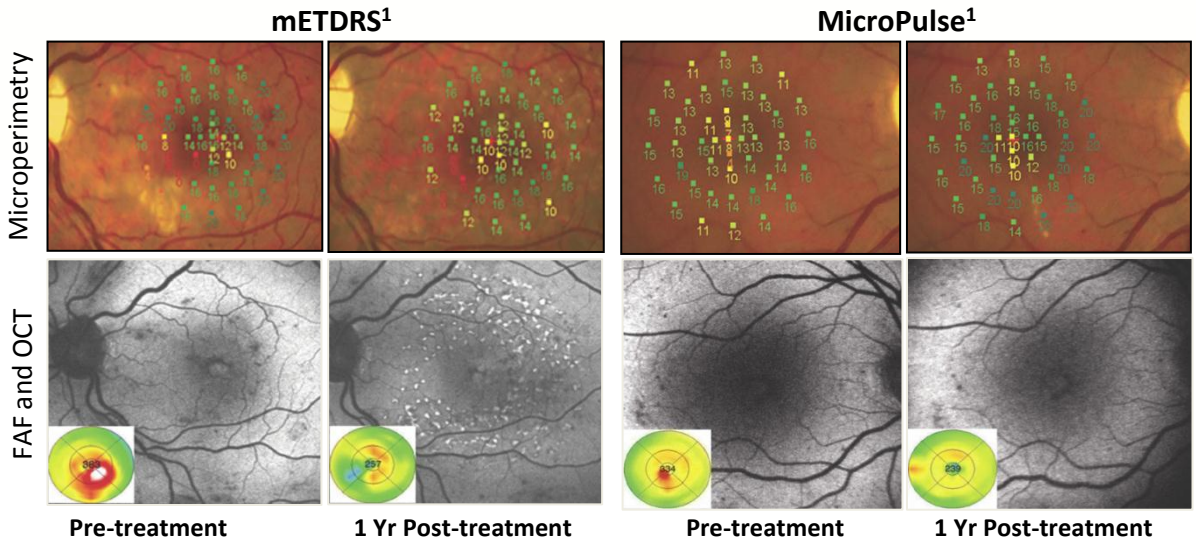
Fovea-Friendly™ MicroPulse® Laser Therapy

IRIDEX | MicroPulse®

MicroPulse = Increased Retinal Sensitivity without Damage



Prospective, Masked, Randomized Clinical Trial[1]

- 62 eyes (50 patients)
- Untreated, center-involving CSME
- Randomized to mETDRS or 810 nm MicroPulse

1 Year Results

- MicroPulse was as effective as mETDRS in
  - stabilizing VA
  - reducing macular edema
- With added benefits of
  - no tissue damage detectable at any time point postoperatively
  - significant improvement in retinal sensitivity

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

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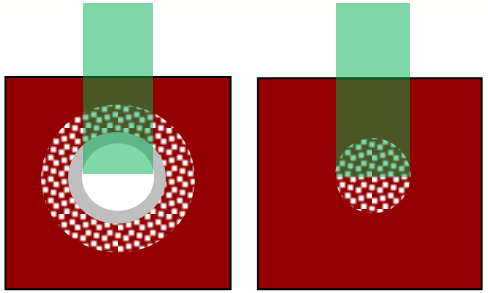
MicroPulse Stimulates Biological Factors

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

Modulation of the expression of intracellular biological factors



Visible Conventional CW (DRS/ETDRS)

Tissue-sparing MicroPulse

MicroPulse laser treatment, produces a stress response and induces beneficial intracellular biological factors that are primarily anti-angiogenic and restorative without tissue damage as seen in CW.

PEDF - plays a role in inhibiting neovascularization by its anti-angiogenic activity

TSP1 - one of the most potent anti-angiogenic factors

SDF1 - plays a key role in recruitment of bone marrow-derived reparative cells

ß-actin - protein that is involved in cell motility, structure and integrity

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.

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Considerations for Incorporating MicroPulse

- Safety
  - Fovea-friendly, no tissue damage, repeatable
  - Absence of laser scars minimizes vision loss over time
- Efficacy
  - Demonstrated through clinical studies and practical experience, durable therapy
- Efficiency
  - Quick and easy treatment
  - Faster than conventional focal or grid laser
- Economics
  - Patient $ ⬇
  - Healthcare System $ ⬇
  - Expense to Practice $ ⬇
  - Dual-laser Platform $ ⬇
  - Practice Revenue $ ⬆

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MicroPulse Efficacy & Safety: 810 nm

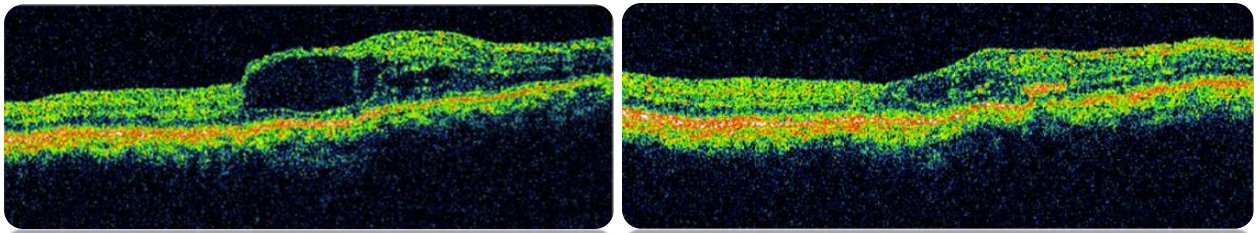
- Long-term retrospective review: 274 consecutive eyes with macular edema due to DME or BRVO were treated with MicroPulse high density laser treatment using various duty cycles (DC) and followed for up to 10 years. 252 eyes met inclusion criteria.
- Results:

  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

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

MicroPulse Efficacy & Safety: 810 nm & 577 nm

- 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

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

"[MicroPulse] should be introduced into the routine treatment protocols of DME as primary treatment in mild DME (<400 µm) or combined with intravitreal injections (both anti VEGF or corticosteroids) in moderate to severe DME."

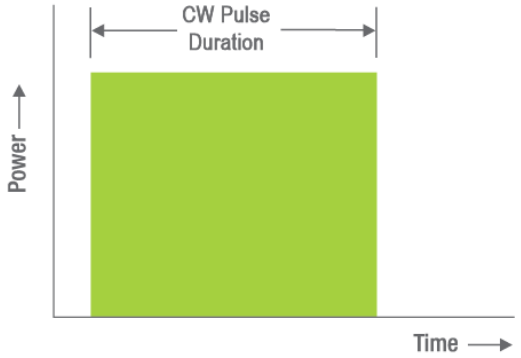
IRIDEX | MicroPulse®

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.

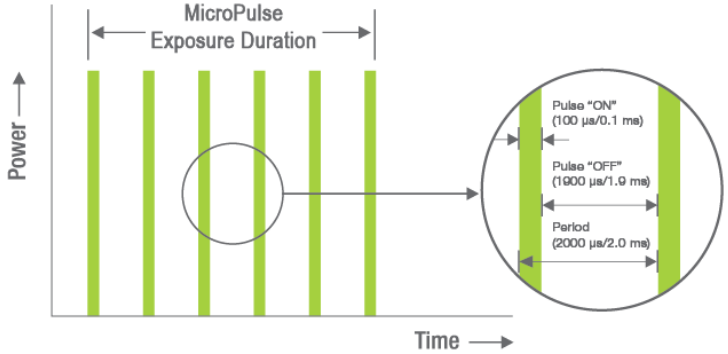
What is MicroPulse Technology?

MicroPulse technology finely controls thermal elevation by “chopping” a continuous-wave (CW) beam into an envelope of repetitive short pulses.

CW Mode



MicroPulse Mode



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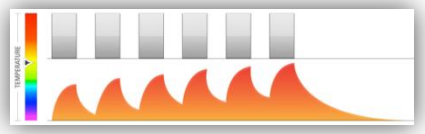
How Does MicroPulse Work?

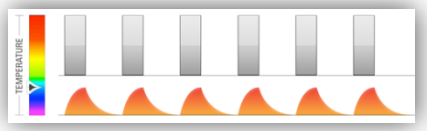
Repetitive short pulses permit tissue to cool between pulses and reduce thermal buildup.

CW Laser Exposure

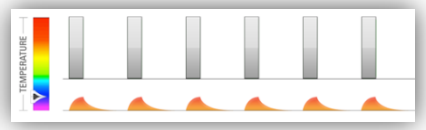
100% Duty Cycle (DC)



MicroPulse High DC (15%)



MicroPulse Medium DC (10%)



MicroPulse Low DC (5%)

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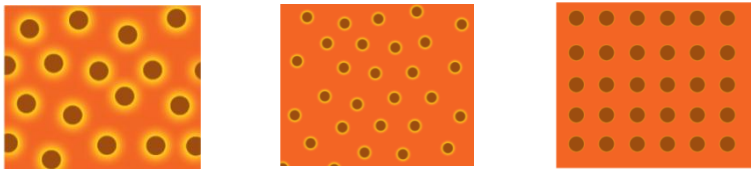
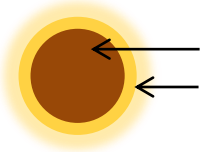
MicroPulse Low Intensity/High Density Application

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

Continuous-wave Laser



High-intensity argon | Low-intensity argon | Pattern Scanning

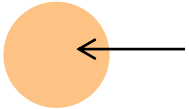


Area of retina damaged by laser

Area of retina affected by laser but not destroyed; able to contribute to the therapeutic effects of laser treatment

MicroPulse Laser

Low-intensity/ low-density | Low-intensity/ high density

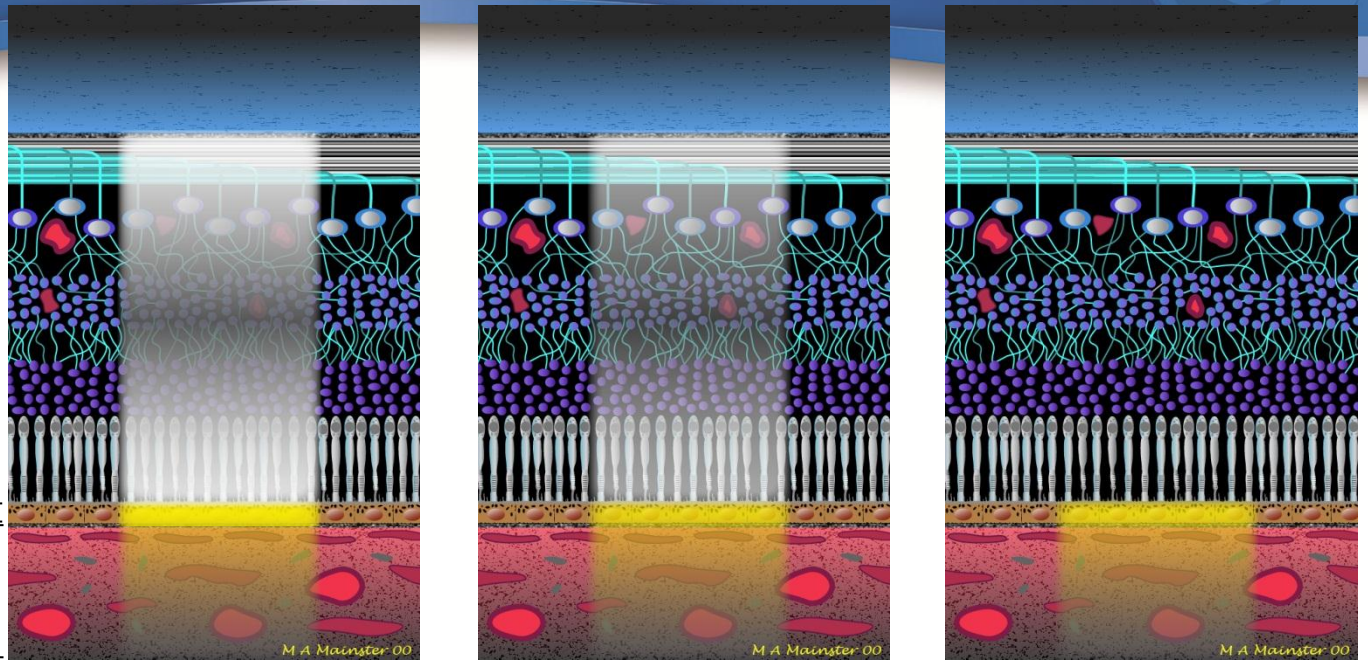


Area of retina affected by laser but not destroyed; able to contribute to the therapeutic effects of laser treatment

IRIDEX | MicroPulse®

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

Evolution of Subthreshold Photocoagulation



Continuous-Wave,
Conventional –DRS / ETDRS

Modified ETDRS

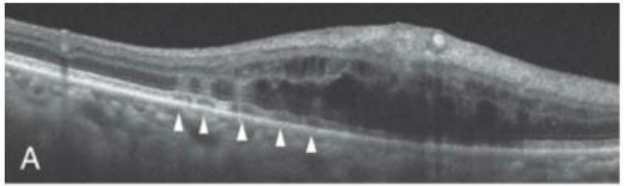
MicroPulse
Invisible By Biomicroscopy

IRIDEX | MicroPulse®

Illustrations compliments of Martin A. Mainster, PhD., MD, FRCOphth

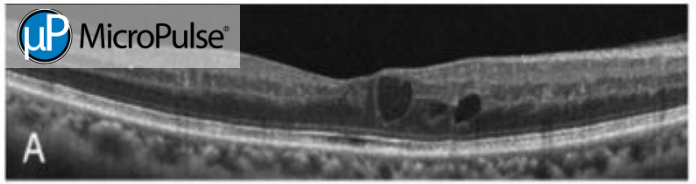
Barely Visible CW Scanning ≠ MicroPulse

Continuous-Wave Barely Visible Scanning



Fluid-like spikes adjacent to ruptured RPE (arrows) Immediately after CW and pattern scanning laser, a hyper-reflective band appeared at the laser sites.

IRIDEX MicroPulse



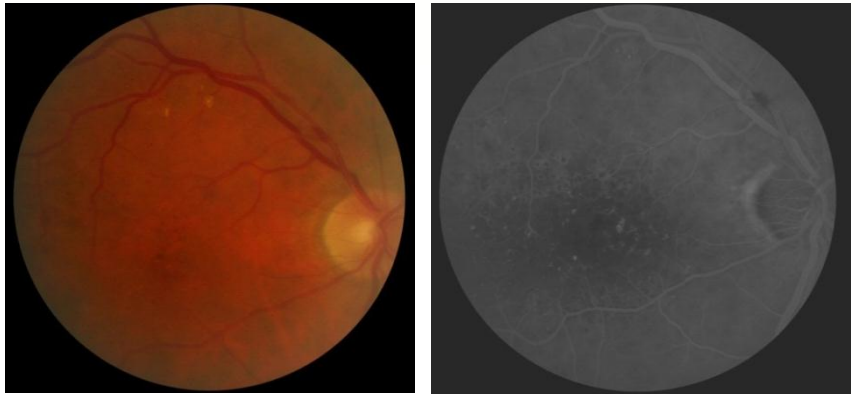
100% of tissue spared Retinal morphology did not change at any time during the observation period after MicroPulse.

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):1592-160

IRIDEX | MicroPulse®

Subvisible CW Scanning ≠ MicroPulse

Subthreshold CW Laser
561 nm; 200 µm spot; 50 mW; 10 ms



Subthreshold CW Laser
532 nm; 200 µm spot; 50 mW; 30 ms

Photos compliments of Sam Mansour, MD

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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 ($P < 0.05$)

IRIDEX | MicroPulse

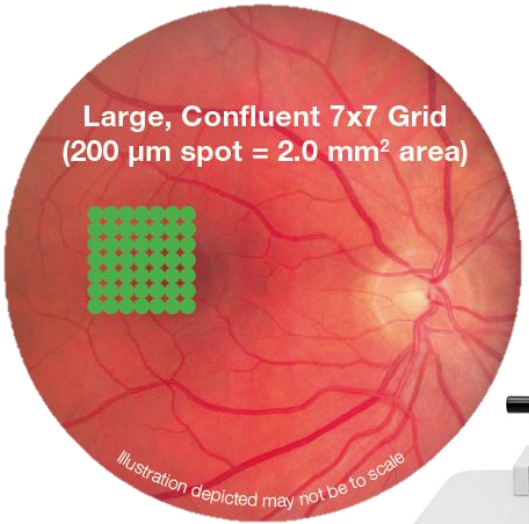
Lavinsky D, Cardillo JA, Melo LA, Jr., Dare A, Farah ME, Belfort R Jr. Invest Ophthalmol Vis Sci 2011

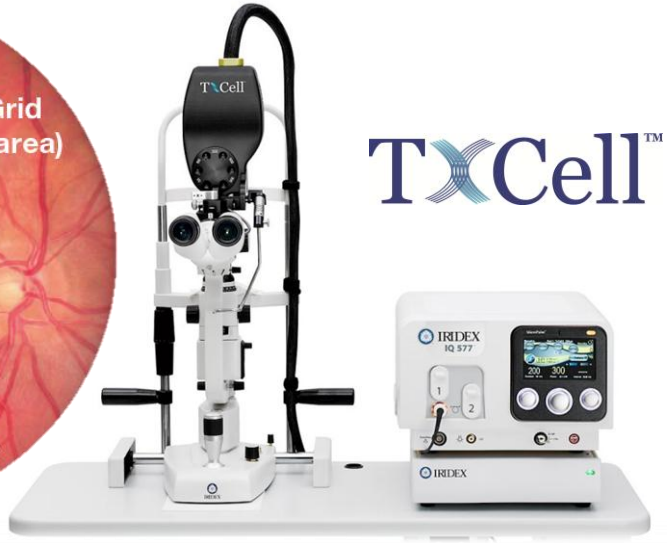
Clinical Success Using Confluent Spacing

Confluent, High-Density Laser Patterns For MicroPulse® Protocols

MicroPulse laser therapy has shown clinical success using confluent spacing.[1-2]

TxCell™ Scanning Laser Delivery System offers confluent, high-density applications in a wide selection of patterns.





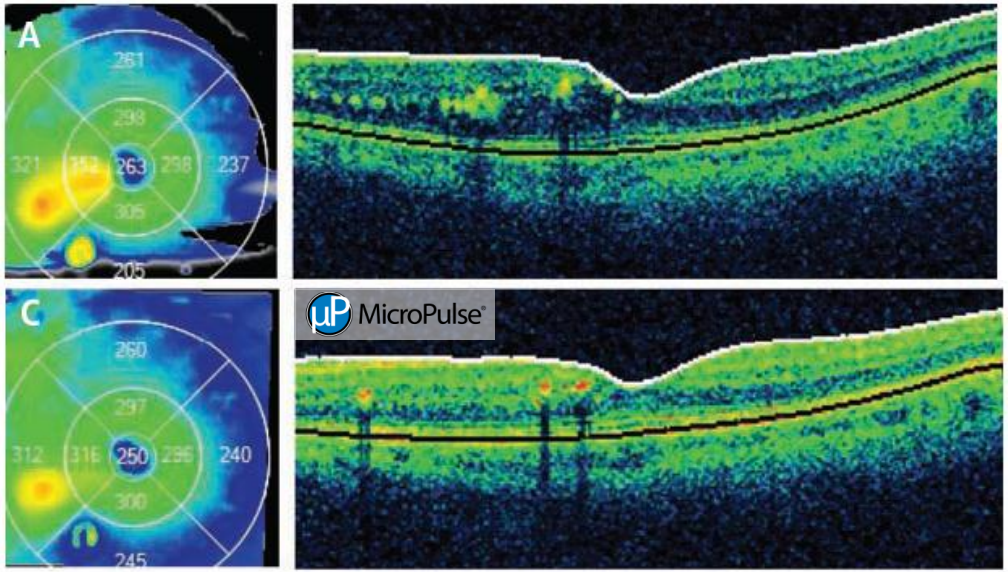
TXCell™

1. Luttrull JK, Sramek C, Palanker D, Spink CJ, Musch DC. *Retina* 2012;32(2):375-86
2. Lavinsky D, Cardillo JA, Melo LA, Jr., Dare A, Farah ME, Belfort R Jr. *Invest Ophthalmol Vis Sci* 2011; 52 (7): 4314-23

IRIDEX | MicroPulse®

TxCell-Guided MicroPulse for Center-Involving ME due to BRVO

Patient: 79-year-old female with BRVO and AMD.



Pre-MicroPulse: VA 20/30
Central retinal thickness 263 µm
Extrafoveal thickness 321 µm
Juxtafoveal thickness 352 µm

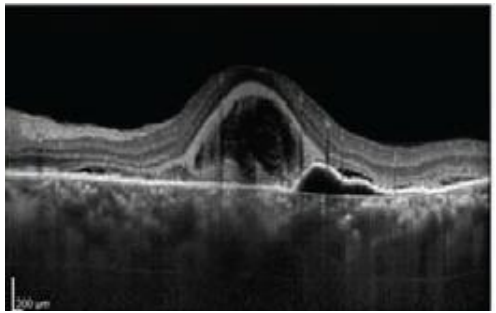
15 Weeks Post-MicroPulse: VA 20/25
Central retinal thickness 259 µm
Extrafoveal thickness 312 µm
Juxtafoveal thickness 329 µm

Read Case Report by Dr. David Gossage

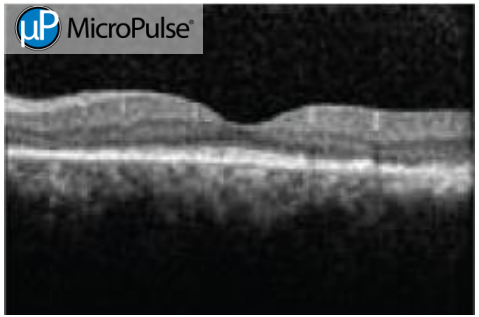
IRIDEX | MicroPulse®

TxCell-Guided MicroPulse for Central Serous Retinopathy

Patient: 54-year-old male with history of bullous CSR and a large persistent neurosensory detachment for 10 months after initial presentation.

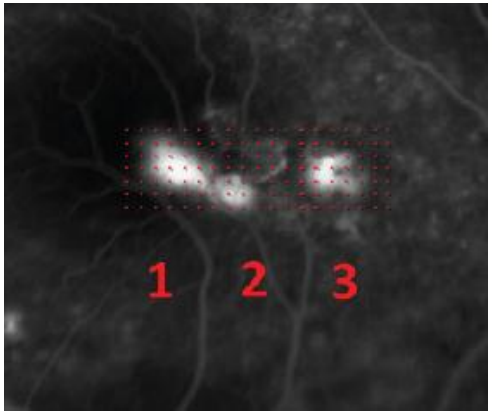


Pre-MicroPulse: VA 20/200
CMT 640 µm



4 mos Post-MicroPulse: VA 20/25
CMT 204 µm with complete resolution of subretinal fluid

Read Case Report by Dr. Gennady Landa

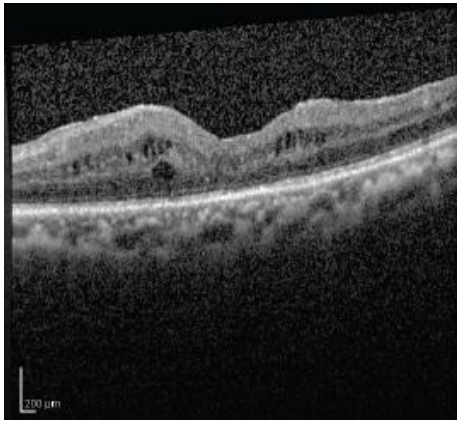


TxCell-guided MicroPulse: three 7x7 treatment grids placed confluently over all areas of leakage or fluid, including in the fovea.

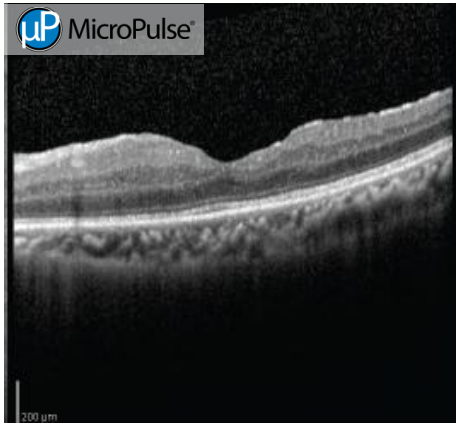
IRIDEX | MicroPulse

TxCell-Guided MicroPulse for DME

Patient: 79-year-old female with insulin-dependent diabetes mellitus and a history of nonproliferative diabetic retinopathy OU.



Pre-MicroPulse: VA 20/60
CST 340 µm



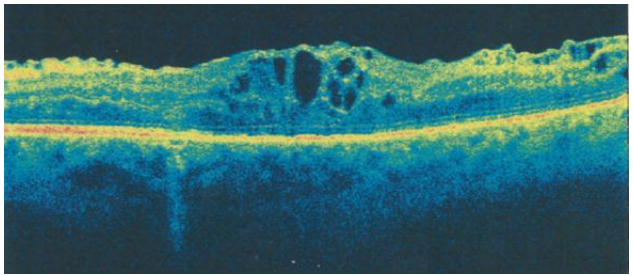
1 mo Post-MicroPulse: VA 20/40*
CST 280 µm *Baseline for patient

Read Case Report by Dr. Johnny Tang

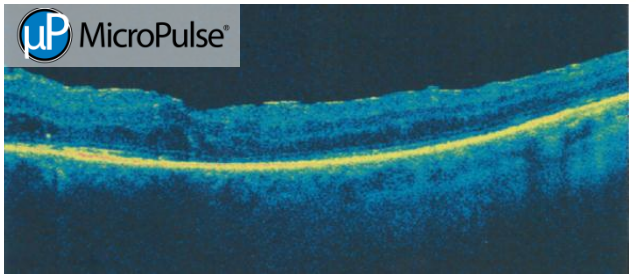
IRIDEX | MicroPulse

Center-Involving DME Refractive to Avastin and Ozurdex

Patient: 63-year-old male with very aggressive refractive DME that would not respond to anti-VEGF or steroid



Pre-MicroPulse: VA 20/200, CRT 438 µm



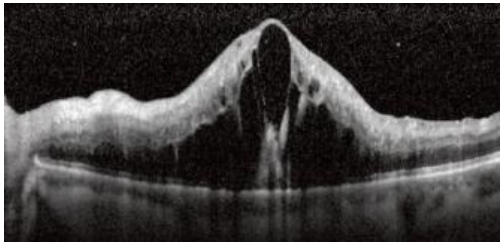
3 Months Post-MicroPulse: VA 20/60, CRT 270 µm

Read Case Report by Dr. Aaron Appiah

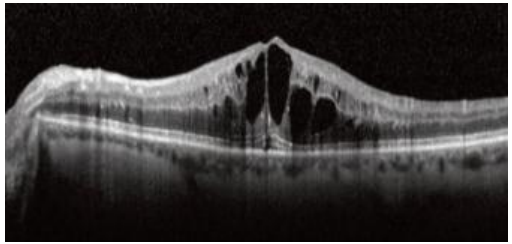
IRIDEX | MicroPulse

Macular Edema Associated with CRVO

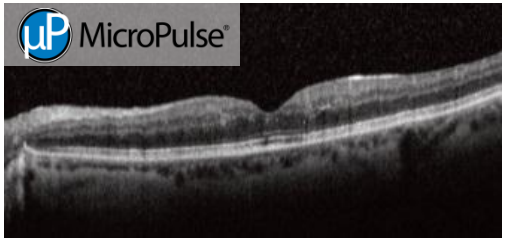
Patient: 64-year-old male with history of systemic hypertension



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



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



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

Read Case Report by Dr. Patrick Caskey

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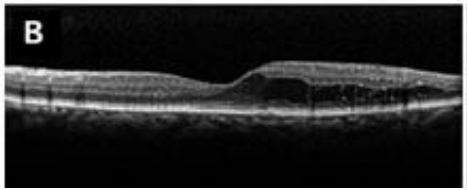
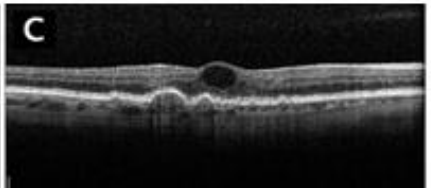
How would you treat these patients with good vision?

All patients have 20/20 to 20/40 VA.

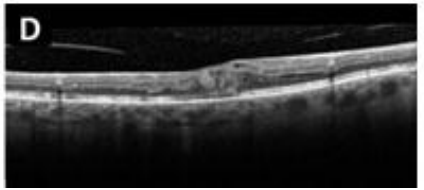
Intrafoveal cysts without retinal thickening.



Intrafoveal thickening with minimal central foveal thickening



Isolated central foveal cyst



Diffuse macular thickening including the fovea

IRIDEX | MicroPulse®

Transfoveal MicroPulse for DME for Patients with Good Vision

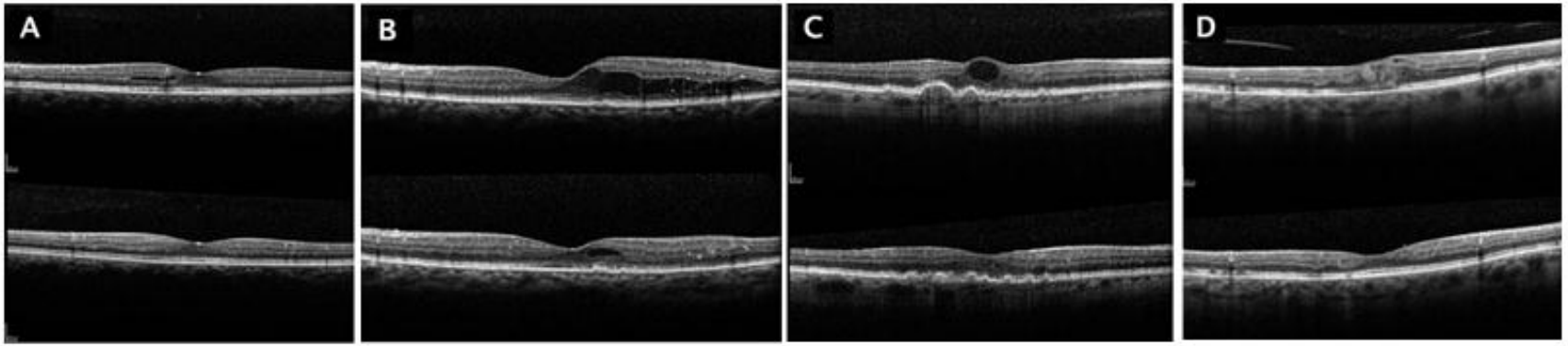
Luttrull. RETINA

SAFETY OF TRANSFOVEAL SUBTHRESHOLD DIODE MICROPULSE LASER FOR FOVEA-INVOLVING DIABETIC MACULAR EDEMA IN EYES WITH GOOD VISUAL ACUITY

JEFFREY K. LUTTRULL, MD,* STEPHEN H. SINCLAIR, MD† **RETINA** 34:2010–2020, 2014

Before

4 – 7 mos Post MicroPulse



Intrafoveal cysts without retinal thickening

Intrafoveal thickening with minimal central foveal thickening

Isolated central foveal cyst

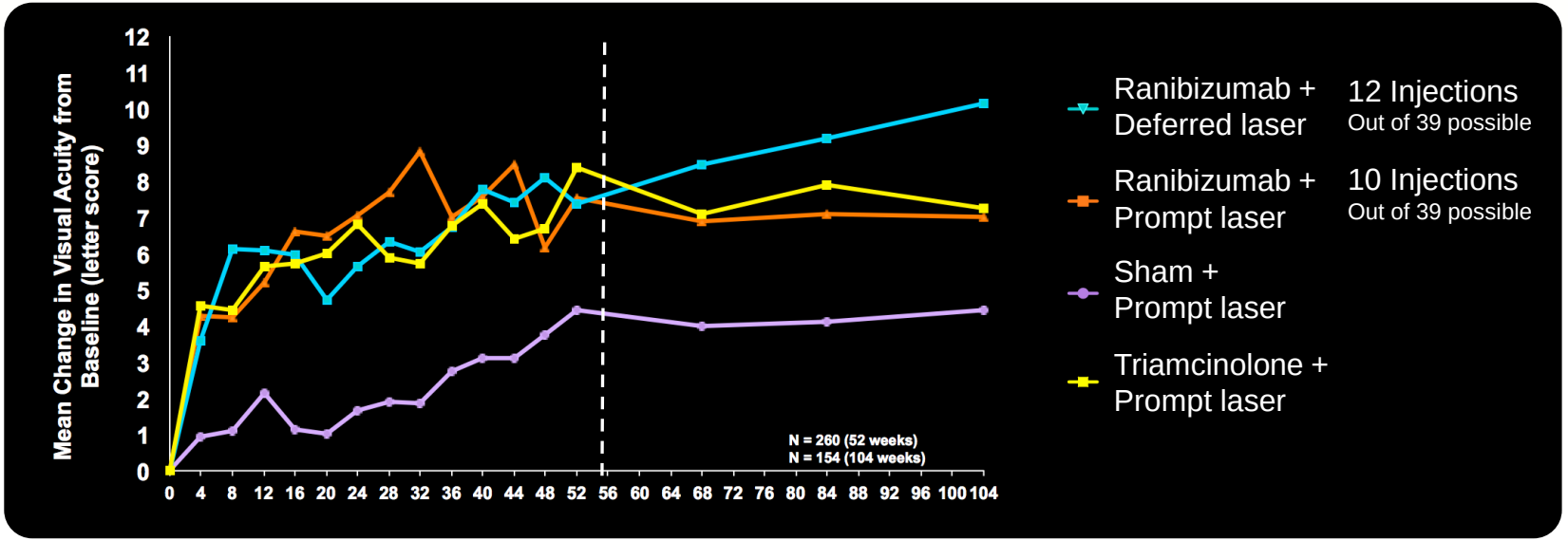
Diffuse macular thickening including the fovea

IRIDEX | MicroPulse®

Laser Still Plays a Critical Role in the Treatment of DME

In Protocol 1, patients with deferred* laser did best

(*deferred= waiting 6 months before treating with laser)



DRCR. Randomized Trial Evaluating Ranibizumab Plus Prompt or Deferred Laser or Triamcinolone Plus Prompt Laser for Diabetic Macular Edema *Ophthalmology* 2010; 117:1064-1077

Considerations for Incorporating MicroPulse

- Safety
  - Fovea-friendly, no tissue damage, repeatable
  - Absence of laser scars minimizes vision loss over time
- Efficacy
  - Demonstrated through clinical studies and practical experience, durable therapy
- Efficiency
  - Quick and easy treatment
  - Faster than conventional focal or grid laser
- Economics
  - Patient $⬇
  - Healthcare System $⬇
  - Expense to Practice $⬇
  - Dual-laser Platform $⬇
  - Practice Revenue $⬆

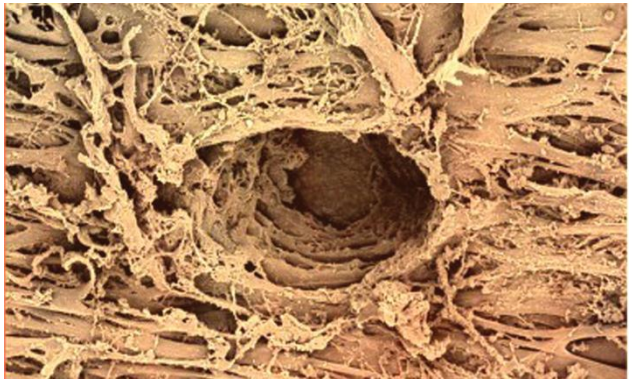
IRIDEX | MicroPulse®

Repeatable
MicroPulse® Laser Trabeculoplasty

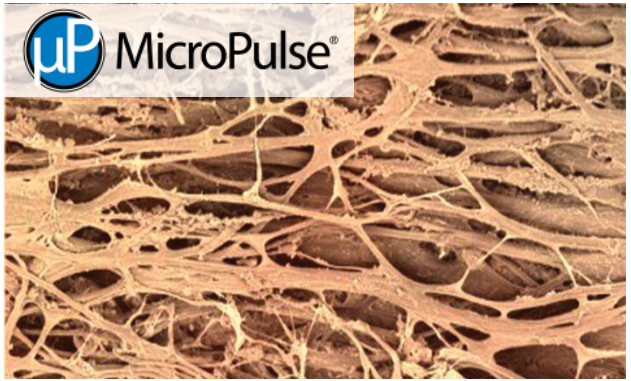
IRIDEX | MicroPulse®

 018PPT-MicroPulse Overview Abbr 01/2015

MicroPulse® Laser Trabeculoplasty (MLT)
for the Treatment of Glaucoma



Trabecular meshwork after ALT
Continuous-wave laser exposures can cause high thermal rise resulting in tissue damage



Trabecular meshwork after MLT
Meshwork remains intact without the signs of tissue damage while still as effective as ALT & SLT.[1]

1. Fudemberg SJ, Myers JS, Katz LJ, et al: Trabecular Meshwork Tissue Examination with Scanning Electron Microscopy: A Comparison of MicroPulse Diode Laser (MLT), Selective Laser (SLT), and Argon Laser (ALT) Trabeculoplasty in Human Cadaver Tissue. *Invest. Ophthalmol. Vis. Sci.* 2008;49(5):1236-.

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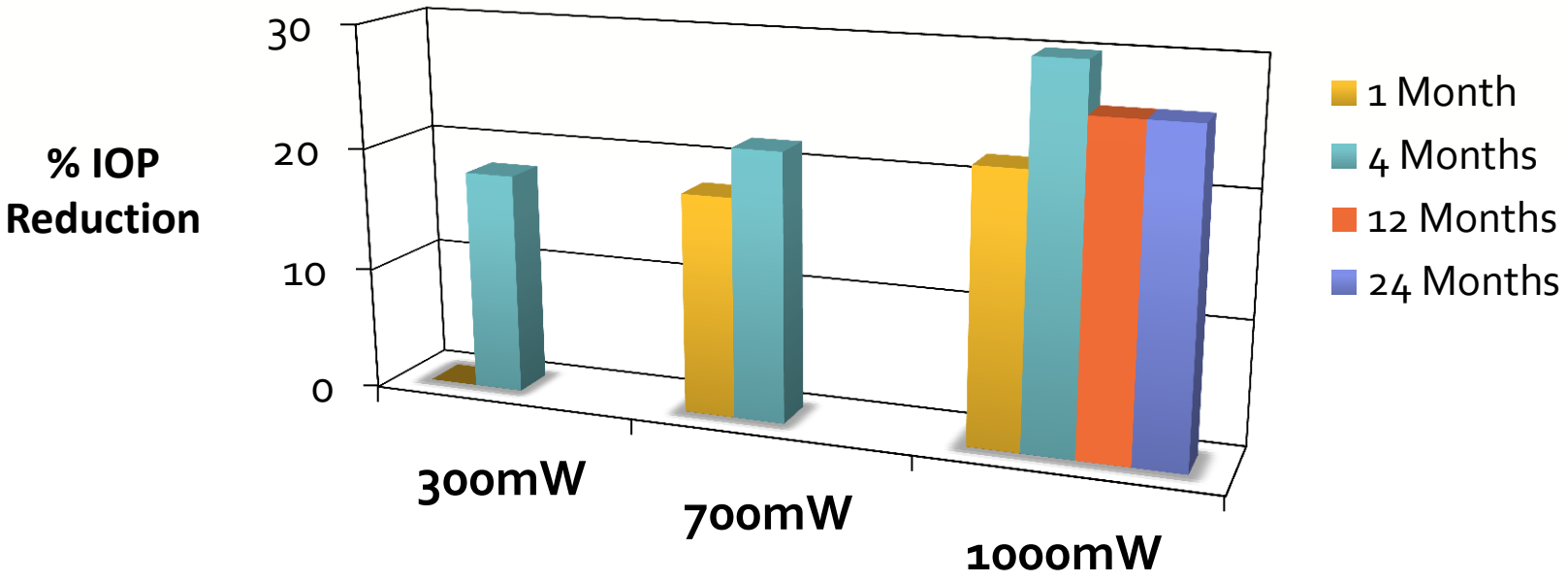
Evidence of Dose Response



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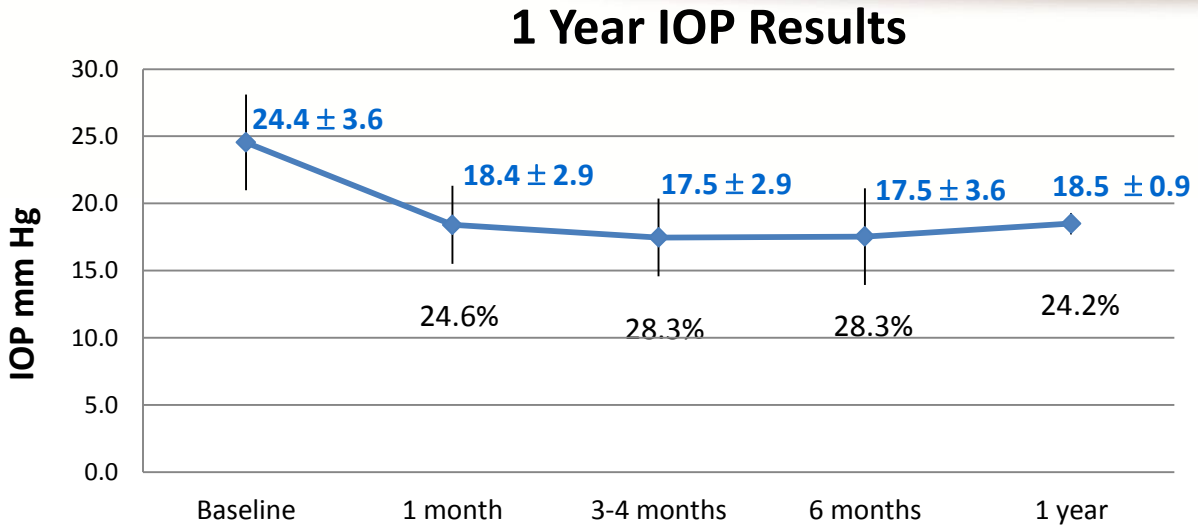
David Gossage, DO, FAOCO, FAAO , Gossage Eye Institute, Hillsdale, MI

Multi-Center 1000 mW MLT

Pre-op ≥ 21 mmHg

~ 6 mmHg drop

~ 25% IOP reduction



Meds
3.0 → 2.8 (NS)

# of pts	40	34	34	13	10

Ike Ahmed, MD, FRCSC, University of Toronto, Toronto, Canada
David Gossage, DO, FAOCO, FAAO , Gossage Eye Institute, Hillsdale, MI
Nathan Radcliffe, MD , Weill Cornell Medical College, New York, NY
Steven Vold, MD , Vold Vision, LLC Fayetteville, AR

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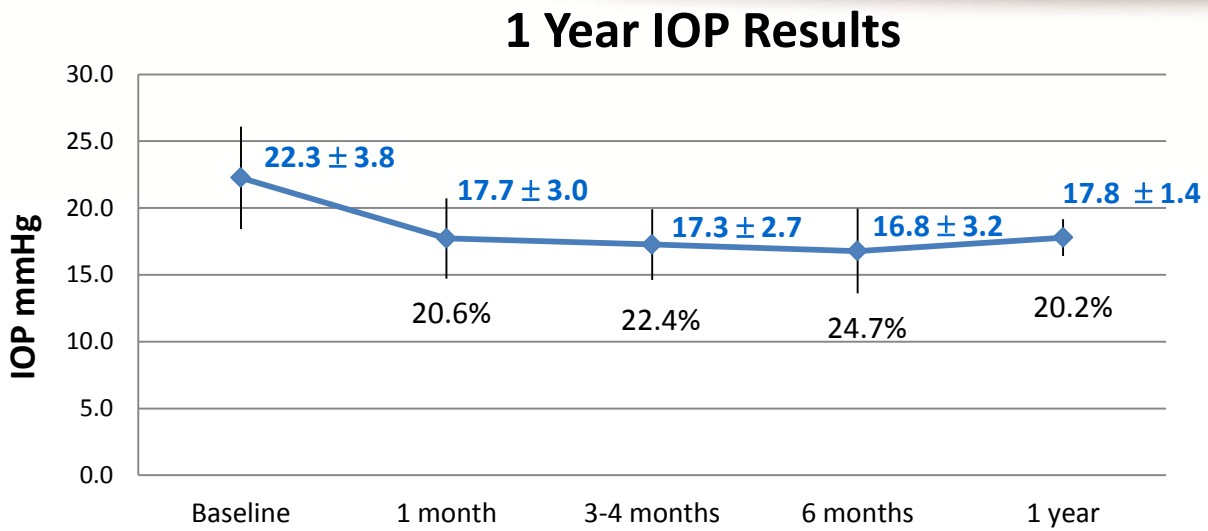
Multi-Center 1000 mW MLT

Pre-op ≥ 18 mmHg

~ 4.5 mmHg drop

~ 20% IOP reduction



Meds
2.9 → 2.3 (NS)

# of pts	66	54	52	23	14

Ike Ahmed, MD, FRCSC, University of Toronto, Toronto, Canada
David Gossage, DO, FAOCO, FAAO , Gossage Eye Institute, Hillsdale, MI
Nathan Radcliffe, MD , Weill Cornell Medical College, New York, NY
Steven Vold, MD , Vold Vision, LLC Fayetteville, AR

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MLT / SLT Comparison

	MicroPulse® Laser Trabeculoplasty (MLT)	Selective Laser Trabeculoplasty (SLT)
Wavelength	532 nm and 577 nm	532 nm
Mechanism	Thermally effects - not destroys - pigmented trabecular meshwork cells without thermal or collateral damage	Selective destruction of pigmented trabecular meshwork cells without thermal or collateral damage
Learning Curve	Easy	Easy
Repeatable	Yes	Yes
Visible signs of treatment intra-or post-operative	No	Yes
Inflammation	No	Yes
Spot Size	300 µm (smaller spot to access narrow angles)	400 µm
Complications	Minimal to none	Post-op IOP spikes are possible
Functionality of laser system	Continuous-wave and MicroPulse treatment for glaucoma and retinal disorders	SLT
Parameter Control	Power, ON/OFF time, number and rep rate of pulses	Pulse energy

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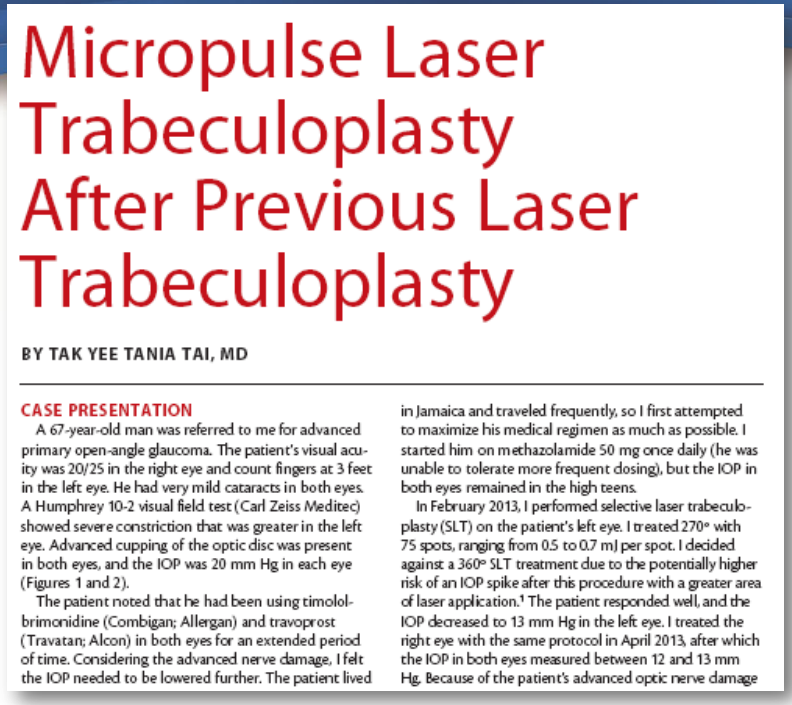
Ahmed I, Gossage D, Vold S. With Years of SLT Data, Why Consider MicroPulse? Webinar, June 2013.

MLT / SLT Comparison



Micropulse Laser Trabeculoplasty After Previous Laser Trabeculoplasty

BY TAK YEE TANIA TAI, MD

CASE PRESENTATION

A 67-year-old man was referred to me for advanced primary open-angle glaucoma. The patient's visual acuity was 20/25 in the right eye and count fingers at 3 feet in the left eye. He had very mild cataracts in both eyes. A Humphrey 10-2 visual field test (Carl Zeiss Meditec) showed severe constriction that was greater in the left eye. Advanced cupping of the optic disc was present in both eyes, and the IOP was 20 mm Hg in each eye (Figures 1 and 2).

The patient noted that he had been using timolol-brimonidine (Combigan; Allergan) and travoprost (Travatan; Alcon) in both eyes for an extended period of time. Considering the advanced nerve damage, I felt the IOP needed to be lowered further. The patient lived in Jamaica and traveled frequently, so I first attempted to maximize his medical regimen as much as possible. I started him on methazolamide 50 mg once daily (he was unable to tolerate more frequent dosing), but the IOP in both eyes remained in the high teens.

In February 2013, I performed selective laser trabeculoplasty (SLT) on the patient's left eye. I treated 270° with 75 spots, ranging from 0.5 to 0.7 mJ per spot. I decided against a 360° SLT treatment due to the potentially higher risk of an IOP spike after this procedure with a greater area of laser application.[1] The patient responded well, and the IOP decreased to 13 mm Hg in the left eye. I treated the right eye with the same protocol in April 2013, after which the IOP in both eyes measured between 12 and 13 mm Hg. Because of the patient's advanced optic nerve damage

Read Case Report by Dr. Tania Tai

Case Report

- Patient IOP rebound post SLT
- Physician concern with SLT repeat treatment because of potential IOP spikes
- MLT performed because no history of inflammation post treatment
- Patient's IOP dropped from 19 to 13 mm Hg and stable for 6 months

"For patients such as this one, with advanced disease and IOP spikes and for whom pharmaceutical treatments and previous laser treatments have failed, MLT is a viable option"

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Tai, *Glaucoma Today* November/December 2014

MicroPulse Technology available in Multi-Functional Laser Systems

IQ 577™

IQ 532™

IQ 810™

- 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 and CE clearance for both conventional and MicroPulse Laser Therapies

*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

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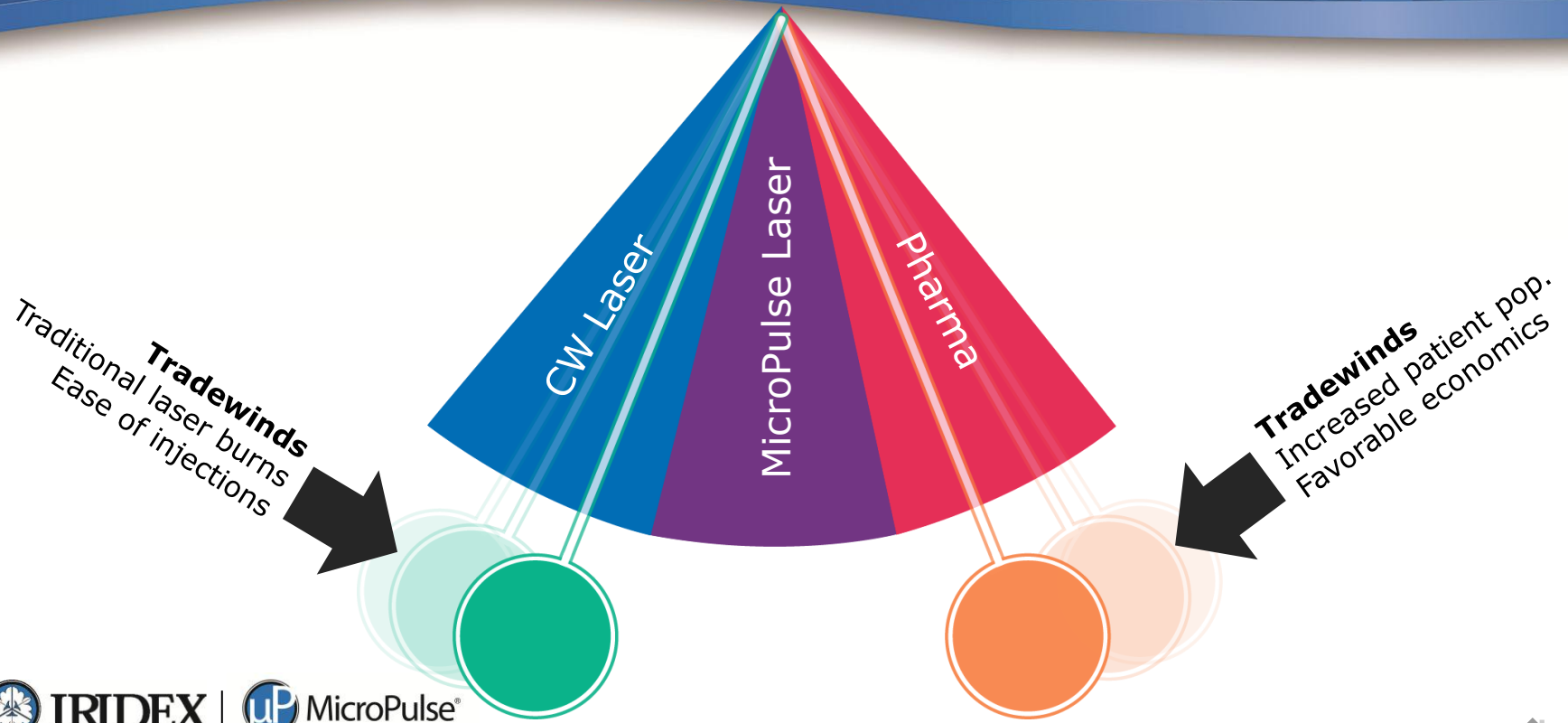
New Standard of Care



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