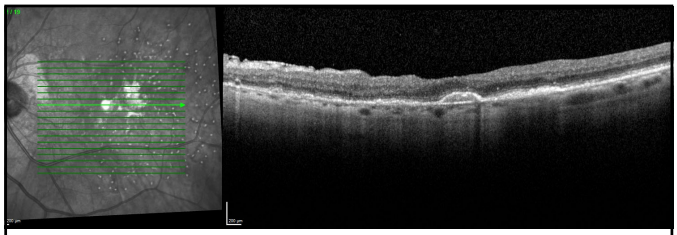
Wet AMD left eye

- Post laser and 2 IVT Avastin
- Vision 20/40



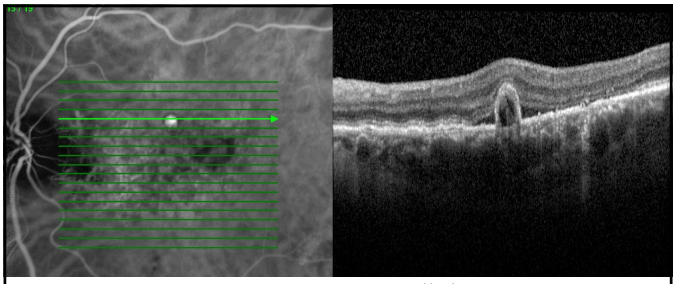
Wet AMD

- 80 year old female
- 9 IVT Eylea since 2017
- Laser 10/10/18
- Vision 20/70



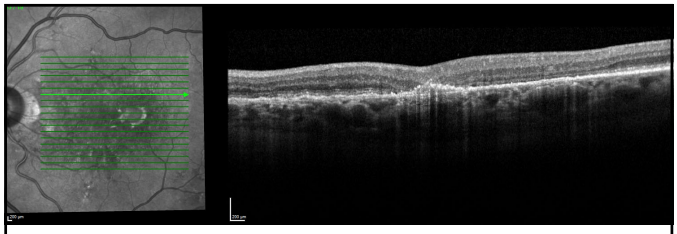
Wet AMD

- 3 months post laser
- No retreatment with anti VEGF since laser
- Vision 20/60



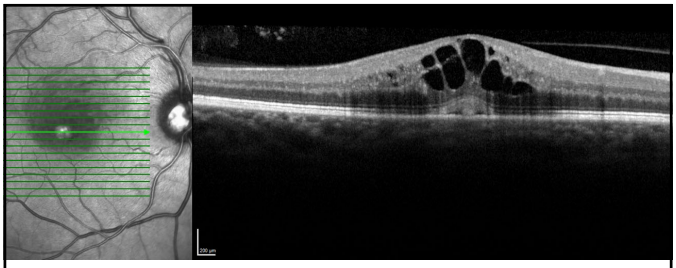
Wet AMD

- 80 year old male
- 13 IVT Eylea q 4-6 weeks
- Laser 9/14/18
- Vision 20/70



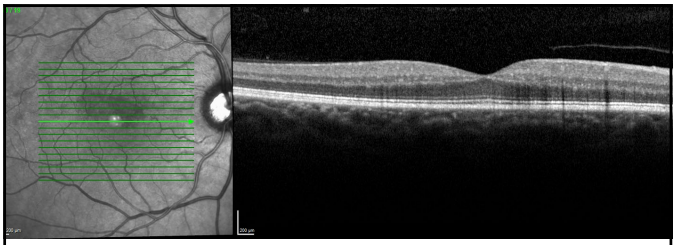
Wet AMD

- 3 months post Laser
- Given 1 IVT Eylea 6 weeks post laser
- Vision 20/60



BRVO

- 57 year old female
- Vision: 20/80
- Given 1 IVT Avastin then laser 2 weeks later

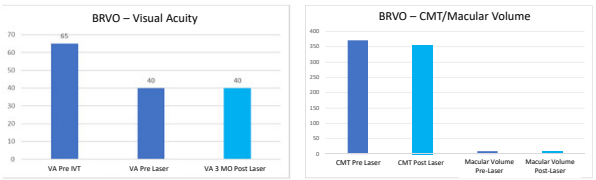


BRVO

- 4 months post IVT Avastin and Laser
- Vision 20/25

BRVO

N=15



Conclusion

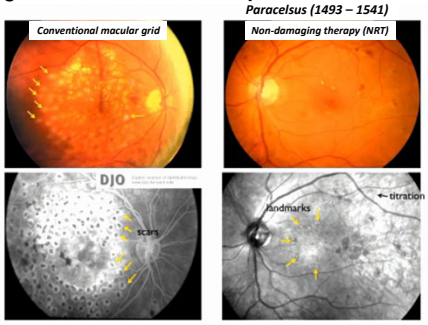
- Subthreshold laser or non damaging retinal laser treatment (NRT) activates endogenous repair mechanisms
- Cells surviving the hyperthermia express HSP and GFAP around the conventional burns and inside non-damaging spots
- Lack of tissue damage allows:
  1. High spot density - essential for boosting clinical efficacy
  2. Periodic retreatments - essential for chronic conditions
  3. Treatment to fovea

Conclusions

- Nearly confluent coverage helps boost clinical efficacy;
  0.25 D spacing corresponds to 50% coverage
  0 spacing corresponds to 70% coverage
  Compared to 9% coverage in conventional laser
- Potential uses of NRT
1. Addition to treatment regimen of suboptimal or non responders to anti VEGF
2. Increase treatment interval between anti VEGF injections

The right dose differentiates a poison and a remedy

Paracelsus (1493 – 1541)



Thank you

- Acknowledgement
  Topcon
  Stephanie Shackelford
  April Daugherty COT