Tissue-Sparing MicroPulse™ Photocoagulation

MicroPulse™

First, do no harm

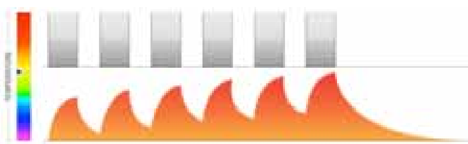
IRIDEX

What is MicroPulse?

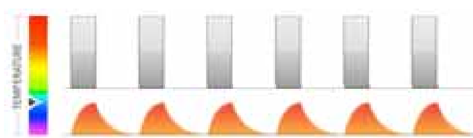
- A technology that finely controls thermal elevation by:
  - “chopping” a CW beam into a train of repetitive microsecond pulses
  - allowing tissue to cool between pulses to reduce thermal buildup

- Resulting in:
  - greater confinement of photothermal effects, and
  - equal or better patient outcomes with little or no collateral damage (vs. conventional laser therapy)

CW Laser Exposure (100%)



MicroPulse High Duty Cycle (DC) (15%)



MicroPulse Medium DC (10%)

MicroPulse Low DC (5%)

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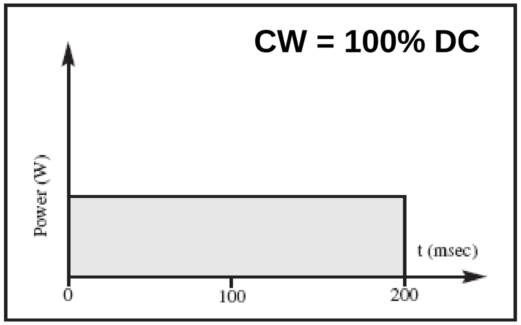
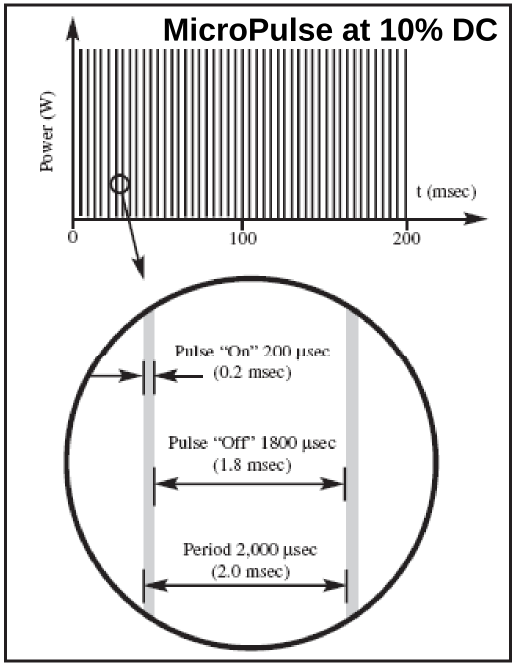
MicroPulse Terminology

- Pulse "On" time (MicroPulse Duration)
- Pulse "Off" time (MicroPulse Interval)
- "Period" or "Envelope"
  (sum of Duration and Interval)
- "Duty Cycle" (percent Duration over Period)

Example:

- Pulse "On": **0.2** ms (200 μs)
- Pulse "Off": 1.8 ms (1800 μs)
- Period: **2.0** ms (2000 μs)
- Duty Cycle: 10% = (**0.2**/**2.0**) x 100





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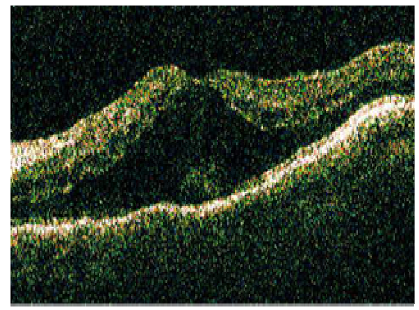
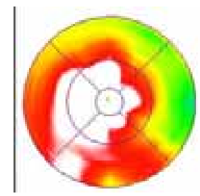
MicroPulse Clinical Applications

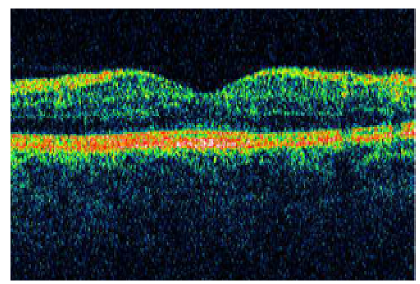
- Retinal Disorders
  - Macular Edema
    - Diabetes
    - BRVO
  - CSC
  - PDR
- Glaucoma Disorders
  - Primary open-angle glaucoma

IQ 577 MicroPulse
Macular edema secondary to BRVO

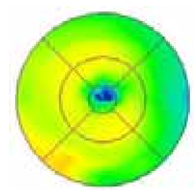


Pre-Treatment: 20/100





6 Months Post One Treatment: 20/20



Images compliments of Stanislav Saksonov, MD; and Sviatoslav Suk, MD, PhD; Eye Microsurgery Center, Laser Unit, Kiev, Ukraine

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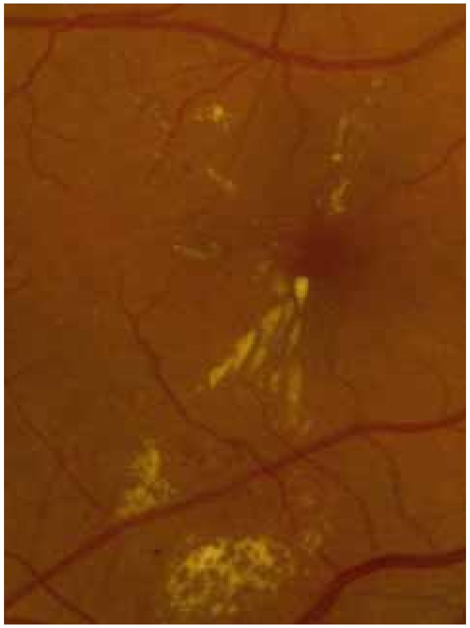
MicroPulse Clinical Applications

810 nm MicroPulse Treatment for DME



Pre-treatment: VA 20/32

4 months post-treatment

1 year post-treatment: VA 20/20.
Note, no signs of laser treatment.

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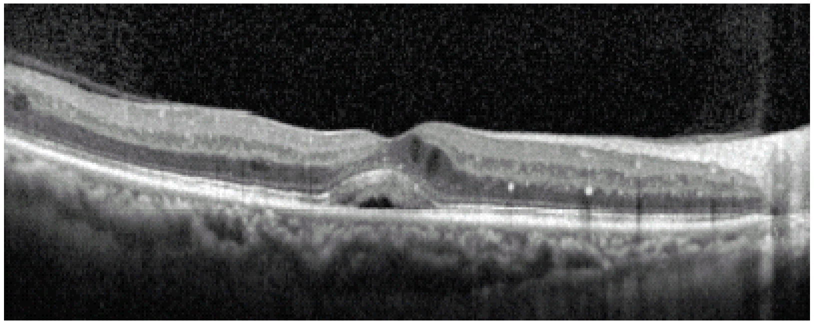
Images compliments of Dr. Victor Chong

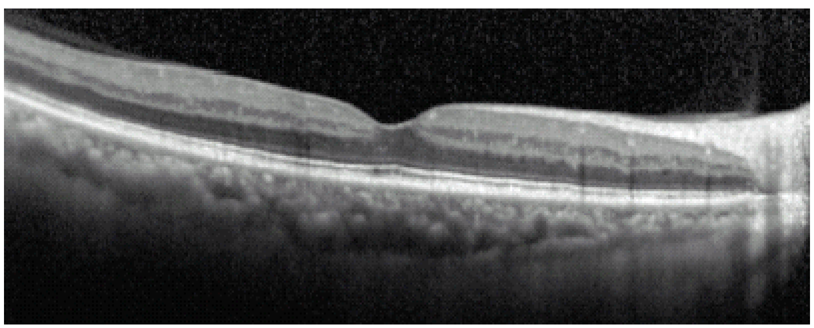
MicroPulse Clinical Applications

IQ 577 MicroPulse Treatment for CSDME

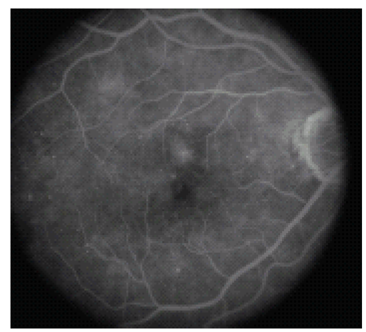


Pre-Treatment: SD-OCT, CRT 326 µm

FA, VA: $20/50^{-1}$



6 Weeks Post-Treatment: CRT 272 µm



VA: $20/25^{-1}$

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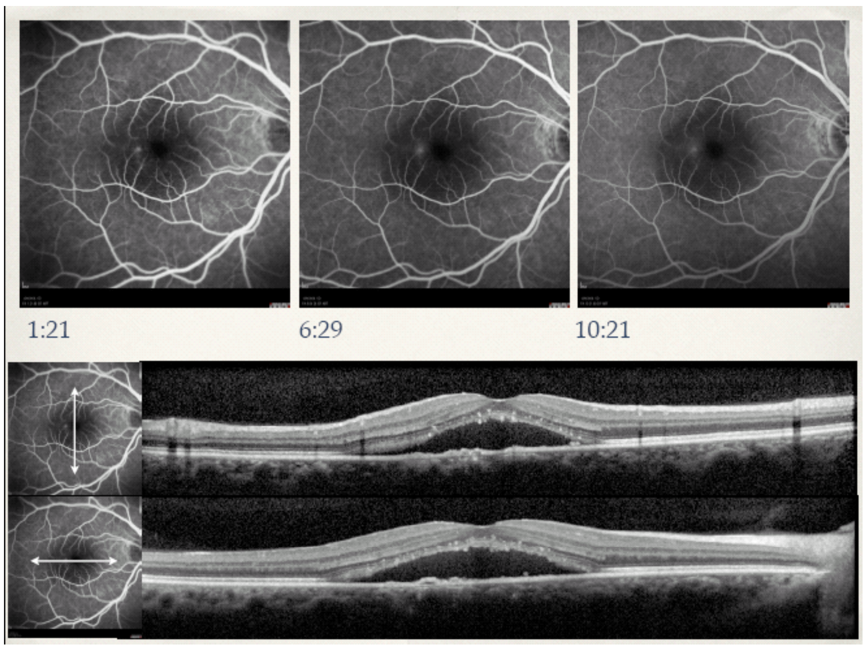
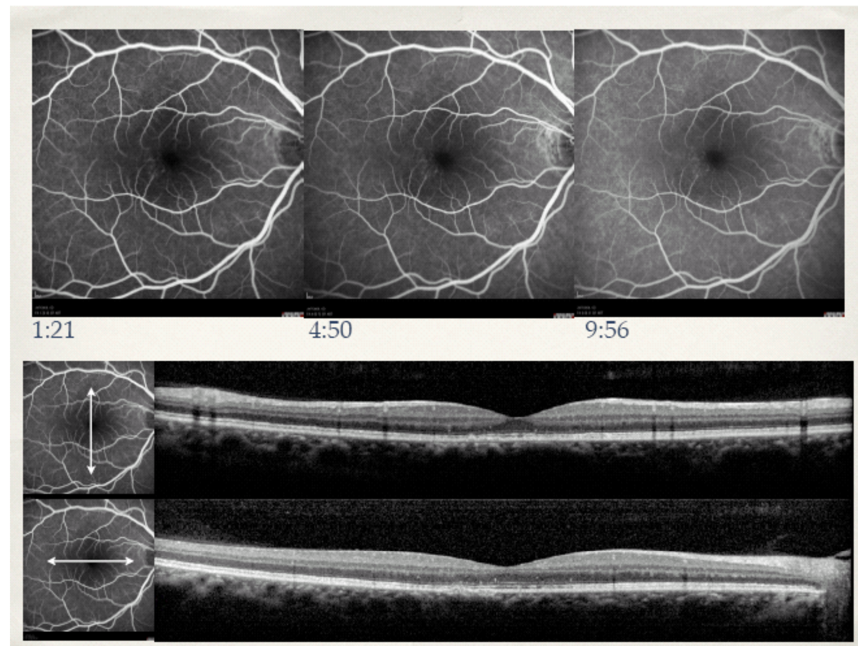
Images compliments of Dr. Sam Mansour

MicroPulse Clinical Applications

IQ 577 MicroPulse Treatment for CSC



Pre-Treatment: VA 20/80 for 8 months. Foveal-involved retinal detachment .



14 days Post-Treatment: VA 20/20. No signs of laser treatment. No leakage.

Images compliments of Dr. André Maia

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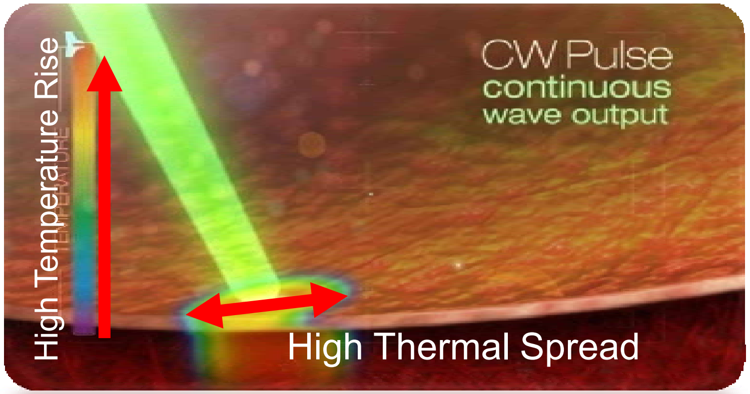
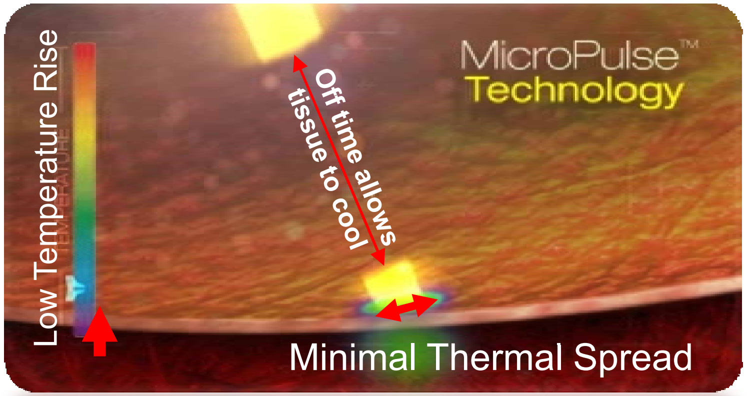
MicroPulse Differences/Advantages

Differences	Advantages
Lack of visible endpoint compared to conventional laser treatment	Absence of laser-induced retinal damage and related consequences associated with conventional laser protocols
Slower resolution of edema compared to pharma	Treatment results more durable than pharma
Risk of under treatment	Retreat as needed





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How does Tissue-Sparing MicroPulse Photocoagulation (PC) Work?

Evolution Towards Tissue-Sparing PC

- PC induces beneficial intracellular biological factors
  - PC up-regulates PEDF[1]
    - PEDF plays a role in inhibiting neovascularization by its anti-angiogenic activity
  - PC 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 PC suggests it may induce the anti-angiogenic properties of this gene which might contribute to the long-term beneficial effects of PC.
- MicroPulse limits thermal elevation below the threshold of tissue damage, and likely stimulates biological factors

IRIDEX

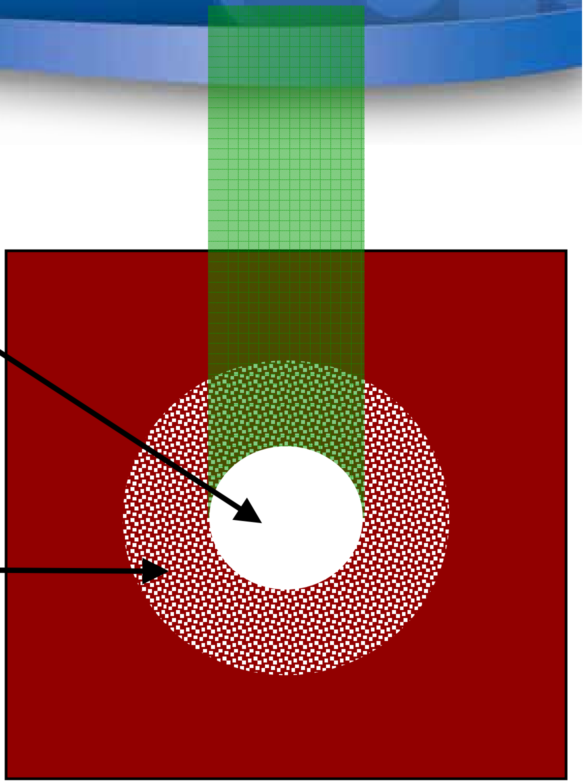
1. Ogata et al. *Am J Ophthalmol* 2001
2. Binz et al. *FASEB* 2006

Evolution Towards Tissue-Sparing PC
Conventional (DRS/ETDRS) PC

- Treatment Endpoint
  - Visible, high intensity lesion

- Response of Directly Heated Tissue
  - Causes retinal blanching, kills 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)
  - ***This is a new paradigm in the mechanism of action of laser photocoagulation***



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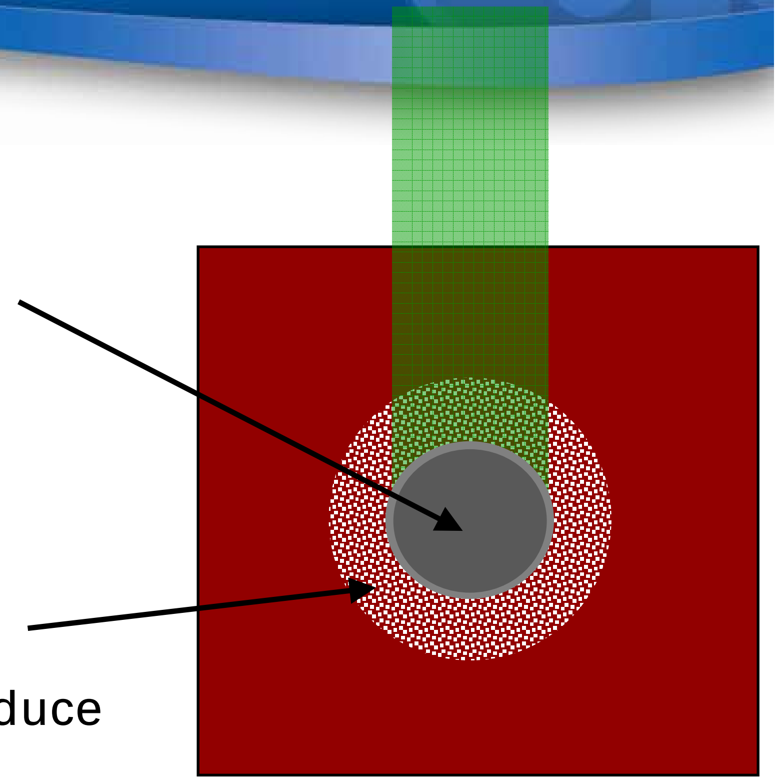
Evolution Towards Tissue-Sparing PC

Modified Conventional (mETDRS) PC

- Treatment Endpoint
  - Barely visible threshold burn
- Response of Directly Heated Tissue
  - Causes *minimal* retinal blanching, kills *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)



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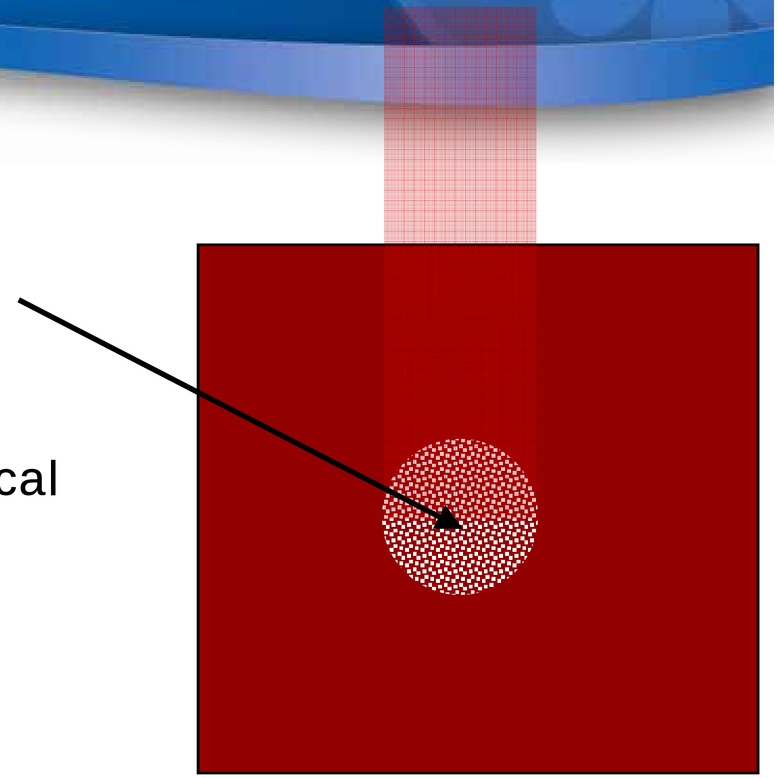
Evolution Towards Tissue-Sparing PC

Subvisible MicroPulse PC

- 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)
  - ***This supports the new paradigm in the mechanism of action of laser photocoagulation***



- Response of Indirectly Heated Tissue
  - Negligible due to minimal thermal expansion to non-directly targeted tissue

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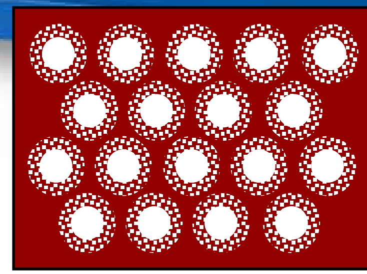
Evolution Towards Tissue-Sparing PC

Treatment Protocols (Intensity and Density)

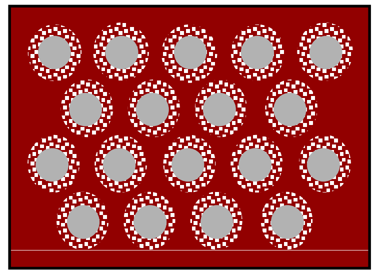
Conventional
High Intensity/Low Density



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

↓

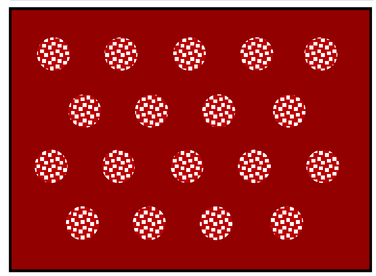
Modified Conventional
Mild Intensity/Low Density



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

↓

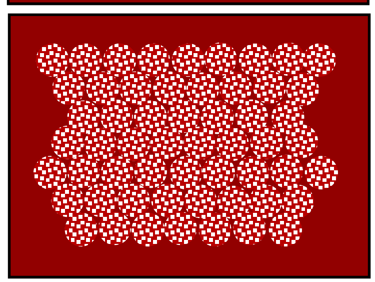
MicroPulse LD
Low Intensity/Low Density (LD)



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

↓

MicroPulse HD
Low Intensity/High Density (HD)



- 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

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Tissue-Sparing MicroPulse Clinical Results for DME

MicroPulse Clinical Results – Vujosevic

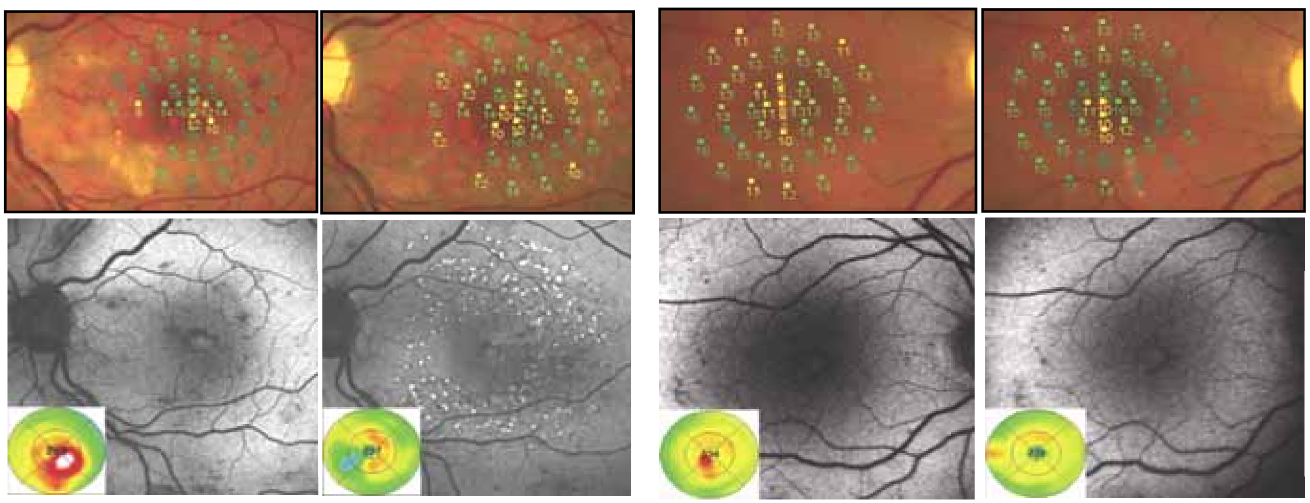
Using Low Intensity / High Density Protocol for DME

- 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

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 year
- Results:

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

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

IRIDEX

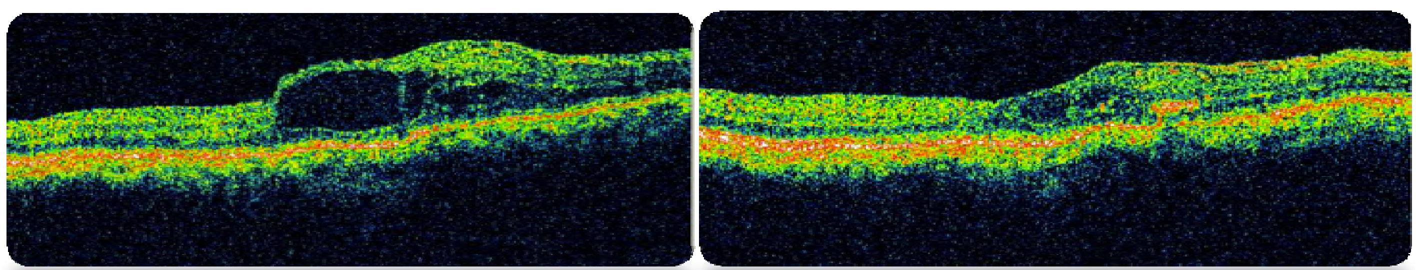
Lavinsky D, Cardillo JA, Melo LA, Jr., Dare A, Farah ME, Belfort R Jr. *Invest Ophthalmol Vis Sci* 2011

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

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

MicroPulse Clinical Results – DME

Using Low Intensity / High Density Protocols

High Density (HD) MicroPulse Therapy for DME		
Author	**Authors' Conclusions**	**Follow-up**
Vujosevic *Retina* 2010[1]	Effective as mETDRS laser in stabilizing visual acuity 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.	1 year
Lavinsky *IOVS* 2011[2]	Superior to the mETDRS based on BCVA improvement and CMT reduction.	1 year
Luttrull *Retina* 2011[3]	Can effectively treat retinovascular macular edema without laser-induced retinal damage.	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

Tissue-Sparing MicroPulse Treatment Guidelines for DME

Treatment Guidelines: 577 nm Tissue-Sparing MicroPulse for DME - Mansour

	Pre-Treatment Test Burn	Subthreshold MicroPulse Treatment
Emission Mode	CW	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 50 mW and titrate power upward by increments of 10 mW until a barely visible tissue reaction is seen, moving to a new location for each test.	2x power determined in the test burn
Technique	Performed outside the vascular arcades on flat retina	Dense treatment – contiguous pattern with the laser over the edematous area based on OCT.
Treatment Endpoint	Barely visible tissue reaction	Not visible – rely on objective post-treatment outcome measures (VA, OCT, FA)

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Sam Mansour, MD; Clinical Professor of Ophthalmology, The George Washington University. Personal communications 2011

Treatment Guidelines:
810 nm Tissue-Sparing MicroPulse for DME

	Luttrull[1]	Vujosevic[2]
Emission Mode	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. Long-term safety, high-resolution imaging, and tissue temperature modeling of subvisible diode micropulse photocoagulation for retinovascular macular edema. *Retina* 2012;32(2):375-86.
2. 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

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Tissue-Sparing MicroPulse Clinical Results for CSC

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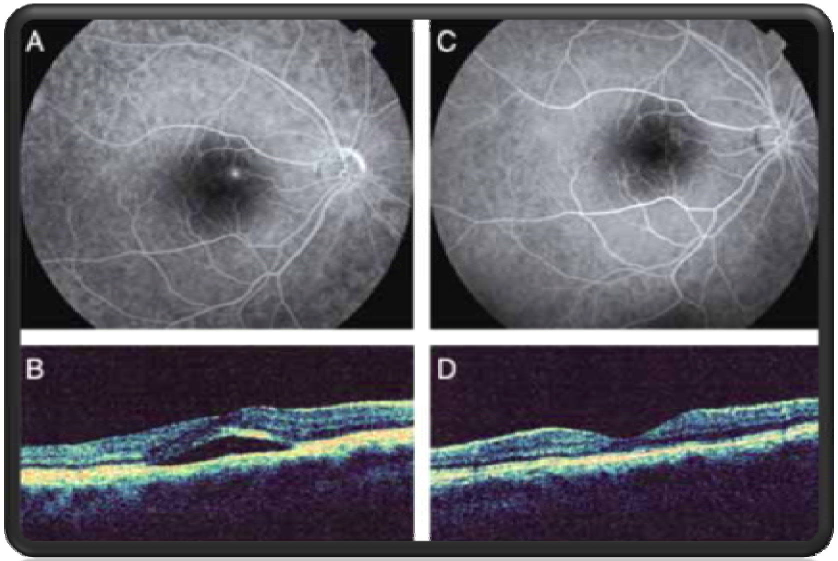
First, do no harm

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.

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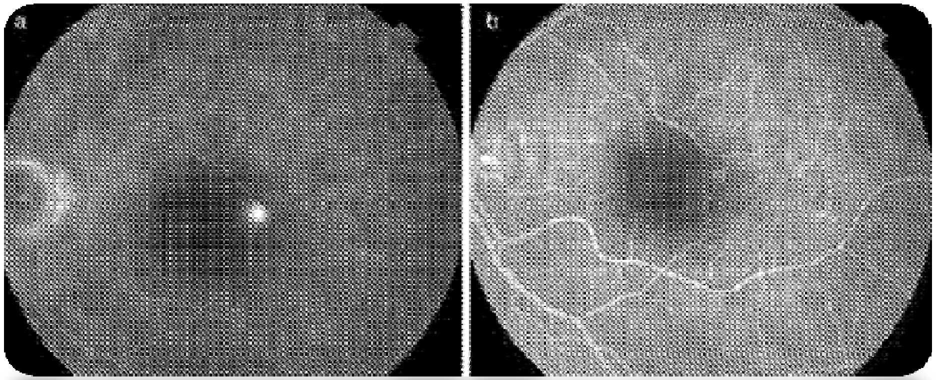
Lanzetta P, Furlan F, Morgante L, Veritti D, Bandello F. *Eur J Ophthalmol* 2008;18(6):934-40.

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.



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

MicroPulse Clinical Results for CSC - Koss

- A comparative, controlled, prospective study comparing MicroPulse, 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

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

MicroPulse Clinical Results - CSC

MicroPulse Therapy for CSC		
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.	14 months (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 PC with no detectable signs of laser-induced iatrogenic damage.	17.1 months (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.	10 months

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1. Lanzetta P, Furlan F, Morgante L, Veritti D, Bandello F. *Eur J Ophthalmol 2008;18(6):934-40.*
2. Gupta B, Elagouz M, McHugh D, Chong V, Sivaprasad S. *Clin Experiment Ophthalmol 2009;37(8):801-5.*
3. Koss MJ, Beger I, Koch FH. *Eye (Lond) 2011* published online ahead of print

Tissue-Sparing MicroPulse Treatment Guidelines for CSC

Treatment Guidelines:
810 nm Tissue-Sparing MicroPulse for CSC - Lanzetta

	Pre-Treatment Test Burn	Subthreshold MicroPulse Treatment
Emission Mode	CW	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.

IRIDEX

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

Treatment Guidelines:
810 nm Tissue-Sparing MicroPulse for CSC - Gupta

	Pre-Treatment Test Burn	Subthreshold MicroPulse Treatment
Emission Mode	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

Treatment Guidelines:
810 nm Tissue-Sparing MicroPulse for CSC - Koss

	Pre-Treatment Test Burn	Subthreshold MicroPulse Treatment
Emission Mode	CW	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.

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

MicroPulse is Commercially Available

- IRIDEX MicroPulse technology is available
  - Laser systems have FDA clearance
  - Available in 810 nm, 577 nm, and 532 nm wavelengths

IQ 810™

IQ 577™

IQ 532™

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MicroPulse
First, do no harm

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MicroPulse Forum >>

The MicroPulse Forum is an online community of leading MicroPulse surgeons and a clinical resource for tissue-sparing therapy protocols. The Forum offers a commonplace for surgeons to access our library of MicroPulse clinical material and review physicians' experiences.

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