Tissue-Sparing
MicroPulse™ Laser Therapy (MPLT)

First, do no harm

Technology

Retina

Parameters

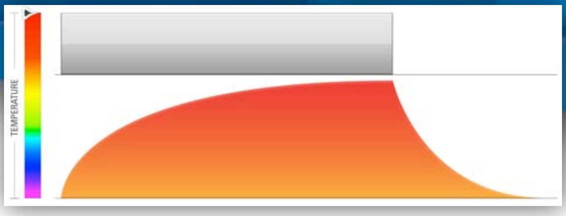
Glaucoma

Parameters

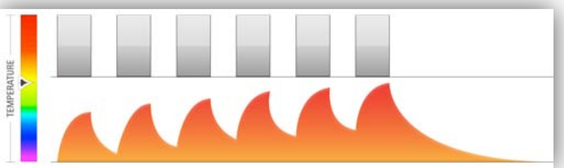
MicroPulse™ Technology

What is MicroPulse Technology?

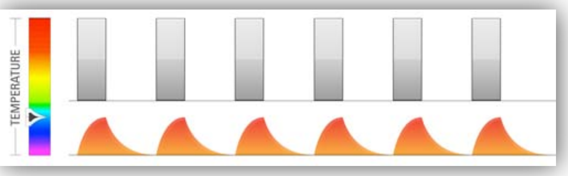
- A technology that "chops" CW laser emission into spaced, repetitive micropulses to allow:
  - Finer control of photothermal effects
    - Lower energy per pulse
    - Tissue cooling between pulses (based on Duty Cycle) More
  - Equivalent or superior clinical outcomes with the benefits of no tissue damage detectable at any time point post-operatively[1]



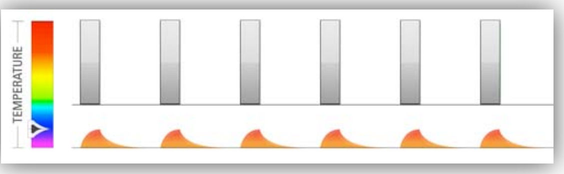
CW Laser Exposure: 100% Duty Cycle (DC)



MicroPulse High DC (15%)



MicroPulse Medium DC (10%)



MicroPulse Low DC (5%)

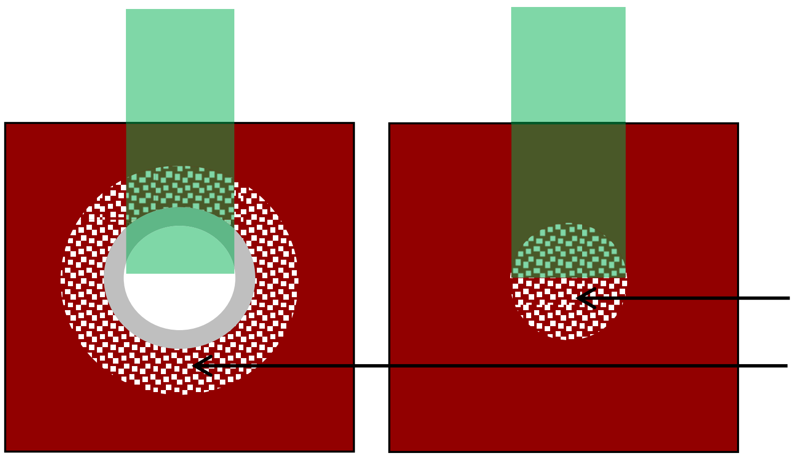
IRIDEX | MicroPulse

1. Vujosevic S, Bottega E, Casciano M, Pilotto E, Convento E, Midena E: Microperimetry and Fundus Autofluorescence in Diabetic Macular Edema: Subthreshold Micropulse Diode Laser Versus Modified Early Treatment Diabetic Retinopathy Study Laser Photocoagulation. *Retina* 2010;30(6):908-916.

How does MicroPulse Laser Therapy Work?

PEDF[1] ↑ | TSP1[2] ↑ | SDF1[3] ↑ | ß-Actin[3] ↑

Modulation of the expression of intracellular biological factors



Visible Conventional CW (DRS/ETDRS)

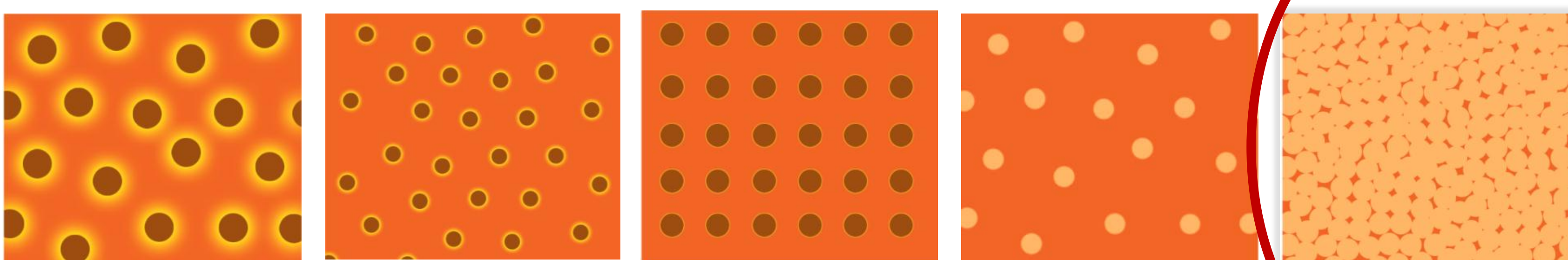
Tissue-sparing MLT

Heated tissue that remains viable after CW or MicroPulse laser treatment, produces a stress response and induces beneficial intracellular biological factors that are primarily anti-angiogenic and restorative. More

1. Ogata N, Tombran-Tink J, Jo N, Mrazek D, Matsumura M: Upregulation of Pigment Epithelium-Derived Factor after Laser Photocoagulation. *Am J Ophthalmol* 2001;132(3):427-9.
2. Binz, N, Graham, CE, Simpson, K, Lai, YK, Shen, WY, Lai, CM, Speed, TP, Rakoczy, PE: Long-Term Effect of Therapeutic Laser Photocoagulation on Gene Expression in the Eye. *FASEB J* 2006;20(2):383-5.
3. Yu, AK, Merrill, KD, Truong, SN, Forward, KM, Morse, LS, Telander, DG: The Comparative Histologic Effects of Subthreshold 532- and 810-Nm Diode Micropulse Laser on the Retina. *Investigative Ophthalmology & Visual Science* 2013;54(3):2216-2224.

MPLT Low Intensity / High Density Application

Low-intensity MicroPulse exposures avoid thermal retinal injury. Therefore, **high-density** (confluent) coverage of the diseased retina is needed to maximize clinical effectiveness of MPLT.[1-8]



High-intensity argon | Low-intensity argon | Pascal | Low-intensity/ low-density MPLT | Low-intensity/ high density MPLT

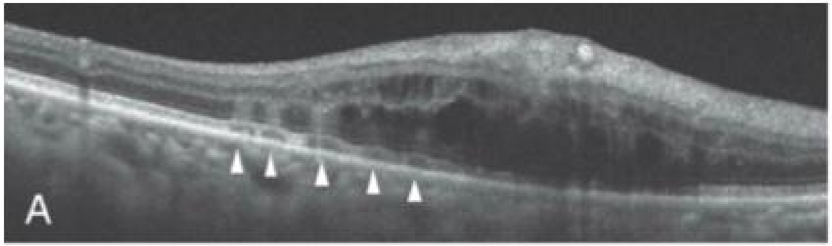
Vermillion = Retina unaffected by laser treatment. Brown = Area of retina destroyed by laser and inactive with respect to ability to produce extracellular cytokines. Yellow = Area of retina affected by the laser but not destroyed, able to contribute to the therapeutic effects of laser treatment via laser-induced alteration / normalization of cytokine expression.[8] More

1. Luttrull, et al. BJO 2005
2. Luttrull, et al. OSLI 2006
3. Luttrull, et al. Eye 2008
4. Vujosevic, et al. Retina 2010
5. Ohkoshi, et al. AJO 2010
6. Lavinsky, et al. IOVS 2011
7. Luttrull, et al. Retina 2012
8. Luttrull J, et al. Curr Diabetes Rev, 2012

IRIDEX | MicroPulse

Subthreshold CW Scanning ≠ MPLT

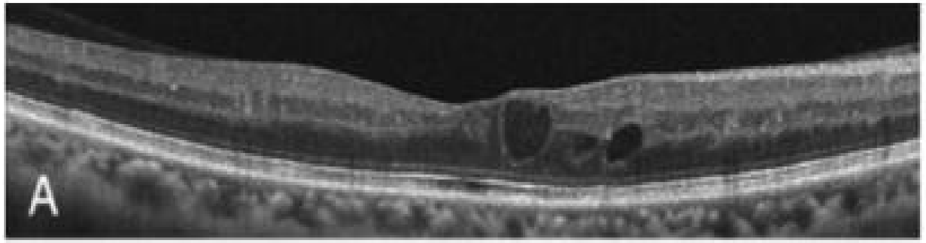
CW Subthreshold Scanning



Fluid-like spikes adjacent to ruptured RPE (arrows)

- SD-OCT imaging of retinal healing within 3 months post CW, pattern scanning, and MicroPulse laser treatments.
- Immediately after CW and pattern scanning laser, a hyper-reflective band appeared at the laser sites.

MicroPulse



100% of tissue spared

- Retinal morphology did not change at any time during the observation period after MicroPulse.

Inagaki K, et al. Spectral-Domain Optical Coherence Tomography Imaging of Retinal Changes after Conventional Multicolor Laser, Subthreshold Micropulse Diode Laser, or Pattern Scanning Laser Therapy in Japanese with Macular Edema. *Retina* 2012;32(8):1592-1600

"Continuous conventional laser can also be delivered in a subthreshold fashion using lower energy, but this is not the same as dividing the energy into micropulses. Micropulse-divided laser energy will heat the tissue less than a continuous pulse laser even if the total amount of energy is the same."

Yu AK, Merrill KD, Truong SN, Forward KM, Morse LS, Telander DG. The Comparative Histologic Effects of Subthreshold 532- and 810-Nm Diode Micropulse Laser on the Retina *Invest Ophthalmol Vis Sci* 2013

IRIDEX | MicroPulse

MicroPulse Technology available in Multi-functional Laser Systems

- Fovea-friendly™ MicroPulse* Laser Therapy[1] for retinal disorders
- Repeatable MicroPulse Laser Trabeculoplasty for glaucoma therapy
- Conventional photocoagulation
- TxCell™ Scanning Laser Delivery Device*: Multi-spot pattern scanning for efficient retinal photocoagulation
- FDA-cleared for both conventional and MicroPulse laser therapies

IQ 577™

IQ 532™

IQ 810™

Retina | Glaucoma

IRIDEX | MicroPulse

*MicroPulse and TxCell are optional with the IQ 577 and IQ 532 lasers

1. Bhagat N, Zarbin M, Mansour S, Chong V, and Cardillo JA. Fovea-friendly MicroPulse Laser. Supplement to Retina Today, May/June 2012

Fovea-friendly™ MicroPulse Laser Therapy

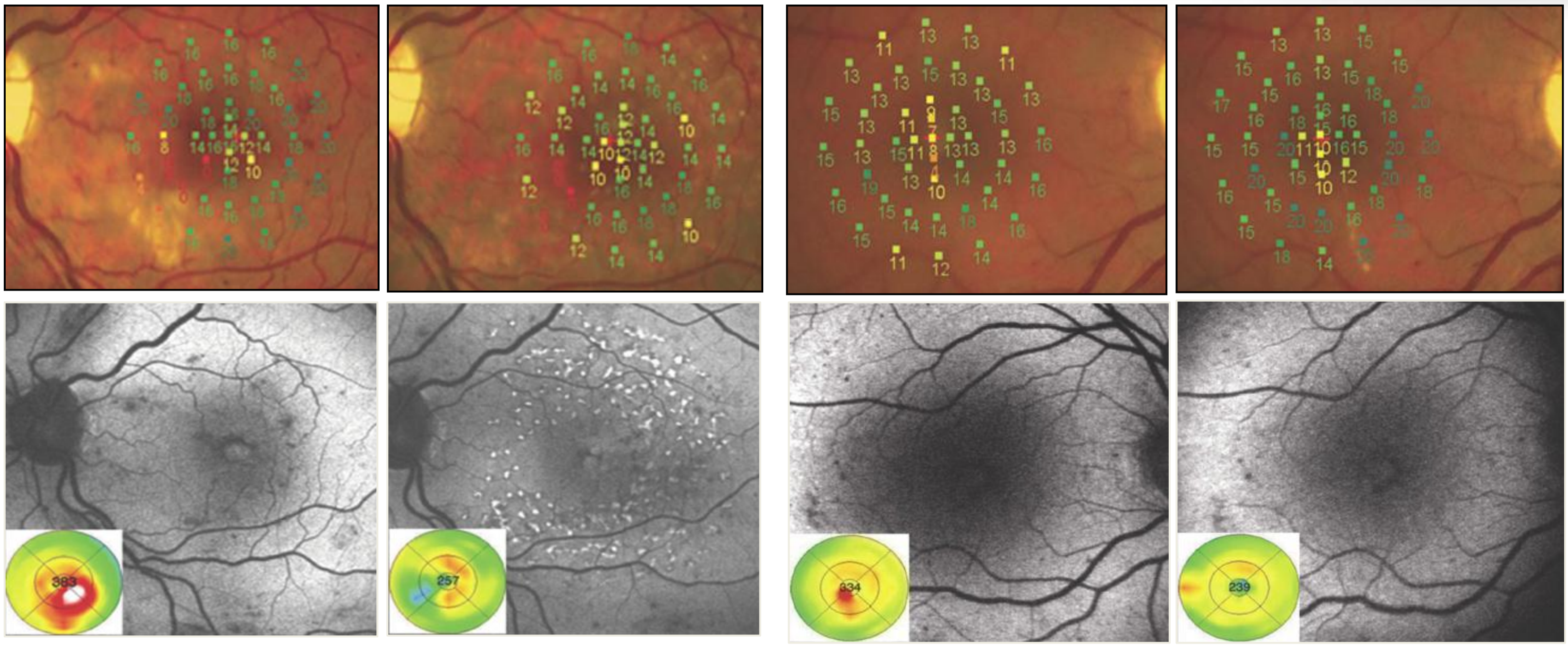
IRIDEX | MicroPulse

MPLT = Clinical Efficacy without Damage

mETDRS[1] **MPLT[1]**

Microperimetry

FAF and OCT



Pre-treatment **1 Yr Post-treatment** **Pre-treatment** **1 Yr Post-treatment**

A prospective, randomized clinical trial on 62 eyes (50 patients) with untreated, center-involving, clinically significant DME. 810 nm MPLT was effective as mETDRS laser in stabilizing VA and in reducing macular edema with the benefits of no tissue damage detectable at any time point postoperatively, and of significant improvement in retinal sensitivity.

IRIDEX | MicroPulse

1. Vujosevic S, Bottega E, Casciano M, Pilotto E, Convento E, Midena E. *Retina* 2010

810 nm MPLT Clinical Results – DME

Using Low Intensity / High Density Protocols

Author	Authors' Conclusions	Follow-up
Vujosevic *Retina* 2010[1]	Effective as mETDRS laser in stabilizing VA and in reducing macular edema with the benefits of no tissue damage detectable at any time point postoperatively, and of significant improvement in retinal sensitivity. More	1 year
Lavinsky *IOVS* 2011[2]	Superior to the mETDRS based on BCVA improvement and CMT reduction. More	1 year
Luttrull *Retina* 2011[3]	Can effectively treat retinovascular macular edema without laser-induced retinal damage. More	Up to 10 years

1. Vujosevic S, Bottega E, Casciano M, Pilotto E, Convento E, Midena E. *Retina* 2010
2. Lavinsky D, Cardillo JA, Melo LA, Jr., Dare A, Farah ME, Belfort R Jr. *Invest Ophthalmol Vis Sci* 2011
3. Luttrull JK, Sramek C, Palanker D, Spink CJ, Musch DC. *Retina* 2012;32(2):375-86

IRIDEX | MicroPulse

810 nm MPLT Clinical Results – CSC

Using Low Intensity / High Density Protocols

Author	Authors' Conclusions	Follow-up
Lanzetta *EJO* *2008*[1]	The majority of eyes achieved anatomic and functional improvements. MicroPulse is a new and promising method for treating a previously untreatable disorder. This minimally invasive and retina sparing treatment may allow the cure of CSC at its earlier stages when irreversible visual loss has not occurred. More	14 mos (mean, range 3 to 36 mos.)
Gupta *Clin Exp Ophth* *2009*[2]	Outcomes confirm long-term efficacy of MicroPulse in the management of CSC. It produces therapeutic effects that appear comparable to those of conventional laser with no detectable signs of laser-induced iatrogenic damage. More	17.1 mos (mean, range 6 to 24 mos.)
Koss *Eye* 2011[3]	Results indicate superior subretinal fluid resolution, and superior VA improvement and other visual functions, for MicroPulse laser compared to anti-VEGF injections, with no tissue reactions observed during and at any point after MicroPulse treatment. More	10 mos

IRIDEX | MicroPulse

1. Lanzetta P, et al. Eur J Ophthalmol 2008
2. Gupta B, et al. Clin Experiment Ophthalmol 2009
3. Koss MJ, et al. Eye (Lond) 2012

Comparison - 810 nm and 577 nm MPLT

- Both 810 nm and 577 nm subvisible MicroPulse laser with 5% duty cycle and fixed power parameters appear to be safe in center involving DME.

- At 6 months, 60 eyes (43 patients) treated with 810 nm and 577 nm showed:
  - No difference in macular volume
  - No signs of inner or outer retinal and choroidal damage
  - No changes shown on FAF or MP1
  - No absolute scotoma
  - Fixation was always central and stable in all patients

More

Treatment Parameters		
Wavelength	**810 nm**	**577 nm**
Eyes	31	29
Spot Size	125 µm	100 µm
Power	750 mW	250 mW
Duration	200 mw	200 ms
Duty Cycle	5%	5%

IRIDEX | µP MicroPulse

Vujosevic S, Martini F, Convento E, Longhin E, Pilotto E, Midena E: Morphologic and Functional Effects of Diode(810nm) and Yellow(577nm) Subthreshold Micropulse Laser in Center-Involving Diabetic Macular Edema. *ARVO Meeting Abstracts* 2013;54(6):2380.

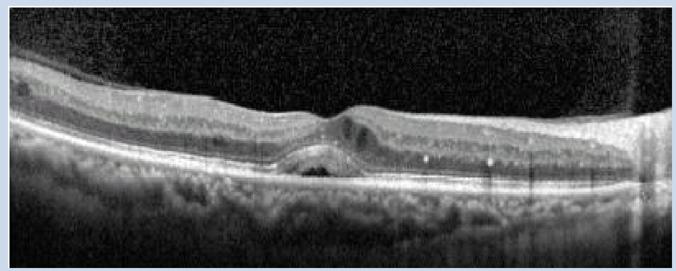
577 nm MPLT Case Reports

DME | CRVO | Uveitis

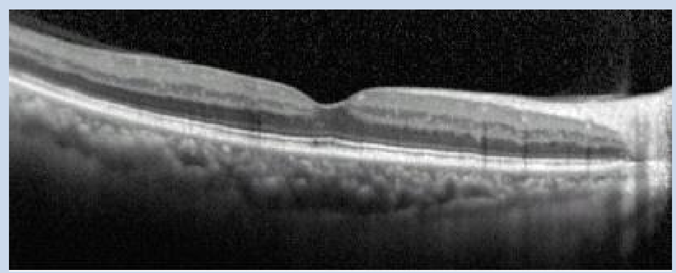
"In my practice: MPLT has now completely replaced conventional laser for macular edema resulting from diabetes or retinal vein occlusion…"

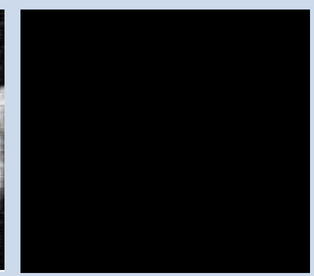
Sam Mansour, MD
Warrenton, VA

View Case Report



Pre-Treatment: SD-OCT, VA 20/50-1, CRT 326 µm





6 Weeks Post-Treatment: VA 20/25-1, CRT 272 µm

IRIDEX | MicroPulse

577 nm MPLT Case Reports

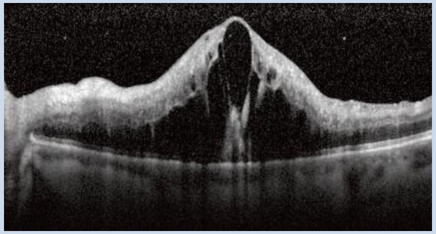
DME | CRVO | Uveitis

"Repeat treatments and treating through the fovea can be done safely using MPLT."

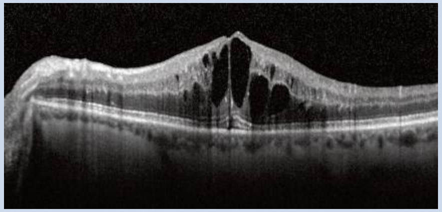
"Utilizing MPLT in the exam lane has streamlined our office flow because patients don't have to move in and out of a separate laser room."

Patrick Caskey, MD
Santa Rosa, CA

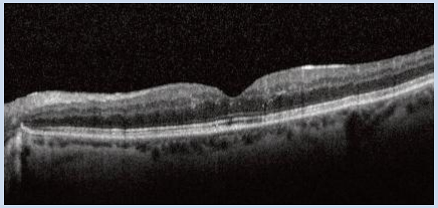
View Case Report



Pretreatment:
VA 20/150, CRT 870 µm.
Clinical exam revealed prominent cystoid macular edema.



6 weeks post third anti-VEGF treatment.
Pre MPLT: VA 20/70-2, CRT 584 µm. Recurrent macular edema noted.



Approximately 5 months Post MPLT: VA 20/40+2, CRT 261 µm. No macular edema observed on clinical exam.

IRIDEX | MicroPulse

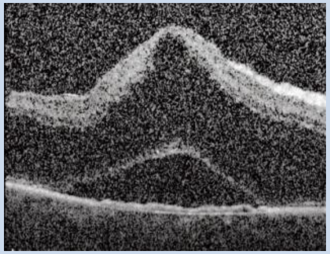
577 nm MPLT Case Reports

DME | CRVO | Uveitis

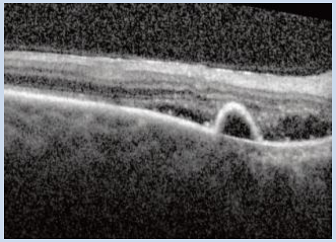
"MPLT was the only attempted treatment that resulted in resolution ofthe macular edema..."

Jeevan Mathura, MD
Washington, DC

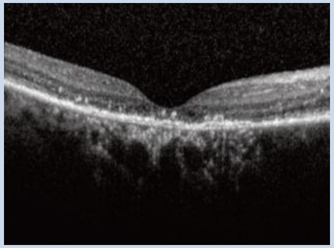
View Case Report



Sept. 2012 | right eye post numerous steroid and intra-vitreal bevacizumab injections | CST >1,078 µm | VA 20/400.



Nov. 2012 | right eye 4 weeks post intravitreal steroid injection | large amounts of fluid, hard exudates, full-appearing optic nerve with blurred margins, CSC and a PED | CST 727 µm | VA 20/200.



Jan. 2013 | right eye 7 weeks post MPLT | CST 164 µm | VA 20/400.

IRIDEX | MicroPulse

Comparison: 810 nm and 532 nm

- Histological study
  - 14 Dutch-belted rabbits received MicroPulse laser using 5%, 10%, 20%, and 40% duty cycles. Right eye received 810 nm; Left eye, 532 nm
- Results showed
  - Equivalent histologic changes from both wavelengths at 2- and 4-week time points.
  - Equivalent protein expressions of SDF1, ß-actin, and VEGF
- Observations
  - During the application of MPLT at all duty cycles, there was no visibly detectable lesions.
  - MPLT delivered at a 5% duty cycle showed no histological changes in 76% (57/75) of cases, while still producing SDF1

Yu, AK, Merrill, KD, Truong, SN, Forward, KM, Morse, LS, Telander, DG: The Comparative Histologic Effects of Subthreshold 532- and 810-Nm Diode Micropulse Laser on the Retina. *Investigative Ophthalmology & Visual Science* 2013;54(3):2216-2224.

IRIDEX | MicroPulse

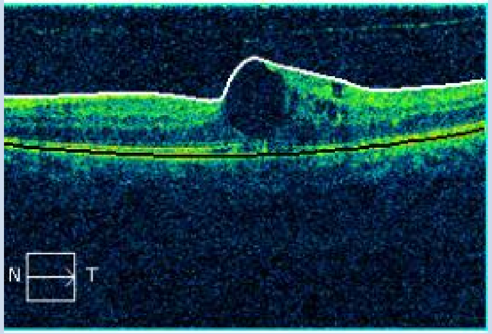
532 nm MPLT Case Reports

DME | DME Refractive to Avastin & Ozurdex | Radiation Retinopathy

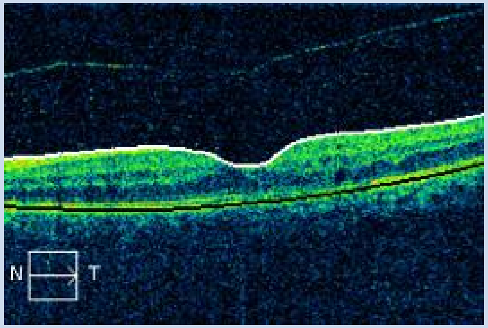
"I feel comfortable knowing that [with subthreshold MicroPulse] I am not creating any thermal damage in the fovea and that I may be able to reduce the amount of anti-VEGF treatments needed in the future for a given patient."

David Gossage, DO
Hillsdale, MI

View Case Report



Pre MPLT: CRT 434 µm, VA 20/50



3 Months Post MPLT: CRT 314 µm; VA 20/30

IRIDEX | MicroPulse

532 nm MPLT Case Reports

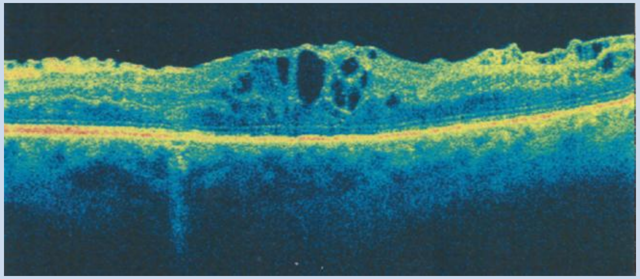
DME | DME Refractive to Avastin & Ozurdex | Radiation Retinopathy

"MPLT has truly revolutionized my practice, not just with DME, but also with any vascular pathology. I can safely treat right through the fovea and get a response without damaging the retina. In fact, I have actually seen retinal sensitivity improve post-treatment."

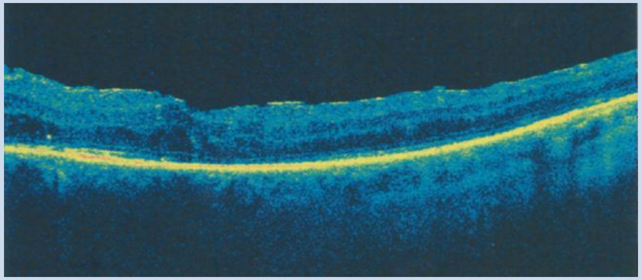
"The repetitive nature of anti-VEGF treatment results in significant cost and inconvenience to the patient. That ultimately compelled me to adopt MPLT."

Aaron Appiah, MD
Tallahassee, FL

View Case Report



Pre-op VA: 20/200, CRT: 438 µm



3 Months Post-Op VA: 20/60, CRT: 270 µm

IRIDEX | MicroPulse

532 nm MPLT Case Reports

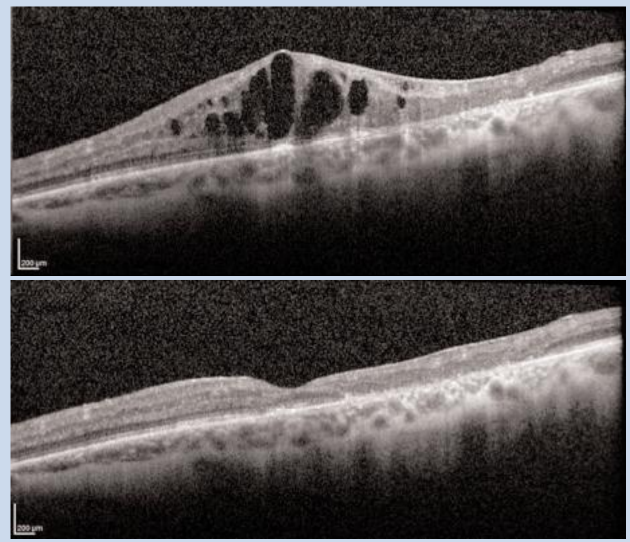
DME | DME Refractive to Avastin & Ozurdex | Radiation Retinopathy

"MPLT is an exciting avenue for new treatment in radiation retinopathy, an area where there is currently no existing standard of care."

"MPLT has been one of the easiest treatments I have ever adopted. Because the therapeutic window for radiation retinopathy is so large, I had no anxiety about MPLT even in treating my first patient."

Timothy Murray, MD
Coral Gables, FL

View Case Report



Before and 3 months after one MPLT treatment in conjunction with anti-VEGF therapy for radiation retinopathy. In this patient, foveal contour was restored and visual acuity improved from 20/100 to 20/25. No further treatment has been required.

IRIDEX | MicroPulse

Treatment Parameters

IQ 577™

- 577 nm MPLT for DME - Mansour More

IQ 532™

- 532 nm MPLT for DME - Gossage More

IQ 810™

- 810 nm MPLT for DME – Luttrull, Vujosevic More
- 810 nm MPLT for CSC – Lanzetta More
- 810 nm MPLT for CSC – Gupta More
- 810 nm MPLT for CSC - Koss More

MicroPulse™

First, do no harm

www.iridex.com/micropulse

Tissue-Sparing Bibliography

Patient Education

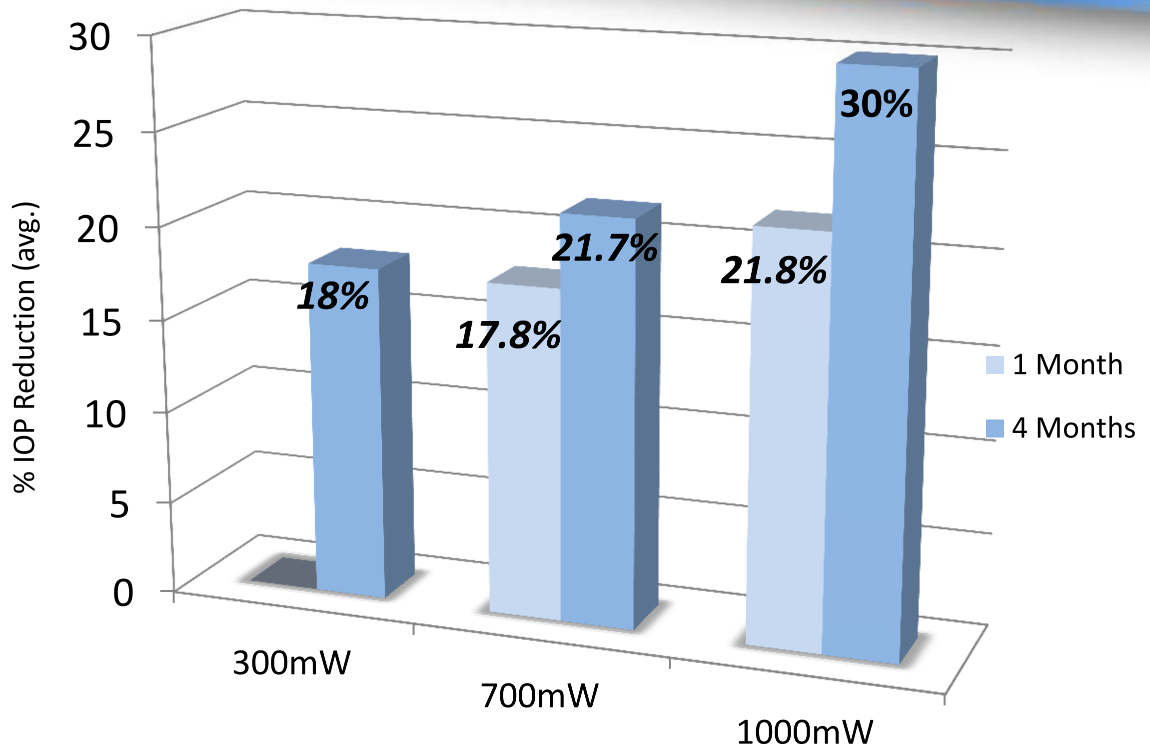
IRIDEX | MicroPulse

Technology Retina Glaucoma

Repeatable
MicroPulse Laser Trabeculoplasty (MLT)
for Glaucoma Therapy

IRIDEX | µP MicroPulse

30% IOP Reduction



532 nm, 1,000 mW = greatest IOP reduction at 1 & 4 mos More

“Even at the highest power, I know that I’m not causing any thermal damage to the trabecular meshwork, and also I’m getting the effect I desire.” *Dr. David Gossage*

IRIDEX | MicroPulse

Ahmed I, Gossage D, Vold S. With Years of SLT Data, Why Consider MicroPulse? Webinar, June 2013.

View Webcast

MLT Treatment Parameters

Wavelength	532 nm
SLA Spot Size	300 µm
Contact Lens	Ritch 4-mirror
Duration	300 ms
Power	1000 mW
Duty Cycle	15%
Treatment Circumference	360° contiguous applications
Post-op Meds	None
Follow-up	1 month May vary based on level of severity

"Most importantly, I have not seen a single spike in IOP with the MLT treatment, a safety profile that I consider unprecedented in laser trabeculoplasty."

Steven Vold, MD
Fayetteville, AR

IRIDEX | µP MicroPulse

Ahmed I, Gossage D, Vold S. With Years of SLT Data, Why Consider MicroPulse? Webinar, June 2013.

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MLT / SLT Comparison

	MLT	SLT
Wavelength	532 nm and 577 nm	532 nm
Mechanism	Thermally effects - not destroys - pigmented TM cells without thermal or collateral damage	Selective destruction of pigmented TM cells without thermal or collateral damage
Learning Curve	Easy	Easy
Repeatable	Yes	Yes
Visible signs of treatment intra-or post-operative	No	Yes
Post-op spikes/inflammation	No	Yes
Spot Size	300 µm*	400 µm
Complications	Minimal to none	Post-op IOP spikes are possible
Functionality of laser system	CW and MicroPulse treatment for glaucoma and retinal disorders	SLT
Parameter Control	Power, ON/OFF time, number and rep rate of pulses	Pulse energy

*Smaller spot to access narrow angles

IRIDEX | MicroPulse

Ahmed I, Gossage D, Vold S. With Years of SLT Data, Why Consider MicroPulse? Webinar, June 2013.

View Webcast

Why Choose MLT?

- Reasonable first-line therapy:
  - Addresses concerns of compliance with medical therapy
  - Advantages over meds: reduce patient cost, no side effects
- Causes less tissue damage than SLT and ALT
- Clinical Efficacy
- Repeatability
- Portability
- Multi-functionality
- Less expensive than SLT

IQ 532™

IQ 577™

IRIDEX | MicroPulse

MicroPulse™

First, do no harm

www.iridex.com/micropulse | Tissue-Sparing Bibliography | Patient Education

IRIDEX | MicroPulse

Technology | Retina | Glaucoma

Appendix

MicroPulse Clinical Results – Vujosevic

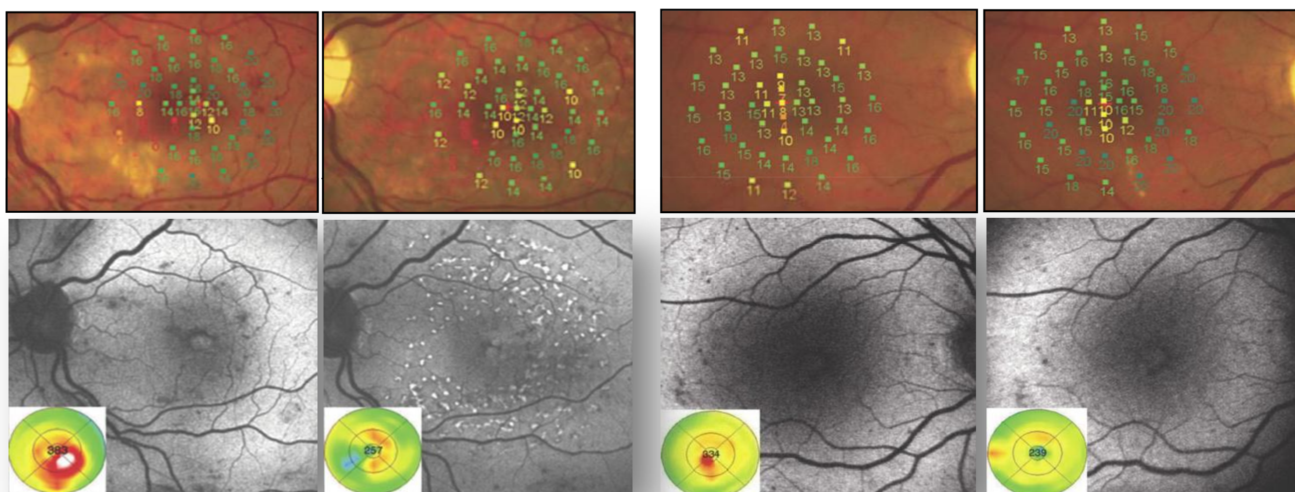
Using Low Intensity / High Density Protocol for DME

- A prospective, randomized clinical trial on 62 eyes (50 patients) with untreated, center-involving, clinically significant DME.
- Significant difference was found in retinal sensitivity using microperimetry. Sensitivity increased in the subthreshold MicroPulse group and decreased in the mETDRS group (*P = 0.04* at 4º and *P* < 0.0001 at 12º)

Modified ETDRS | **Subthreshold MicroPulse**

Microperimetry

Fundus Autofluorescence and OCT



Pre-treatment | 1 Yr Post-treatment | Pre-treatment | 1 Yr Post-treatment

IRIDEX | MicroPulse

Vujosevic S, Bottega E, Casciano M, Pilotto E, Convento E, Midena E. Retina 2010

MicroPulse Clinical Results - Lavinsky

Comparison of mETDRS vs. Low Density vs. High Density Protocols for DME

- A prospective, double-masked, controlled clinical trial on 123 eyes with DME
- Compared three dosing protocols and followed patients for a minimum of 1 yr
- Results:

	Modified ETDRS	MicroPulse High Density	MicroPulse Low Density
Treatment Intensity	Mild	Low	Low
Treatment Density	Low	High	Low
OCT-CMT (Δ)	-126 µm	-154 µm	-32 µm
BCVA (Δ letters)	+4	+12*	-1
Gain ≥15 letters	23%	48%*	5%

*Indicates significant improvement compared to mETDRS ($P < 0.05$)

Lavinsky D, Cardillo JA, Melo LA, Jr., Dare A, Farah ME, Belfort R Jr. Invest Ophthalmol Vis Sci 2011

MicroPulse Clinical Results - Luttrull

Lesion Intensity vs. Duty Cycle for DME

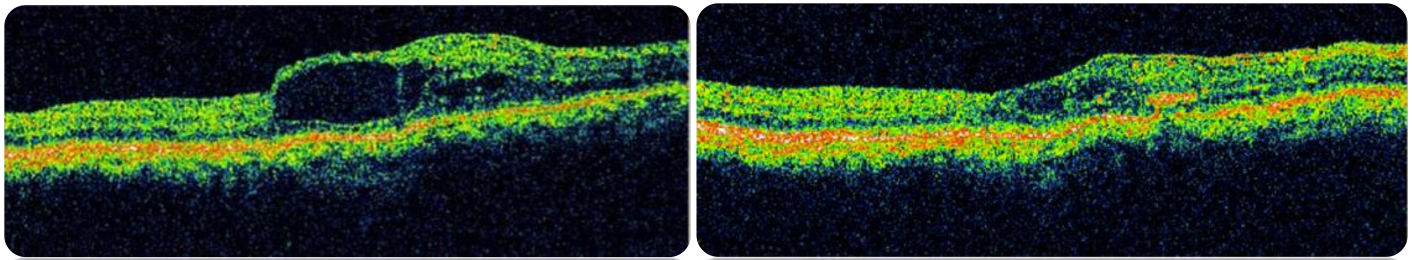
- Long-term retrospective review: 274 consecutive eyes with macular edema due to DME or BRVO were treated with MicroPulse high density laser treatment using various duty cycles (DC) and followed for up to 10 years. 252 eyes met inclusion criteria.
- Results:

Frequency of laser-induced retinal damage:

- Eyes treated with 10-15% DC 8% (7/84)
- Eyes treated with 5% DC 0% (0/168)

- **5% DC treated eyes showed no detectable retinal damage using infrared, red-free or FAF photos; FA, ICGA; or SD-OCT at 12 months**

MicroPulse Treatment for CSDME



Pre-treatment

3 Months Post-treatment

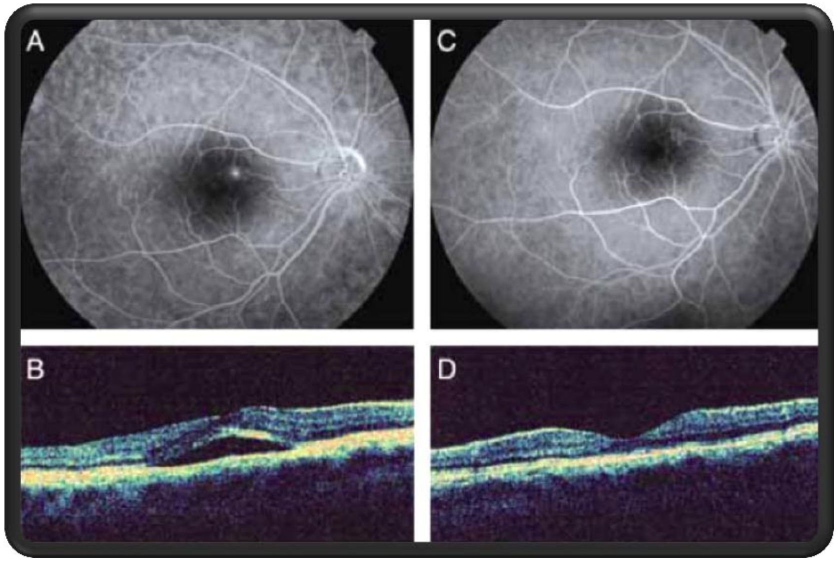
Images compliments of Dr. Jeffrey Luttrull

IRIDEX | MicroPulse

Luttrull JK, Sramek C, Palanker D, Spink CJ, Musch DC. Retina 2012;32(2):375-86

MicroPulse Clinical Results for CSC - Lanzetta

- A prospective study of 24 eyes with CSC for more than 3 months with no prior intervention were treated with nonvisible MicroPulse laser.
- At 14 months (mean, range 3 to 36 months) follow-up:
  - Subretinal fluid completely absorbed in 17 eyes. Mean RT was 328 µm preop; 168 µm at end of follow-up (*P* < 0.0001)
  - VA improved or had no change in 22 eyes
  - No evidence of RPE or retinal changes due to laser treatment was discernible in any eye treated with power < 2 W
  - No patients had any complications from treatment



Pre-op: **(A)** FA shows focal leak of dye**. (B)** Subretinal fluid is visible at OCT. At 6 months post 1 treatment: FA **(C)** and OCT **(D)** confirm resolution of leakage and neuroretinal detachment.

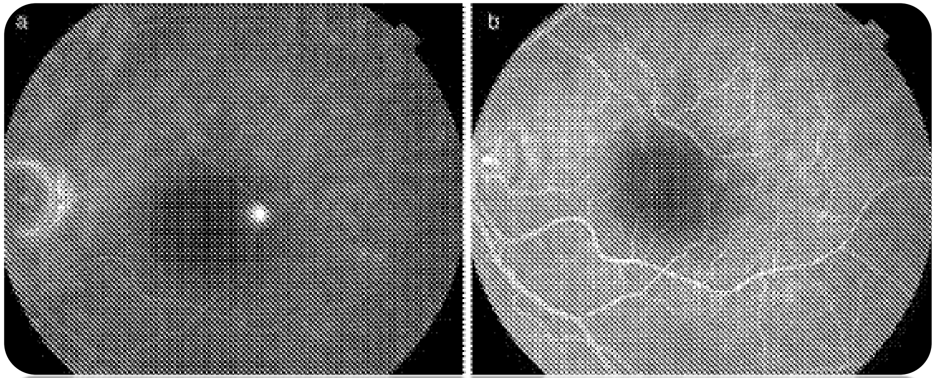
Lanzetta P, et al. Eur J Ophthalmol 2008

IRIDEX | MicroPulse

MicroPulse Clinical Results for CSC - Gupta

- A retrospective case series of 5 patients with CSC treated with MicroPulse.
- At 17.1 months (mean, range 6 to 24 months) follow-up, 4 of 5 patients had complete resolution of symptoms.

(A) FFA showing pretreatment juxtafoveal leakage. MicroPulse was applied to the area of focal juxtafoveal angiographic leakage.
(B) Decreased leakage postop. Symptoms of distortion resolved within 2 days, the central dim area resolved in 5 days. VA improved from 6/12 to 6/6 and remains stable at 20 months follow-up.



Gupta B, Elagouz M, McHugh D, Chong V, Sivaprasad S. Clin Experiment Ophthalmol 2009;37(8):801-5.

IRIDEX | MicroPulse

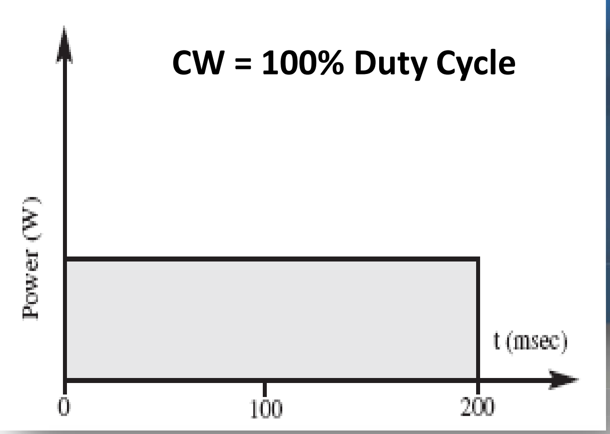
MicroPulse Clinical Results for CSC - Koss

- A comparative, controlled, prospective study comparing MPLT, intravitreal BCZ injection, and observation for the treatment of CSC in 52 eyes of 52 patients.
- At 10 months, results showed:
  - BCVA, macular perimetry, and metamorphopsia improved after MicroPulse, whereas the control group showed no improvements; 80% of patients in the BCZ group had persistent metamorphopsia.
  - MicroPulse treated eyes showed superior to BCZ for resolution of subretinal fluid with no tissue reactions during and at any point after treatment.

			Post treatment		
		Baseline	6 Wks	6 Mos	10 Mos
MicroPulse	Leakage activity	16/16 (100%)	10/16 (62.5%)	7/16 (43.75%)	2/16 (12.5%)
	CMT (µm)	419	387	329	325
	BCVA (total ltrs)	45.4	47.8	50.5	51.6
BCZ	Leakage activity	10/10 (100%)	3/10 (30%)	6/10 (60%)	6/10 (60%)
	CMT (µm)	393	355	334	355
	BCVA (total ltrs)	44.1	41.9	42.4	43.5
Control	Leakage activity	26/26 (100%)	26/26 (100%)	24/26 (92%)	24/26 (92%)
	CMT (µm)	388	396	388	415
	BCVA (total ltrs)	46.4	46.3	44.9	44.5

Koss MJ, Beger I, Koch FH. *Eye (Lond)* 2011 published online ahead of print

MicroPulse Technology



- Pulse ON time: Duration of each MicroPulse
- Pulse OFF time: Interval between MicroPulses
- Period (T): ON time + OFF time
- Duty Cycle (%): Pulse ON time/T x 100
- Exposure Duration (Envelope) = # of MicroPulses x T

Example:

- Pulse ON: 0.1 ms (100 µs)
- Pulse OFF: 1.9 ms (1900 µs)
- Period (T): 2.0 ms (2000 µs)
- Duty Cycle (%): 5% (0.1/2.0 x 100)
- Exposure Duration: 200 ms (100 MicroPulses x 2.0 ms)

MicroPulse 5% Duty Cycle

100 µs (0.1 ms)

1900 µs (1.9 ms)

2000 µs (2.0 ms)

IRIDEX | MicroPulse

Modulation of Intracellular Biological Factors

- Laser photocoagulation alters the expression of intracellular biological factors
  - Up-regulates PEDF[1]
    - PEDF plays a role in inhibiting neovascularization by its anti-angiogenic activity
  - Up-regulates TSP1 gene expression[2]
    - TSP1 is one of the most potent anti-angiogenic factors known.
    - Ninety days after PC, TSP1-positive cells were seen at the edges of the laser lesions along the RPE cells.
    - Long-term up-regulation of TSP1 after photocoagulation suggests it may induce the anti-angiogenic properties of this gene which might contribute to the long-term beneficial effects of photocoagulation.
- MPLT alters the expression of intracellular biological factors
  - Stimulates SDF1[3]
    - SDF1 plays a key role in recruitment of bone marrow-derived reparative cells.
  - Stimulates ß-actin[3]
    - ß-actin is a protein that is involved in cell motility, structure and integrity

IRIDEX | MicroPulse

1. Ogata et al. Am J Ophthalmol 2001
2. Binz et al. FASEB 2006
3. Yu, et al. Invest Ophthalmol Vis Sci 2013

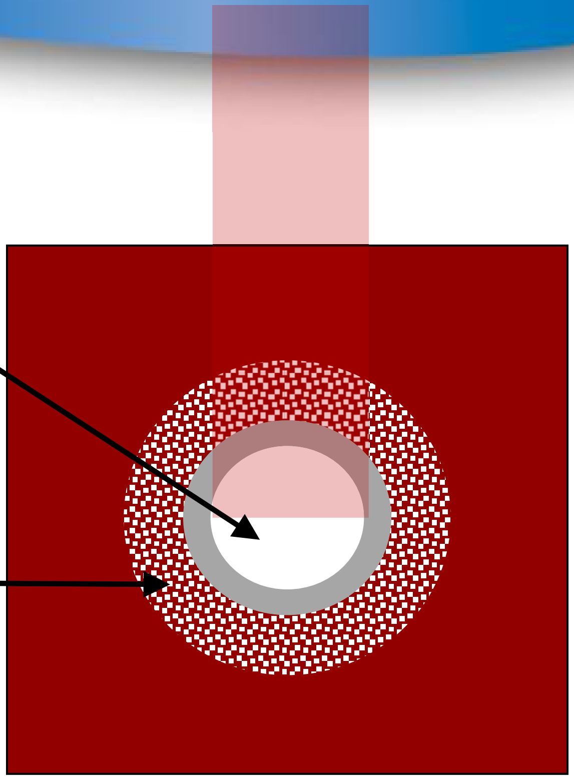
Evolution Towards Tissue-Sparing PC

Conventional (DRS/ETDRS) PC

- Treatment Endpoint
  - Visible, high intensity lesion

- Response of Directly Heated Tissue
  - Causes retinal blanching, destroys tissue, and results in post-treatment scarring which expands with time

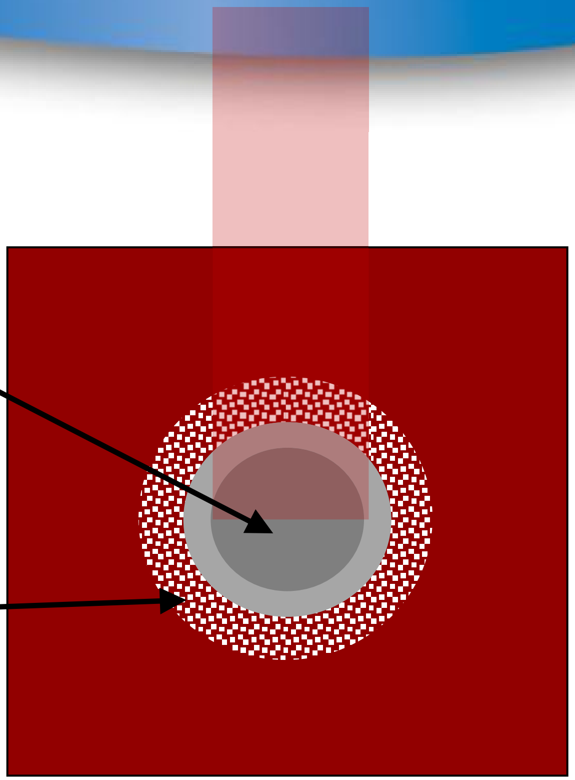
- Response of Indirectly Heated Tissue
  - Tissue remains viable and able to produce a stress response
  - Induces beneficial intracellular biological factors primarily anti-angiogenic and restorative (i.e. PEDF, TSP1)



IRIDEX | MicroPulse

Evolution Towards Tissue-Sparing PC
Modified Conventional (mETDRS) PC

- Treatment Endpoint
  - Barely visible threshold burn
- Response of Directly Heated Tissue
  - Causes *minimal* retinal blanching, destroys *less* tissue, but still results in some post-treatment scarring which expands with time
- Response of Indirectly Heated Tissue
  - Tissue remains viable and able to produce a stress response
  - Induces beneficial intracellular biological factors primarily anti-angiogenic and restorative (i.e. PEDF, TSP1)

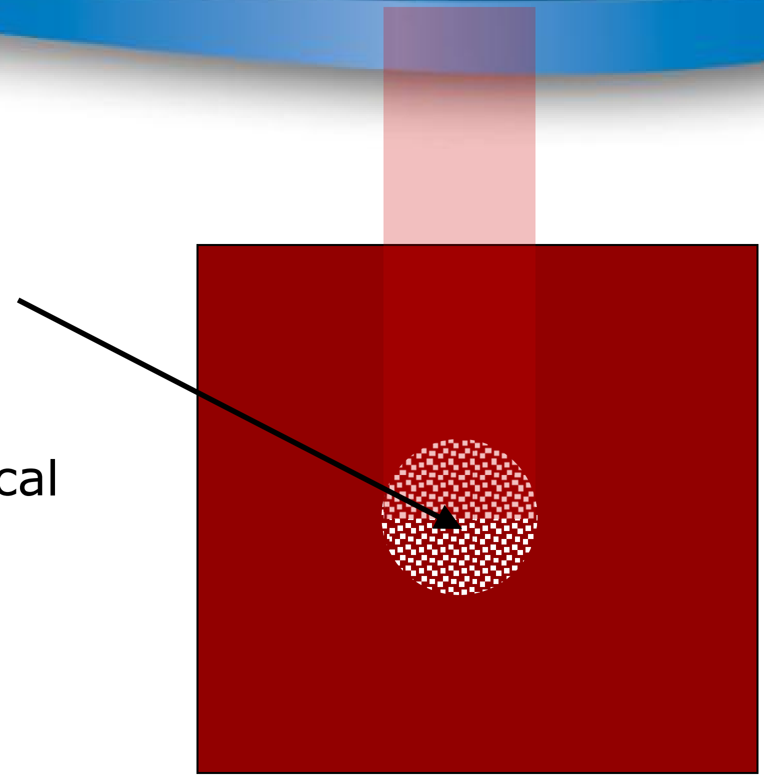


IRIDEX | MicroPulse

Evolution Towards Tissue-Sparing PC

Subvisible MicroPulse

- Treatment Endpoint
  - Subvisible
- Response of Directly Heated Tissue
  - Tissue remains viable and able to produce a stress response
  - Induces beneficial intracellular biological factors primarily anti-angiogenic and restorative (i.e. PEDF, TSP1)
- Response of Indirectly Heated Tissue
  - Negligible due to minimal thermal expansion to non-directly targeted tissue



IRIDEX | MicroPulse

Comparison - 810 nm and 577 nm MPLT

- Masked, independent grading of images, included
  - Retinal thickness and volume
  - Integrity and reflectivity of inner and outer retinal layers and choroidal microstructure on SD-OCT
  - Presence of hyper/hypo autofluorescence on FAF
  - Leakage and laser scars on FA
  - Mean central retinal sensitivity
  - Presence of absolute scotomas
  - Site and stability of fixation on MP1

	Baseline		**6 Months Follow-up**	
Wavelength	**810 nm**	**577 nm**	**810 nm**	**577 nm**
CRT	313.68±4.83 µm	323.14±6.76 µm	280.75±4.43 µm	291.74±6.65 µm
Macular Volume	11.28±0.18 mm^3	11.62±0.24 mm^3	11.10±0.16 mm^3	11.23±0.23 mm^3
Retinal Sensitivity	15.4±0.6 dB	14.7±0.5 dB	14.2±0.8 dB	13.2±0.7dB

IRIDEX | MicroPulse

Vujosevic S, Martini F, Convento E, Longhin E, Pilotto E, Midena E: Morphologic and Functional Effects of Diode(810nm) and Yellow(577nm) Subthreshold Micropulse Laser in Center-Involving Diabetic Macular Edema. *ARVO Meeting Abstracts* 2013;54(6):2380.

Treatment Guidelines: 810 nm MPLT for DME – Luttrull, Vujosevic

	Luttrull[1]	Vujosevic[2]
Emission Mode	810 nm MicroPulse	
SLA Spot Size Selection	125 µm	
Contact Lens & Mag.	Mainster Focal Grid (1.05X)	
Duration	300 ms	200 ms
Duty Cycle	5%	
Power	950 mW	750 mW
Technique	Confluent treatment of macular thickening up to FAZ. About 600 spots / macular quadrant	Laser spots are delivered in a multiple and continuous fashion up to 250 µm to 300 µm from the FAZ
Treatment Endpoint	None	

1. Luttrull JK, Sramek C, Palanker D, Spink CJ, Musch DC. *Retina* 2012;32(2):375-86.
2. Vujosevic S, Bottega E, Casciano M, Pilotto E, Convento E, Midena E. *Retina* 2010;30(6):908-916

IRIDEX | MicroPulse

Treatment Guidelines:
577 nm MPLT for DME - Mansour

	577 nm Subthreshold MPLT
Emission Mode	MicroPulse
SLA Spot Size Selection	200 µm
Contact Lens & Mag.	Mainster Focal Grid (1.05X)
Duration	200 ms
Duty Cycle	5%
Power	400 to 600 mW based on pigmentation*
Technique	Approximately 100 - 400 spots. Place dense treatment with contiguous applications over the entire edematous area based on OCT.
Treatment Endpoint	No visible tissue reaction during treatment

*For first time MicroPulse users, Dr. Mansour recommends performing a pre-treatment test burn to determine the MicroPulse treatment power. The test burn is performed in CW mode in a mildly edematous region > 2 DD from foveal center. Start at 50 mW and titrate power upward by increments of 10 mW (moving to a new area each time) until a barely visible tissue reaction is seen.

IRIDEX | MicroPulse

1. Mansour S, Gossage D. MicroPulse for the Ultimate Skeptic. Seeing is Believing. Educational Workshop. Hawaiian Eye, 2013.

Treatment Guidelines:
532 nm MPLT for DME - Gossage

	Pre-Treatment Test Burn	Subthreshold MicroPulse Treatment
Emission Mode	532 nm CW	532 nm MicroPulse
SLA Spot Size Selection	100 µm	
Contact Lens & Mag.	Mainster Focal Grid (1.05X)	
Duration	100 ms	200 ms
Duty Cycle	100 % (CW)	5%
Power	Start at 100 mW and titrate power upward by increments of 10 – 50 mW (moving to a new area each time)	2x power determined in the test burn
Technique	Performed in a non-edematous area of the retina.	High density (confluent) applications over edematous area.
Treatment Endpoint	White burn	No visible tissue reaction during treatment

IRIDEX | MicroPulse

Ahmed I, Gossage D, Vold S. MicroPulse Educational Webinar: With Years of SLT Data, Why Should I Consider MicroPulse. June 2013.

Treatment Guidelines: 810 nm MPLT for CSC - Lanzetta

	Pre-Treatment Test Burn	Subthreshold MicroPulse Treatment
Emission Mode	810 nm CW	810 nm MicroPulse
SLA Spot Size Selection	200 µm	
Contact Lens & Mag.	3 Mirror Goldmann (1.08X)	
Duration	200 ms	
Duty Cycle	100 % (CW)	15%
Power & Technique	Power to observe mild retinal whitening obtained at the posterior pole.	Power determined in the test burn. Multiple overlapping spots placed over and adjacent to the area of RPE leak(s) or zones of RPE decompensation.
Treatment Endpoint	Retinal whitening	No visible change at the retina level was evident during and after irradiation when powers below 2 W were applied.

Lanzetta P, Furlan F, Morgante L, Veritti D, Bandello F. Eur J Ophthalmol 2008;18(6):934-40.

IRIDEX | MicroPulse

Treatment Guidelines:
810 nm MPLT for CSC - Gupta

	Pre-Treatment Test Burn	Subthreshold MicroPulse Treatment
Emission Mode	810 nm MicroPulse	
SLA Spot Size Selection	125 µm	
Contact Lens & Mag.	Area Centralis (1.06X)	
Duration	200 ms	
Duty Cycle	15%	
Power & Technique	Test exposures applied outside the treatment area and power increased until a threshold burn was obtained using MicroPulse mode.	Reduce power (determined by test burn) by 20% increments until there is no visible reaction. A grid of 5 – 10 exposures was applied at the area of leakage on FFA.
Treatment Endpoint	Threshold burn	None

Gupta B, Elagouz M, McHugh D, Chong V, Sivaprasad S. Clin Experiment Ophthalmol 2009;37(8):801-5

IRIDEX | µP MicroPulse

Treatment Guidelines:
810 nm MPLT for CSC - Koss

	Pre-Treatment Test Burn	Subthreshold MicroPulse Treatment
Emission Mode	810 nm CW	810 nm MicroPulse
SLA Spot Size Selection	125 µm	
Contact Lens & Mag.	Area Centralis (1.06X)	
Duration	200 ms	
Duty Cycle	100 % (CW)	15%
Power & Technique	In the nasal mid periphery, start at minimum setting and adjust upward the power until a light grayish visible burn is observed.	2x power determined in the test burn. Three repeated applications were delivered at leakage site(s), paying attention to subtle RPE color changes during laser treatment that would have prompted the immediate cessation of the laser treatment.
Treatment Endpoint	Grayish visible burn	No tissue reaction during and at any point after laser treatment.

Koss MJ, Beger I, Koch FH. Eye (Lond) 2012

IRIDEX | MicroPulse

Treatment Parameters

IQ 577™

- 577 nm MPLT for DME - Mansour More

IQ 532™

- 532 nm MPLT for DME - Gossage More

IQ 810™

- 810 nm MPLT for DME – Luttrull, Vujosevic More
- 810 nm MPLT for CSC – Lanzetta More
- 810 nm MPLT for CSC – Gupta More
- 810 nm MPLT for CSC - Koss More

IRIDEX | MicroPulse

MLT Treatment Parameters

Wavelength	532 nm
SLA Spot Size	300 µm
Contact Lens	Ritch 4-mirror
Duration	300 ms
Power	1000 mW
Duty Cycle	15%
Treatment Circumference	360° contiguous applications
Post-op Meds	None
Follow-up	1 month May vary based on level of severity

"Most importantly, I have not seen a single spike in IOP with the MLT treatment, a safety profile that I consider unprecedented in laser trabeculoplasty."

Steven Vold, MD
Fayetteville, AR

Ahmed I, Gossage D, Vold S. With Years of SLT Data, Why Consider MicroPulse? Webinar, June 2013.

View Webcast

Evolution towards Low Intensity & High Density Protocols

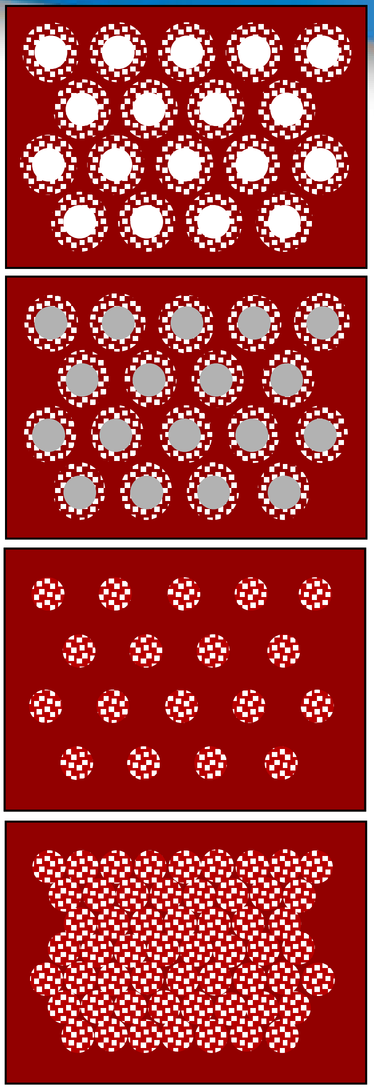
Conventional
High Intensity/Low Density

Modified Conventional
Mild Intensity/Low Density

MicroPulse LD
Low Intensity/Low Density (LD)

MicroPulse HD
Low Intensity/High Density (HD)

IRIDEX | µP MicroPulse



- **DRS Research Group. Ophthalmology 1978**
- **ETDRS Research Group. Arch Ophthalmol 1985**
- **and others**

- **Bandello, et al. Semin Ophthalmol 2001**
- **Bandello, et al. BJO 2005;**
- **Fong, et al. Arch Ophthalmol 2007**
- **and others**

- **Laursen, et al. BJO 2004**
- **Sivaprasad, et al. Clin Experiment Ophthalmol 2007**
- **Figueira, et al. BJO 2009**
- **Nakamura, et al. Eye 2010**
- **and others**

- **Luttrull, et al. BJO 2005**
- **Luttrull, et al. OSLI 2006**
- **Luttrull, et al. Eye 2008**
- **Vujosevic, et al. Retina 2010**
- **Ohkoshi, et al. AJO 2010**
- **Lavinsky, et al. IOVS 2011**
- **Luttrull, et al. Retina 2012**

MLT Clinical Efficacy

- 3 studies, all patients presented with POAG
  - Inclusion criteria: No previous laser treatment, previous ALT or MLT, with or without meds.
- Treatment parameters: 532 nm, 300-µm spot size, 300-ms duration, 15 % duty cycle, 360°, no post-op meds
- Power varied for each study:
  - 300 mW (13 eyes, 13 pts)
  - 700 mW (14 eyes, 14 pts)
  - 1000 mW (18 eyes, 18 pts)
- Results: At 4 months, a 30% reduction in IOP was obtained using 1000 mW

IRIDEX | MicroPulse

Ahmed I, Gossage D, Vold S. With Years of SLT Data, Why Consider MicroPulse? Webinar, June 2013

View Webcast