When to use thermal laser, when to use subthreshold laser?

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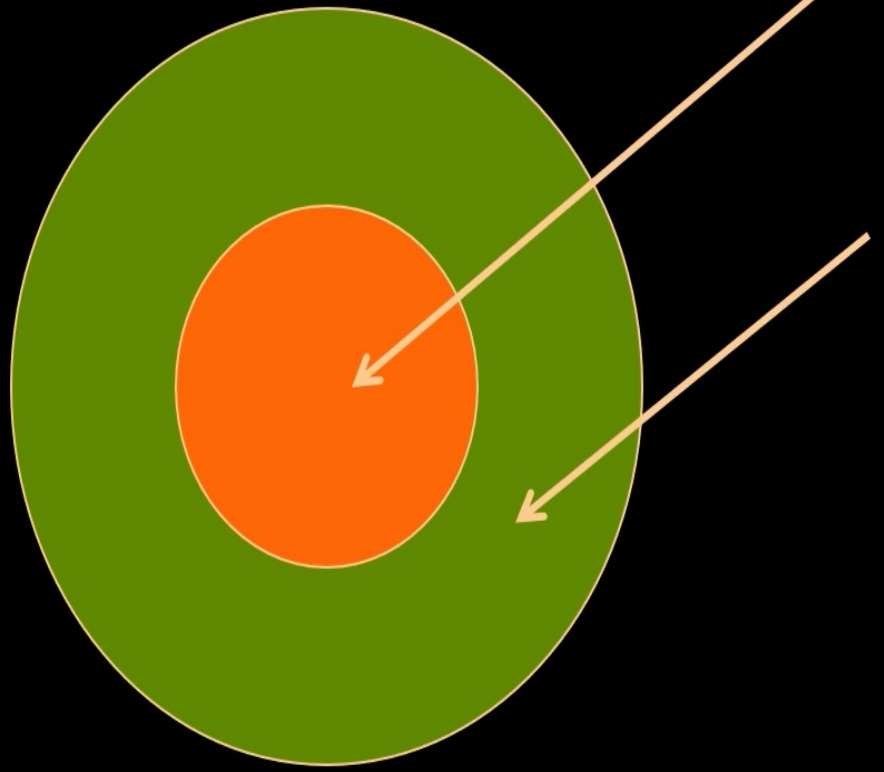
How does laser work in macular disease

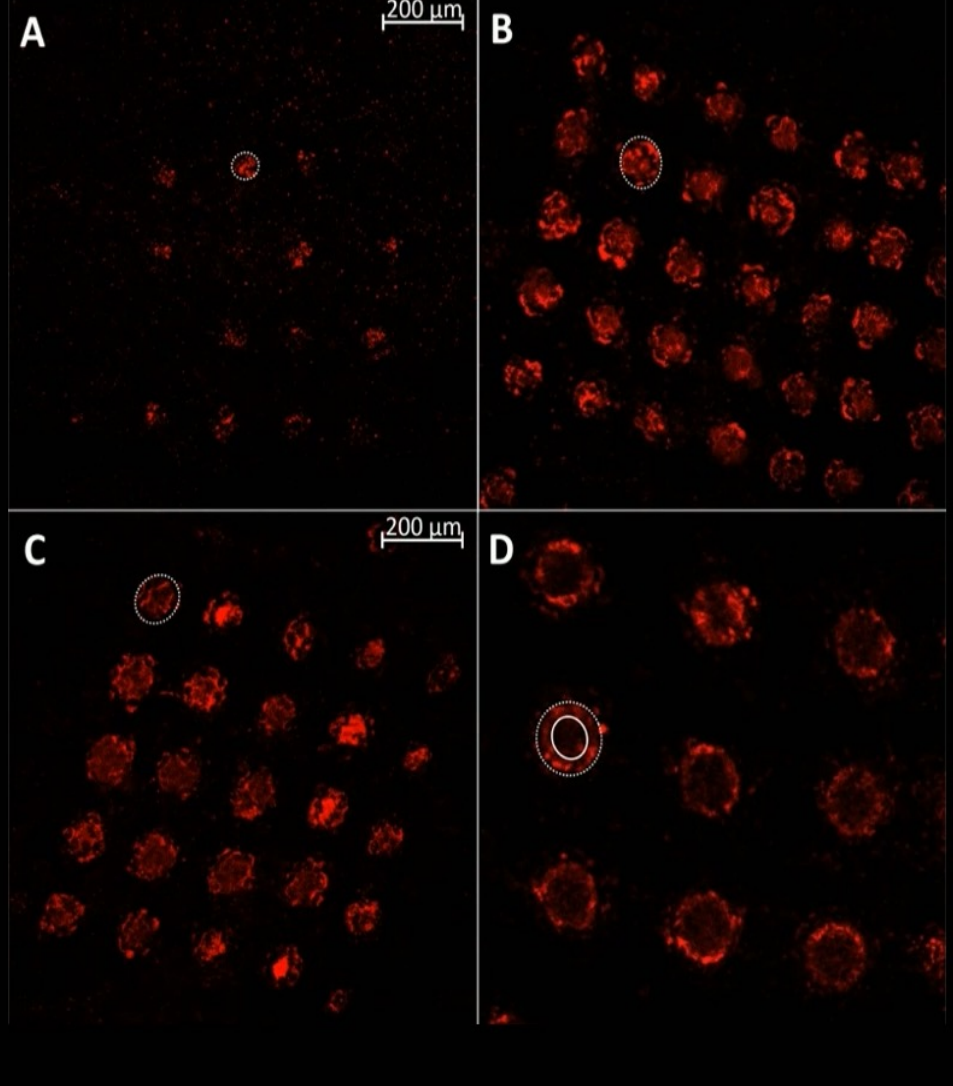
- Historically, “shot the red dots” !
  - Direct coagulation
- We now know, energy absorbed by the RPE change microenvironment
  - Leading to closure of microaneurysms
  - Reduce edema

So the target is RPE and not RETINA

How laser works



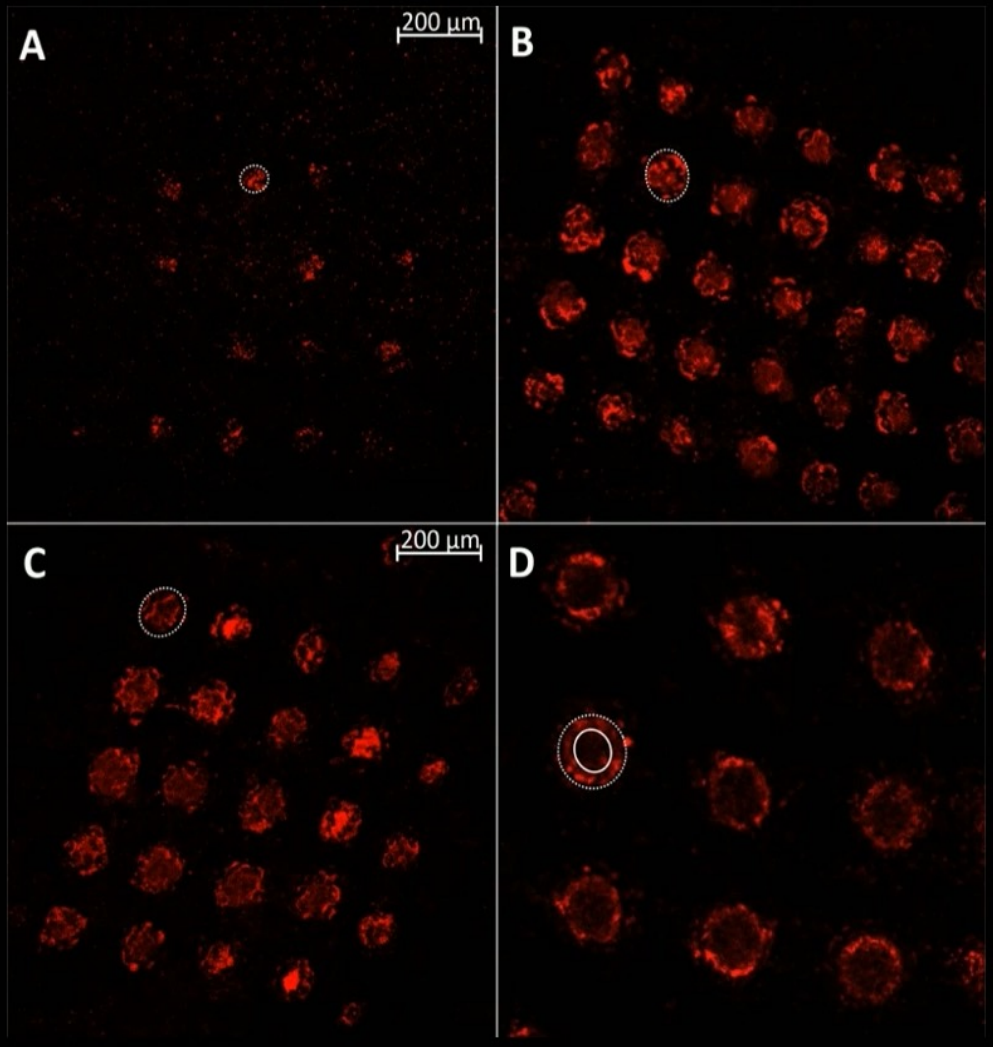
Increase the sublethal zone and reduce the de zone by reducing power in rabbit



A: Energy too low
B: Just right
C: A bit more damage
D: Too much damage

Lavinsky et al., IOVS 2016 May; 57(6): 2488-

Increase the sublethal zone and reduce the dead zone by reducing power in rabbit

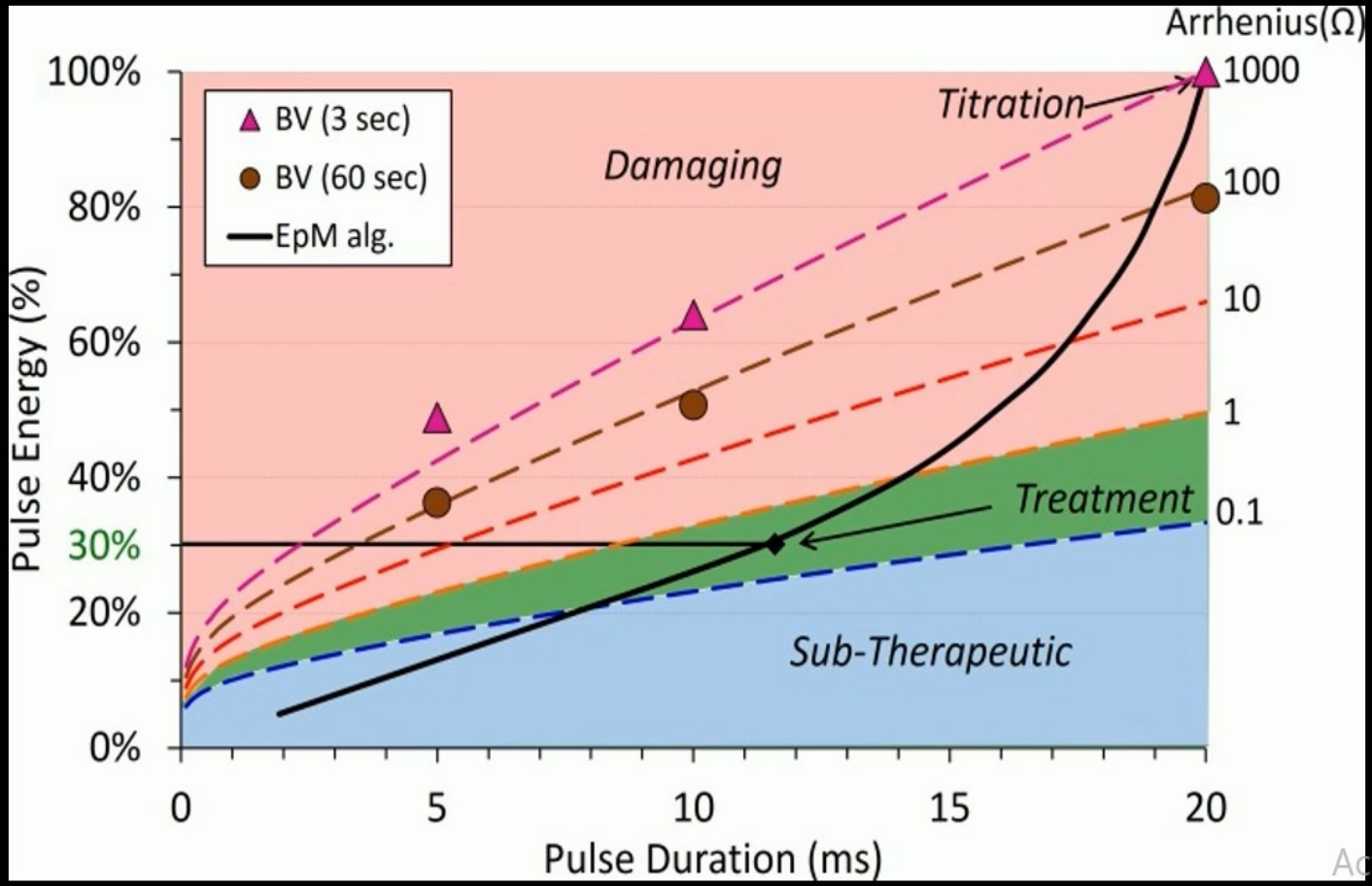


A: Energy too low
B: Just right
C: A bit more damage
D: Too much damage

A: 25% of just visible
B: 30% of just visible
C: 40% of just visible
D: 100% of just visible

Lavinsky et al., IOVS 2016 May; 57(6): 2488–2500

The therapeutic window is very small



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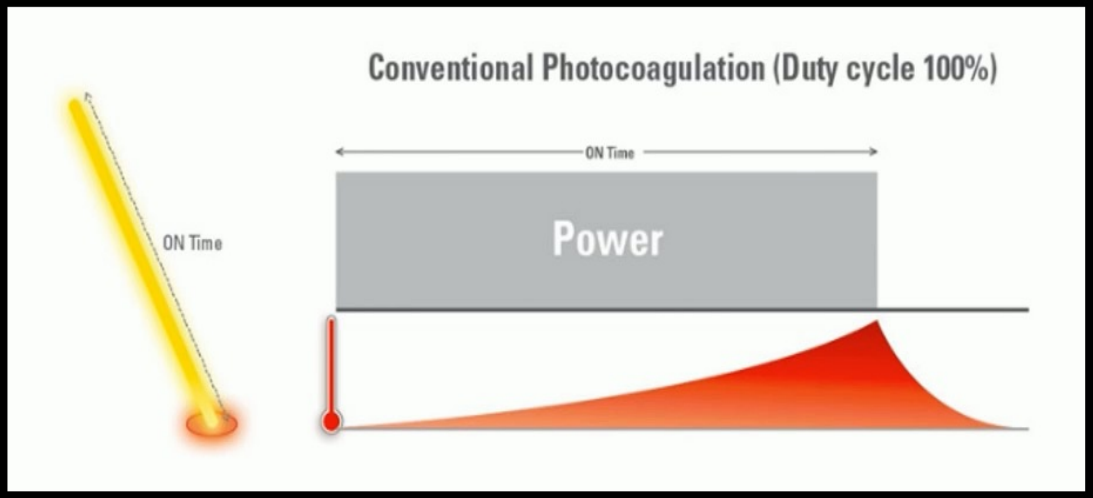
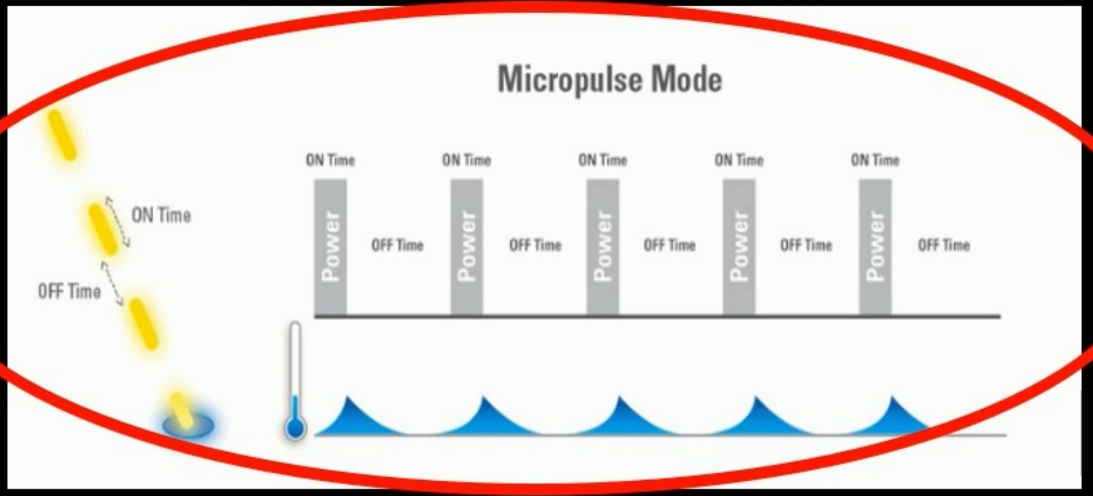
Micropulse / Subliminal laser
Deliver more energy without damage





Micropulse also known as Subliminal

Multiple publications showing efficacy on DME and CSR

Table 4 Treatment outcome after SML, PDT, observation and conventional laser for CSC, DME, and BRVO

	Treatment	Change in CRT (µm)	Change in BCVA (ETDRS letters)
CSC	SML	−131 (range −69.7 to −204)[a]	6.34 (range −15 to 20)[d]
	PDT	−85 (range −76 to −109.8)[b]	3.87 (range 2 to 8.5)[b]
	Observation	−25 (range 26 to −89)[c]	0.67 (range −2.1 to 2.5)[c]
DME	SML	−74.9 (range −138 to 48)[e]	1.26 (range −6.6 to 19)[e]
	Conventional laser	−43.6 (range −145 to 28.7)[f]	−0.29 (range −7.3 to 7.5)[f]
BRVO	SML	−122.59 (range −272 to −40.5)[g]	2.98 (range −3.5 to 9.5)[g]

CSC central serous chorioretinopathy, *DME* diabetic macular edema, *BRVO* branch retinal vein occlusion, *BCVA* best corrected visual acuity, *CRT* central retinal thickness, *ETDRS* Early Treatment Diabetic Retinopathy Study Group letters, *PDT* photodynamic therapy, *SML* subthreshold micropulse laser

[a] 199 patients from 11 studies, 7 studies excluded from the calculations, one due to prior PDT treatment [37], six due to absence of information about the CRT

[b] 100 patients from 3 studies

[c] 49 patients from 3 studies

[d] 216 patients from 14 studies, two studies excluded due to prior PDT [37, 41], two due to absence of information about the concrete BCVA [28, 31]

[e] 613 patients from 11 studies

[e] 195 patients from 7 studies

[f] 80 patients from 3 studies, one study excluded from the calculation due to prior conventional laser treatment [56]

Scholz et al., Adv Ther 2017 34: 1528-55

ELSEVIER

Ophthalmology

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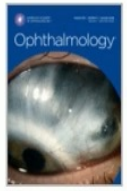


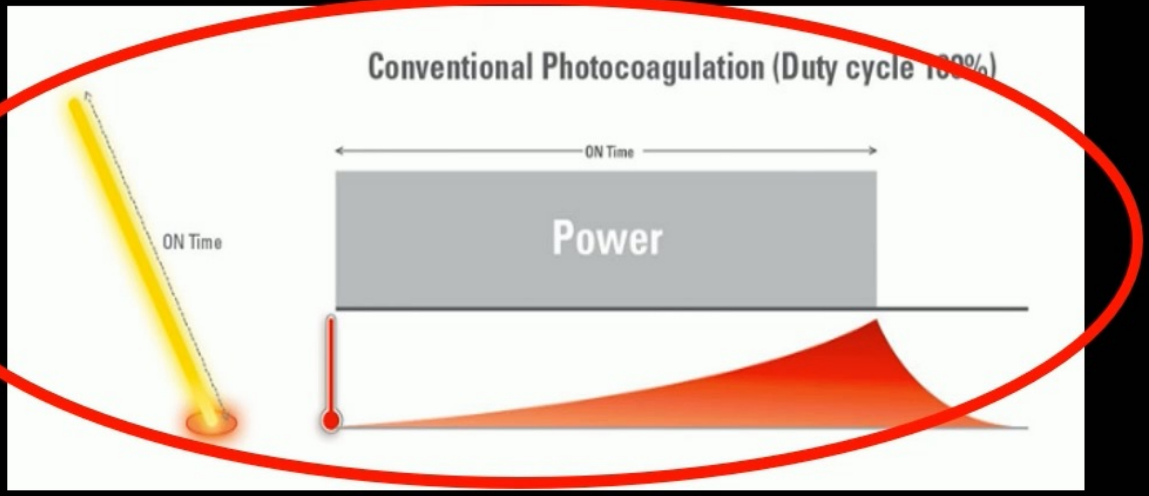
Original Article

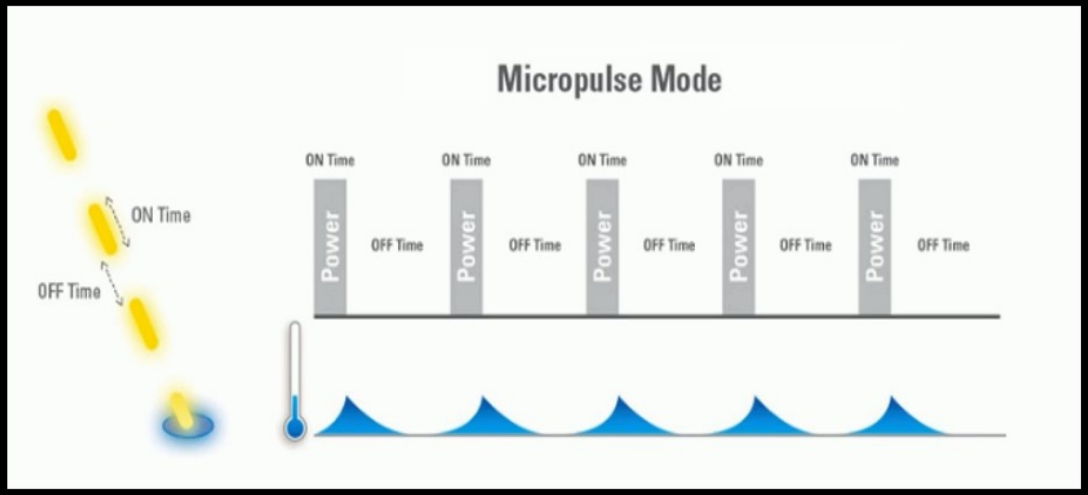
Diabetic Macular Edema and Diode Subthreshold Micropulse Laser: A Randomized Double-Masked Noninferiority Clinical Trial

Noemi Lois MD, PhD [1], Christina Campbell BSc(Hons) [2], Norman Waugh MRCP(UK) [3], Augusto Azuara-Blanco MD, PhD [4], Mandy Maredza PhD [3], Hema Mistry PhD [5], Danny McAuley MR, PhD [1 6], Nachiketa Acharya MD [7], Tariq M. Aslam MD [8], Clare Bailey MD [9], Victor Chong MD [10], Louise Downey MD [11], Haralabos Eleftheriadis MD [12], Samia Fatum MD [13], Sheena George MD [14], Faruque Ghanchi MD [15], Markus Groppe MD [16], Robin Hamilton MD [17], Geeta Menon MD [18], Ahmed Saad MD [19 20]…Mike Clarke PhD [2 4]

- CI-DME with < 400 µr
- Total 266 patients recru
- Multiple centres
- Non inferiority design
- Showed equivalent

Thermal Laser





Micropulse also known as Subliminal

Proliferative diabetic retinopathy - NVD

NVD disappeared after PRP

Thermal laser

Proliferative Diabetic Retinopathy

Retinal tear

Retinal tumor

Russell JF et al Retinal Physi
Haddad NMN et al Seminars

Take home messages

- Subthreshold laser
  - Improve RPE function without killing them
  - Diabetic Macular Edema
  - Central Serous Retinopathy
- Thermal laser
  - Killing RPEs and photoreceptors
  - Proliferative Diabetic Retinopathy (ischemic retina)
  - Retinal hole / detachment (create barrier)
  - Tumor (destroy lesion)

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Subthreshold Laser Therapy

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Laser Technology

Through the years, laser technology also evolved dramatically!

- Plato (400BC) – "Don't look at the sun!"
- Czerny in (1867) Deutschmann (1882) – focused sunlight into rabbits eyes
- Magiore (1927) – Sunlight (Unreliable, long exposure time)
- Meyer-Schwickerath (1949) - Carbon arc lamp (short filament life span, unpredictable retinal burns)
- Xenon arc laser (full thickness burns, many side effects)
- Maiman (1960) – Ruby crystal (red)
- Argon blue laser
- Argon green laser
- Krypton Red
- Semiconductor diode (1980s)
- Photodynamic Laser Therapy (PDT)
- Multispot and Subthreshold Technologies
- 577nm fiber laser technology

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Technology

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Retina therapy

Although intravitreal injections have become the first line of treatment of macular pathologies such as diabetic macular edema (DME), laser application within clinical settings continues to prove efficacious in macular conditions.

TABLE 5. DME TREATMENT THROUGH 1 YEAR: ANTI-VEGF AND LASER

	AFLIBERCEPT N = 208	BEVACIZUMAB N = 206	RANIBIZUMAB N = 206	*P* VALUE
# of Injections (Max = 13)				
Mean	9.2	9.7	9.4	
Median (25th, 75th percentile)	9 (8, 11)	10 (8, 12)	10 (8, 11)	.045†
At least one focal/grid laser	**37%**	**56%**	**46%**	<.001‡

†Global (overall 3 group comparison) *P* value. Pairwise comparisons (adjusted for multiple comparisons): aflibercept-bevacizumab: *P* = .045, aflibercept-ranibizumab: *P* = .19, bevacizumab-ranibizumab: *P* = .22.
‡Global (overall 3 group comparison) *P* value. Pairwise comparisons (adjusted for multiple comparisons): aflibercept-bevacizumab: *P* < .001, aflibercept-ranibizumab: *P* = .058, bevacizumab-ranibizumab: *P* = .061.

DRCR.net Protocol T compared the effectiveness of the three anti-VEGF agents:

- In this study about 40% of the patients had prior laser
- About 40% to 60% of patients who received 9 to 10 anti-VEGF injections in the first year of the study also received laser.

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Laser Photocoagulation

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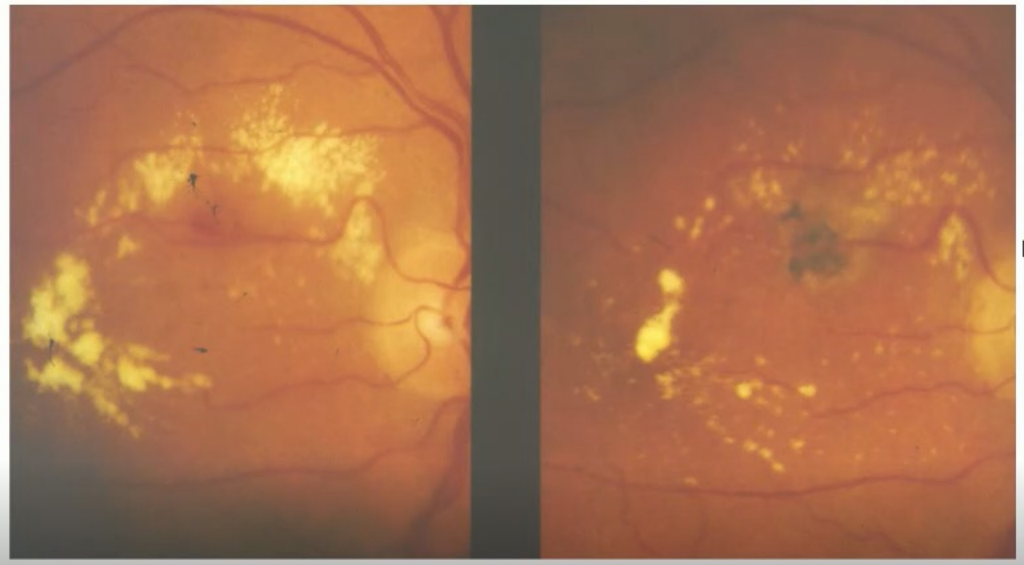
Conventional Photocoagulation

When introduced more than 50 years ago, macular laser was initially used as a photocoagulator to destroy lesions.



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Conventional Photocoagulation

Conventional continuous wave laser photocoagulation is intended to damage the retinal tissue as treatment for the disease, usually to reduce ischemic effects (PRP).

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Minimizing Laser Damaging Effects

- After healing, retinal atrophy and thinning occur in the regions of laser application, sometimes causing scotomas and post-laser lesion enlargement.
- These concerns regarding the destructiveness of laser therapy have led to numerous investigations to provide the same therapeutic effect of lasers while minimizing the damaging effects of lasers.
- Further studies have shown that full thickness retinal damage is not needed to obtain the beneficial effects of lasers.

PRP: Multispot Laser Treatment

DME: Subthreshold Laser Treatment

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Subthreshold Laser Therapy

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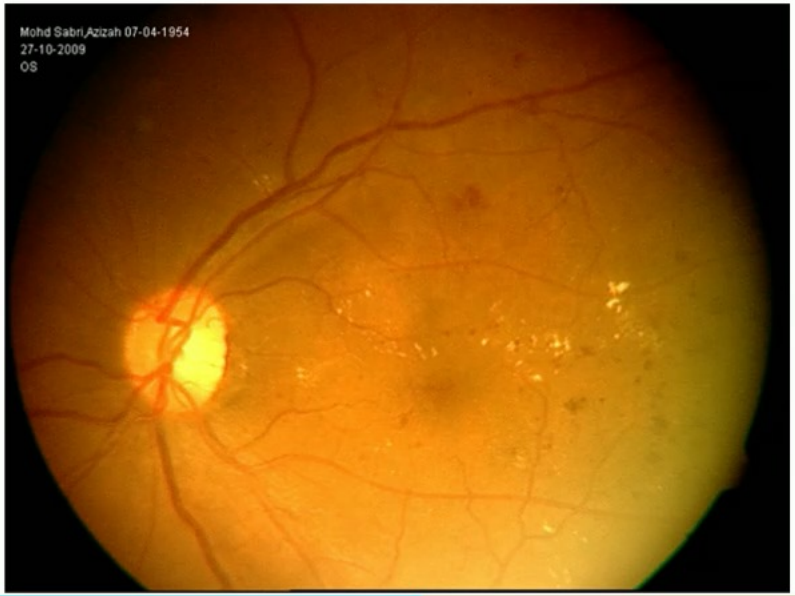
Subthreshold Laser

- Advancement of laser technology has led to the development of subthreshold lasers.
- These lasers encompass all types of treatment that show no visible signs or color change of damage to the eye of the examiner.



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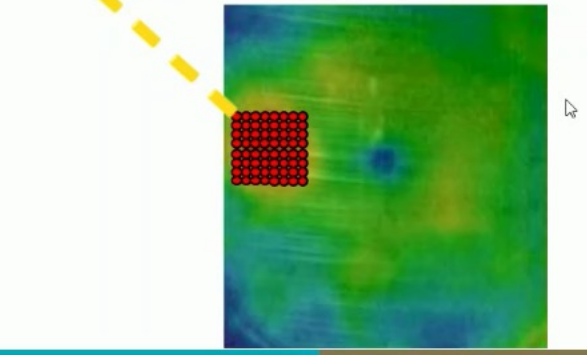
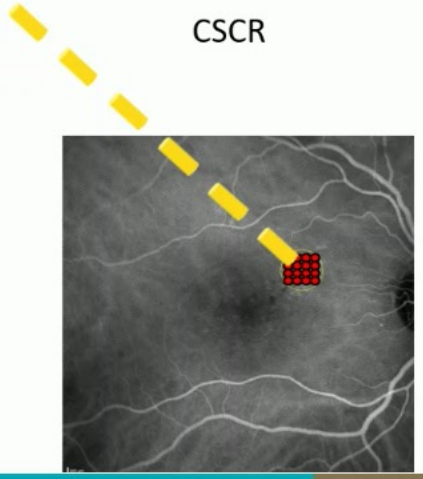
Subthreshold Laser

- Advancement of laser technology has led to the development of subthreshold lasers.
- These lasers encompass all types of treatment that show no visible signs or color change of damage to the eye of the examiner.
- This treatment method is currently most commonly used in macular diseases such as:

DME



CSCR



Images courtesy of Alejandro Filloy Rius, MD. Ph.D - Tarragona, Spain

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Subthreshold Lasers

Today, lasers can be customized to deliver energy in different ways by varying power settings, shortening duration, and employing a train of pulses to achieve a targeted endpoint.

Although sub-threshold laser denotes any laser application below the visible threshold, there are 3 principal types of modern subthreshold laser:

- **SubLiminal / Micropulse:**
  Based on the emission of short repetitive pulses that last for microseconds, allowing for significant cooling in between these short pulses.
- **Endpoint Management:**
  Based on continuous delivery with decreased power levels and duration in an attempt to achieve no visible scarring with positive clinical effect.
- **Nanosecond / Rejuvenation:**
  Using similar specifications to selective laser trabeculoplasty (SLT laser).

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Which one should be favoured?

SUBTHRESHOLD LASERS AVAILABLE ON THE MARKET			
	SubLiminal	Endpoint management	Nanosecond/Rejuvenation
Duration of laser in each pulse	0.1 ms	10 to 20 ms	0.000003 ms
OCT change after treatment	None visible	Clearly visible	Seen in some cases
AF imaging after treatment	None visible	Clearly visible	No published data but RPE changes visible on color fundus photos
Randomized controlled trials published	Several in DME and CSC	None	Reduced AMD progression (in post-hoc analysis)

Figure 1. Comparison of available subthreshold lasers available on the market.

How new generation lasers are different from each other?

Victor Chong

Consultant Ophthalmic Surgeon, Ophtiqua Eye Hospital, University of Oxford and Royal Free Hospital, London, United Kingdom

This review is based on a talk given during OPTIMUM Eye Center 12th Scientific Conference "New Trends in Laser Therapy, Glaucoma & Retinal Diseases in Warsaw, 1.12.2018.

ABSTRACT

Laser has changed a lot over the years, the newer laser can deliver energy in different ways, by reducing the duration to 10–20 ms, in a train of pulses of 0.1 ms as in the micropulse / subliminal laser, and extremely short duration of 0.0017 ms as in the nanosecond laser. Clinical studies have shown that micropulse laser is efficacious in multiple macular conditions. Reducing the power and duration using end-point management has yet to demonstrate clinical efficacy beyond CSR. The ability to reduce the progression of intermediate AMD is intriguing, after all the LEAD (Laser intervention in early stages age-related macular degeneration) trial failed the primary endpoint. Nonetheless, there is evidence to support that it may be effective in a highly selected sub-group of intermediate AMD patients. More studies are required to see whether other lasers such as micropulse laser can have the same effect, and whether micropulse lasers with a slightly higher energy leading to a few RPE cell deaths is needed to have the same effect.

key words: macular diseases, diabetic macular edema, micropulse laser, subliminal laser, non-damaging laser, nanosecond laser

HIGHLIGHTS

The author would explain how laser works in macular diseases, how the treatment protocol has been modified and also how new generation lasers are different from each other?

NAJWAŻNIEJSZE

Autor opisuje sposób działania laseroterapii w chorobach plamki, a także historię zmian protokołów prowadzenia laseroterapii oraz nowe generacje urządzeń i cechy odróżniające je od poprzedników.

STRESZCZENIE

Lasery okulistyczne do leczenia schorzeń siatkówki przeszły znaczną ewolucję w ciągu ostatnich lat. Najnowsze urządzenia zapewniają krótszy czas dostarczania energii (10–20 ms) w impulsach trwających 0,1 ms w laserze mikropulsowym/podprogowym i w impulsach o ultrakrótkim czasie trwania – 0,0017 ms – w laserze nanosekundowym. Badania kliniczne wykazały, że laser mikropulsowy jest skuteczny w wielu stanach chorobowych plamki żółtej. Trwają badania nad określeniem skuteczności klinicznej przy zastosowaniu mniejszej mocy i krótszego czasu aplikacji, uzyskanych dzięki metodzie *end-point management* we wskazaniach innych niż centralna retinopatia surowicza. Możliwości spowolnienia progresji średnio zaawansowanego zwyrodnienia plamki żółtej (AMD) wydają się realne, mimo że w badaniu LEAD (*Laser Intervention in Early Stages Age-related Macular Degeneration*) nie udało się osiągnąć tego założonego pierwszorzędowego punktu końcowego. Dysponujemy jednak licznymi doniesieniami wskazującymi, że sukces jest możliwy w precyzyjnie wyselekcjonowanej podgrupie pacjentów z AMD. Potrzebne są zatem kolejne badania, aby jednoznacznie stwierdzić, czy urządzenia takie jak laser mikropulsowy mogą zapewnić satysfakcjonujący efekt terapeutyczny i czy lasery mikropulsowe o nieco większej energii, które powodują zmiażdżenie większej liczby komórek RPE, są niezbędne do osiągnięcia tego efektu.

Słowa kluczowe: choroby plamki, cukrzycowy obrzęk plamki, laser mikropulsowy, laser podprogowy, laser nieuszkadzający, laser nanosekundowy

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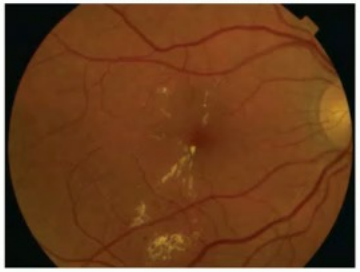
Which one should be favoured?

DO WE NEED TO SEE VISIBLE CHANGES WHILE WE ARE DOING THE LASER FOR THE TREATMENT TO BE EFFECTIVE?

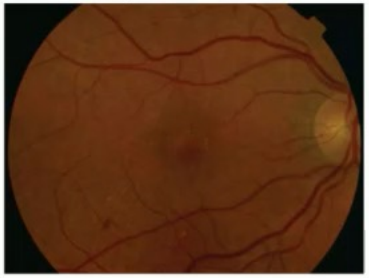
As mentioned, you would like to deliver energy to the RPE cells without damaging the photoreceptors. It is now clear that no visible changes are needed as multiple studies have shown efficacy without any visible changes on the retina.

Fundus photo of pre-laser in patients with DME.



Fundus photo of patients with DME, 4 months after a single micropulse laser treatment.

Fundus photo of patients with DME, 12 months a single micropulse laser treatment showing exudation reduction and no visible laser scar.



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SubLiminal Laser

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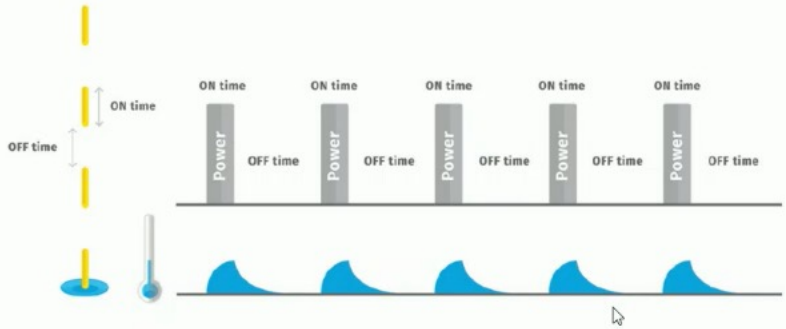
SubLiminal Technology

- SubLiminal laser therapy is based on a stimulation concept, which allows for a cooling period between pulses resulting in no visible scarring (even with fundus autofluorescence imaging and OCT), and no detectable photoreceptor loss. This further results in the improvement of retinal sensitivity in edematous retina and reading speed, while also preventing retinal damage.



- Over 50 studies using SubLiminal / Micropulse laser showed efficacy in DME and CSC including control trials by a number of investigators using a number of different treatment protocols(1).

(1) Scholz P, Altay L, Fauser S. A Review of Subthreshold Micropulse Laser for Treatment of Macular Disorders. Adv Ther 2017; 34(7): 1528--1555.

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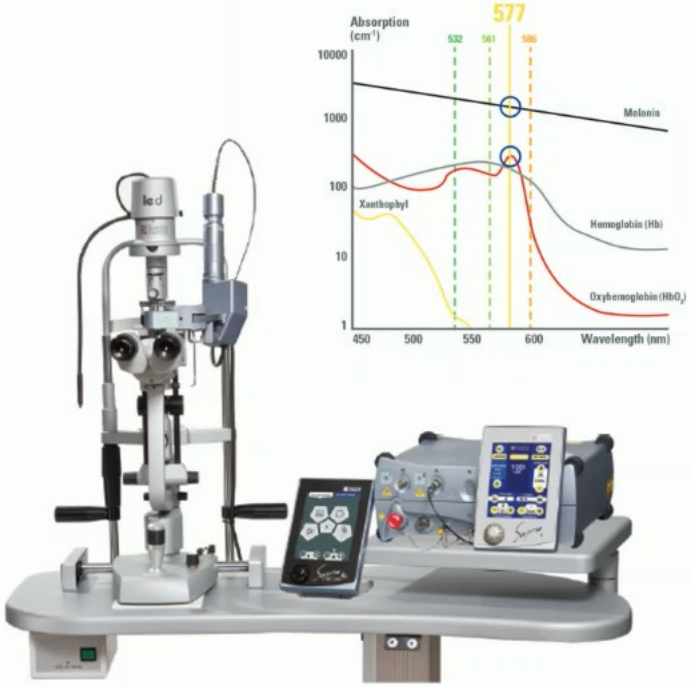

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Original article
https://doi.org/10.35119/myjo.v3i3.226

Subthreshold 577 nm laser photocoagulation vesus conventional 532 nm laser photocoagulation for diabetic macular oedema

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Department of Ophthalmology, University of Malaya, Kuala Lumpur, Malaysia

Abstract

Purpose: To evaluate the visual and anatomic outcomes of the subthreshold micropulse 577 nm yellow diode laser (MYL) and to compare its efficacy with the conventional green 532 nm diode laser (CGL) in Asian eyes with diabetic macular oedema (DME).
Study design: Prospective randomized controlled clinical trial
Methods: Sixty-seven eyes of 43 patients with clinically significant macular oedema (CSME) were randomized to receive either MYL ($n = 37$) or CGL ($n = 30$) at baseline and were followed up for 12 months. Titration in the MYL group was performed with 15% duty cycle, 300 ms duration, and double the threshold power, while the modified Early Treatment of Diabetic Retinopathy Study (mETDRS) protocol was used for the CGL arm with the power titrated to a barely visible burn. Parameters noted included best-corrected visual acuity (BCVA) (logMAR), central subfoveal thickness (CST), macular volume (MV), and average macular thickness (AMT) using optical coherence tomography, and presence of visible laser scars on colour fundus photographs and fundus autofluorescence, at baseline and at 12 months.
Results: At 12 months follow-up, BCVA improved by 4.7 and 8.8 letters, respectively, for the MYL and CGL treatment arms ($p < 0.05$). There was a significant reduction in all retinal thickness parameters (CST, MV, and AMT) when compared to baseline

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E-mail: drlindaong@hotmail.com

10:15 - 11:15 Laser for retina and vitreous: All you need to know in 2023.

CHAIR : VICTOR CHONG

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COMMENT

Check for updates

Subthreshold laser therapy guidelines for retinal diseases

Jay Chhablani[1✉] and SOLS (Subthreshold Laser Ophthalmic Society) writing committee*

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Subthreshold laser therapy has been utilised in clinical practice for more than three decades, and numerous randomised and real-life studies has proven its efficacy and safety in various retinal diseases [1–10]. However, despite decades of usage, we still do not have a standard protocol for subthreshold laser applications and settings. The Subthreshold Ophthalmic Laser Society (SOLS) is comprised of global experts (10) in subthreshold lasers and has a goal to establish subthreshold laser guidelines and establish level 1 evidence on subthreshold laser in ophthalmology.

Here we report consensus guidelines by SOLS for the subthreshold laser settings and applications in diabetic macular oedema (DMO) and central serous chorioretinopathy (CSCR). These guidelines were based on 43 questions based on different aspects of subthreshold laser applications in these diseases. Responses were collected from each expert in a masked fashion in first round and two virtual meetings were performed to discuss these questions to reach final consensus.

For DMO, the experts support the role of subthreshold laser in both centre-involving and non-centre involving macular oedema in conjunction with or without anti-VEGF therapy. Subthreshold laser settings for DMO include 5% duty cycle, 200 ms pulse duration, and 150–200 µm spot size with no spacing between laser spots using integrated pattern system. SOLS experts support titration for subthreshold laser application with 50% of threshold power (achieved with subthreshold laser). SOLS experts suggest treating oedematous area with subthreshold laser, however, does not mandate focal treatment of microaneurysm. SOLS experts consider transfoveal treatment safe with settings described earlier, however, they emphasis the careful application and reconfirmation of subthreshold laser safe settings before application. Considering no visible or structural changes following subthreshold laser treatment, experts do not recommend any specific structural imaging studies to evaluate laser spots, however, autofluorescence or OCT could be carefully evaluated during follow up visits for any laser scars. Experts recommend follow-up evaluation at 6–8 weeks after subthreshold laser application, however, repeat subthreshold laser is suggested after 2–3 months of initial application, in case of poor response. Experts recommend adjunctive therapies such as anti-VEGF or steroid therapy for diabetic macular oedema as per the physician's discretion.

For CSCR, SOLS experts recommend subthreshold laser for both acute as well chronic types. Unlike conventional observation for 3–4 months for acute CSCR, considering the safety profile of subthreshold laser, SOLS experts recommend subthreshold laser application in 1 month if there is no self-resolution. For chronic CSCR, SOLS expert support subthreshold laser as first line as well as combination therapy with other treatment options. Recommended settings for subthreshold laser application are 5% duty cycle, 200 ms pulse duration and 100–200 µm spot size. Settings are same for both acute and chronic CSCR with no spacing between the spots using integrated pattern system. SOLS experts support these settings safe for the transfoveal laser application, with reconfirmation of subthreshold settings. SOLS experts suggest titration with 50% of threshold power (threshold estimation using subthreshold laser mode) (Table 1). Regarding area covered, for acute CSCR, focal leak and adjacent area should be treated with subthreshold laser. In case of chronic CSCR, SOLS experts suggest areas of focal as well as diffuse hyperfluorescence on fluorescein angiography. Considering no visible or structural changes following subthreshold laser, experts do not recommend any specific structural imaging studies to evaluate laser spots, however, autofluorescence or OCT could be carefully evaluated during follow up visits for any laser scars. Evaluation at 6–8 weeks is recommended and in case of poor response or persistence of the subretinal fluid, a repeat treatment with same settings is recommended, in addition to adjuvant treatment options as per physician discretion.

These consensus guidelines do not suggest management of these disease but suggest laser application guidelines using different subthreshold laser deliver systems. These guidelines would help to establish standard subthreshold laser applications in clinical practice.

Table 1. Subthreshold laser consensus guideline settings for diabetic macular oedema and central serous chorioretinopathy by the Subthreshold Ophthalmic Laser Society (SOLS).

Subthreshold laser settings	Diabetic macular oedema	Central serous chorioretinopathy
Duty cycle	5%	5%
Pulse duration	200 ms	200 ms
Spot size	150–200 µm	100–200 µm
Spacing between spots	No	No
Titration	Yes	Yes
Titration power	50% of threshold power	50% of threshold power

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SPRINGER NATURE

OASISEYE SPECIALISTS

SubLiminal Laser – How does it work?

RPE stimulation producing of heat shock proteins (HSP)

- It is believed that the main mechanism of action of subthreshold laser is to stimulate RPE for the production of heat shock proteins (HSP) and, this way, immunomodulate its metabolism and improve its function (2).
- Inagaki et al. prove the up-regulation of Hsp70 in the culture of human epithelial ARPE-19 cells after the application of subthreshold laser, without any thermal damage (3).

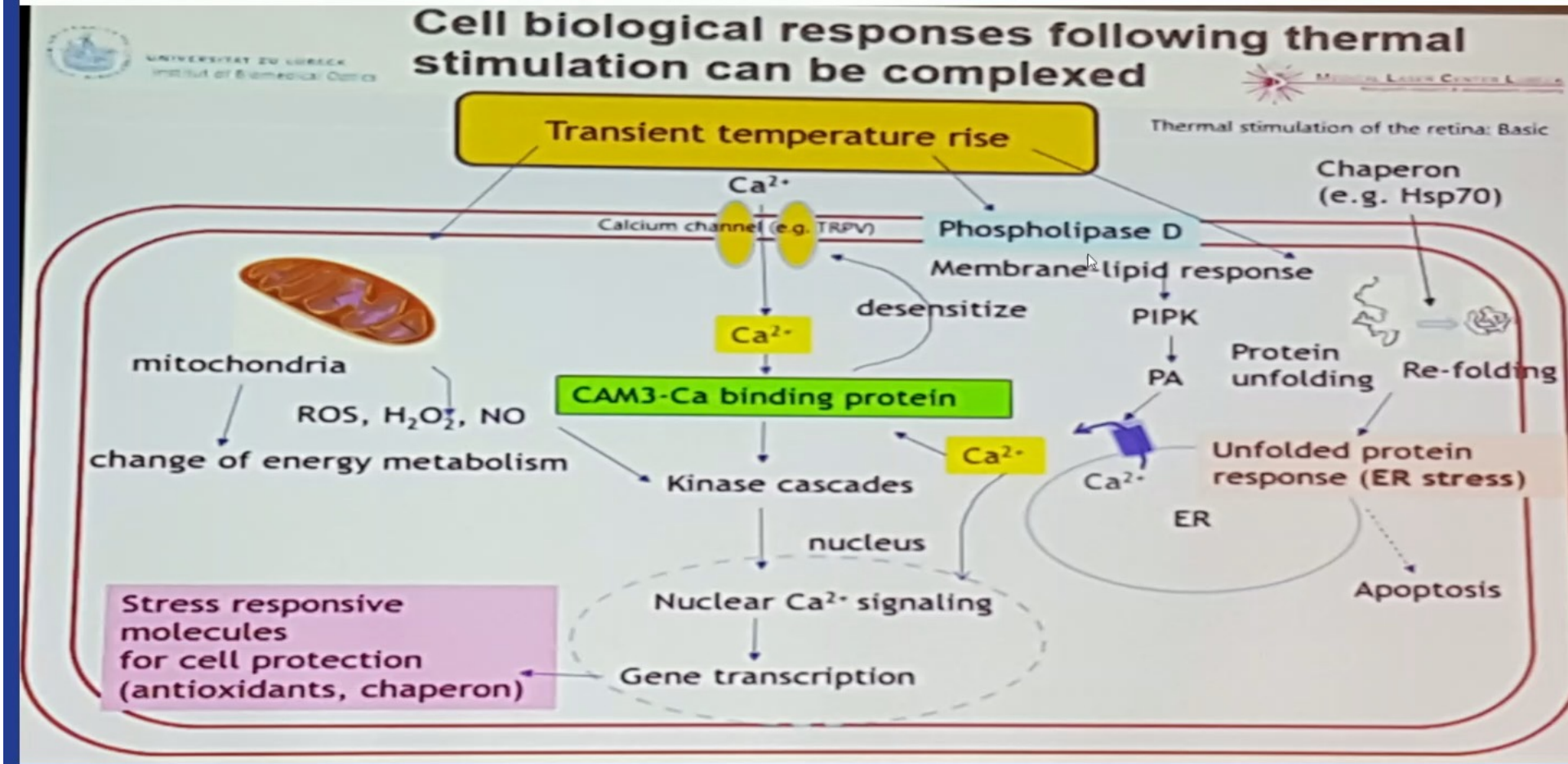
Suppression of the production of neovascular promoting cytokines:

- Li et al. on the RPE of mice, shown that subthreshold laser suppresses the production of neovascular promoting cytokines, such as VEGF, and then up-regulates angiogenic inhibitors, such as the pigment epithelium-derived factor (PEDF), without damaging the cells (4).

2. Maciej Gaw,ecki. Micropulse Laser Treatment of Retinal Diseases. Journal of clinical medicine
3. Inagaki et al. Stimulation with a Micropulse Laser Induces Heat Shock Protein Expression in ARPE-19 Cells. J. Ophthalmol. 2015, 2015, 729792
4. Li et al. Biological Modulation of Mouse RPE Cells in Response to Subthreshold Diode Micropulse Laser Treatment. Cell Biochem. Biophys. 2015, 73, 545–552

OASISEYE SPECIALISTS

Subthreshold Laser – How does it work?



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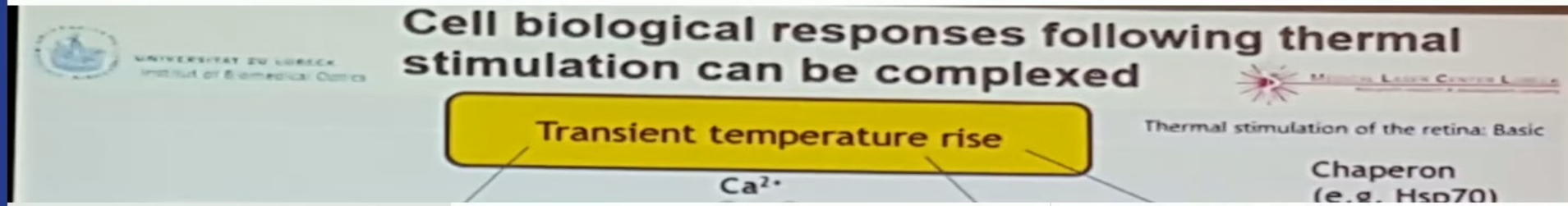
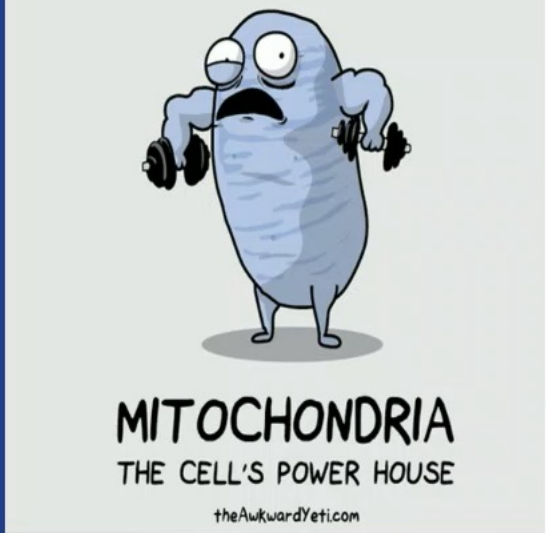
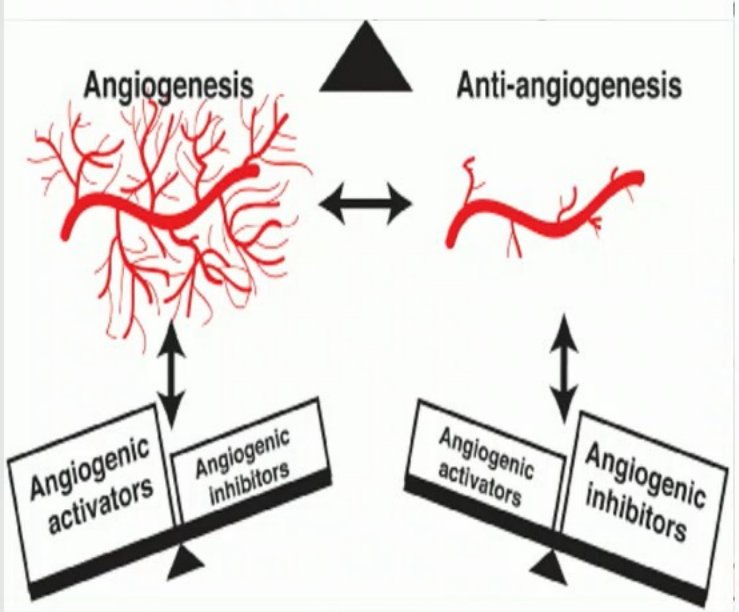
Subthreshold Laser – How does it work?

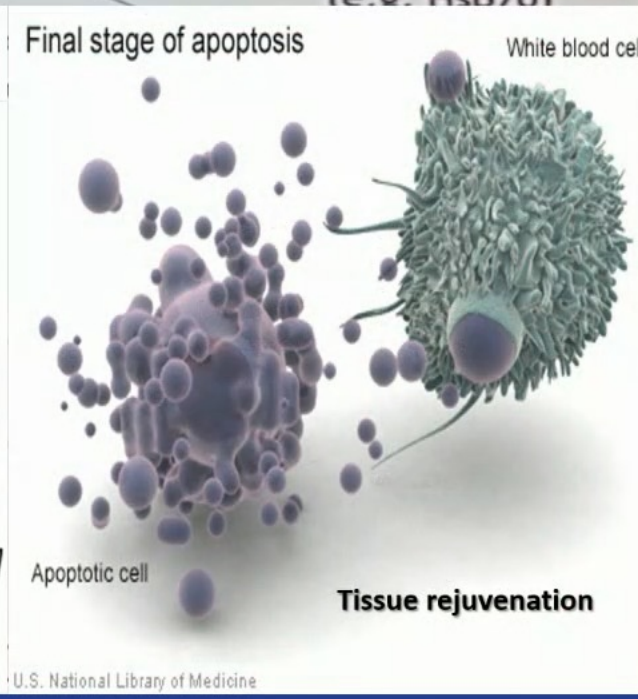


Enhanced cellular respiration



Anti-angiogenic factors release





OASISEYE SPECIALISTS

Subthreshold Laser – How does it work?

Sublethaly heated tissue that remains viable after Subliminal, stimulates the RPE, and triggers a stress response :

* Over-express between 35 and 55 genes (n° is temparature dependant).
  These genes represent diverse biological functions :
    * Modulates beneficial intracellular biological factors
  (PEDF, TSP1, SDF1, ß-Actin, VEGF)
    * Alteration and normalization of cytokine expression
    * Heat Shock Proteins :
        - Inhibit protein aggregation
        - Guide proteins to the correct organ

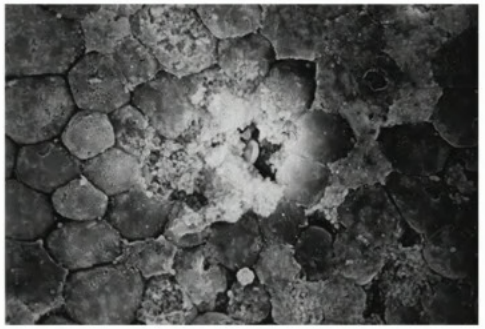


Fig. 4. Scanning electromicrograph of a human retinal pigment epithelial cell monolayer following irradiation with a micropulsed diode laser. Note the relatively limited number of cells damaged by the laser pulse.

Surv Ophthalmol 55 (6) November–December 2010

These factors are primarily anti-angiogenic and restorative

Shafiee A, IOVS 2000; Figueroa J, BJO 2009; Vojosevic S, Retina 2010
Lavinsky D, Retina 2014
Wilson AS,et al: Invest Ophthalmol Vis Sci. 2003; 44:1426-1434
Wilson AS,et al: Invest Ophthalmol Vis Sci. 2003; 44:1426-1434
Sramek C, et al: Invest Ophthalmol Vis Sci. 2011; 52:1780-7

OASISEYE SPECIALISTS

SubLiminal Laser – How does it work?

Reduction of VEGF levels and the restoration of Muller cell (MC) function

- Midena et al. research on human subjects shown a reduction of VEGF levels and the restoration of Muller cell (MC) function as a result of subthreshold laser (5).

Restoration the oxidant/antioxidant balance within the retinal tissue:

- Recent research on mice models shown that subthreshold laser restores the oxidant/antioxidant balance within the retinal tissue and, this way, modulates retinal cell apoptosis, counteracting the programmed cell death (6).

Improvement of retinal perfusion:

- Vujosevic et al. also shown that Subthreshold laser can also improve retinal perfusion in DME (7).

5. Midena et al. Changes of aqueous humor müller cells' biomarkers in human patients affected by diabetic macular edema after subthreshold micropulse laser treatment. Retina 2018.
6. De Cillà et al.The subthreshold micropulse laser treatment of the retina restores the oxidant/antioxidant balance and counteracts programmed forms of cell death in the mice eyes. Acta Ophthalmol. 2018.
7. Vujosevic et al. Optical coherence tomography angiography changes after subthreshold micropulse yellow laser in diabetic macular edema. Retina 2018.

OASISEYE SPECIALISTS

My current treatment parameters
(For Quantel EasyRet system)

- OCT guided (Thickness map).
- 5% duty cicle
- 50% Power titration after visible burn seen outside macula area
- Spot size: 160 microns
- Treat large areas centered at the peak of the thickened retina. (dense pattern)
- Evaluate at 12 weeks with OCT and AF

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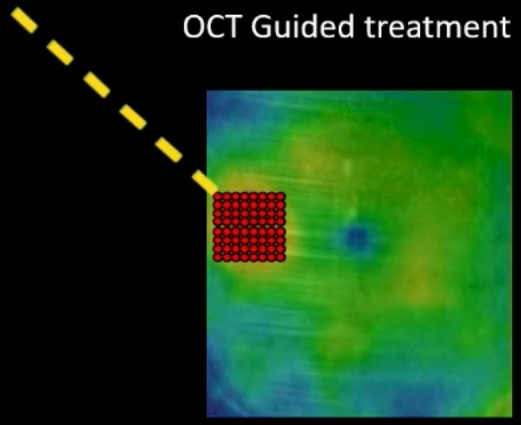
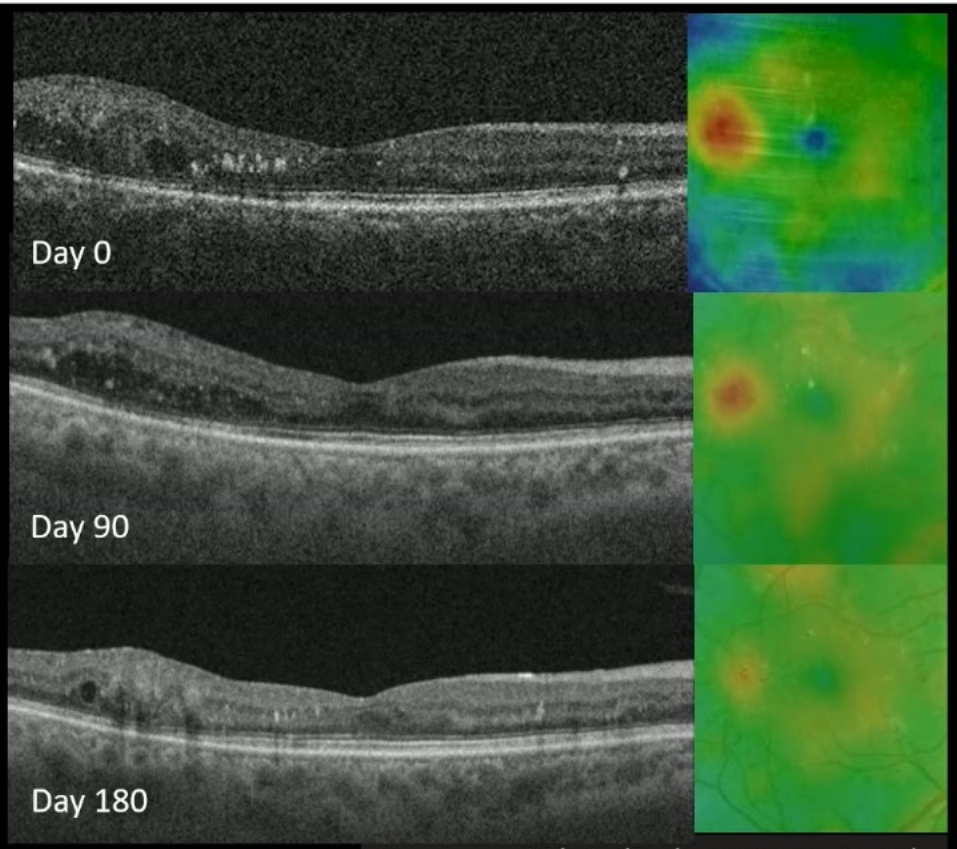
Diabetic Macular Edema (DME)

Non-center involved diabetic macular edema

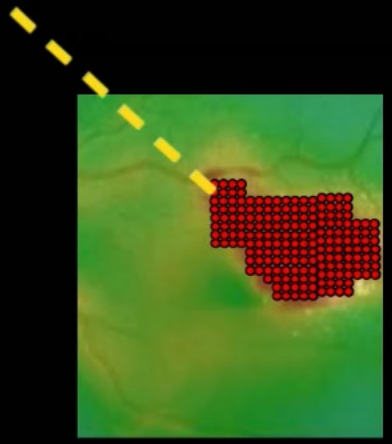


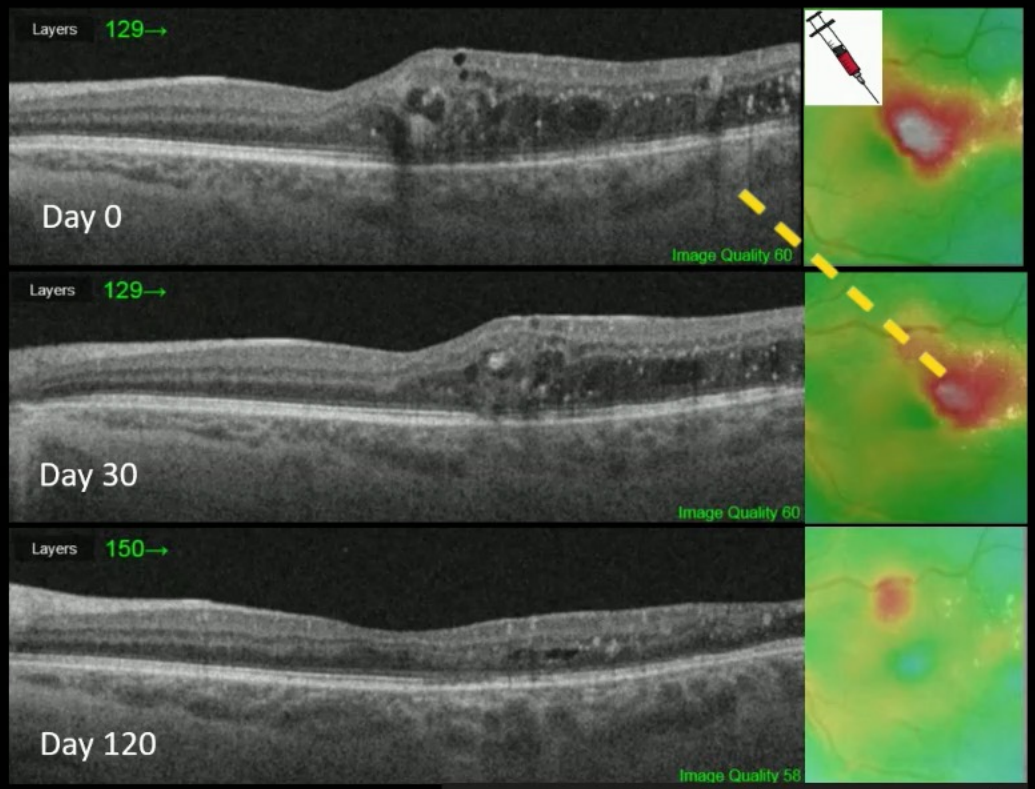


Images courtesy of Alejandro Filloy Rius, MD. Ph.D - Tarragona, Spain

Foveal involved diabetic macular edema

OCT Guided treatment





Images courtesy of Alejandro Filloy Rius, MD. Ph.D - Tarragona, Spain

10:15 - 11:15 Laser for retina and vitreous: All you need to know in 2023.

CHAIR : VICTOR CHONG

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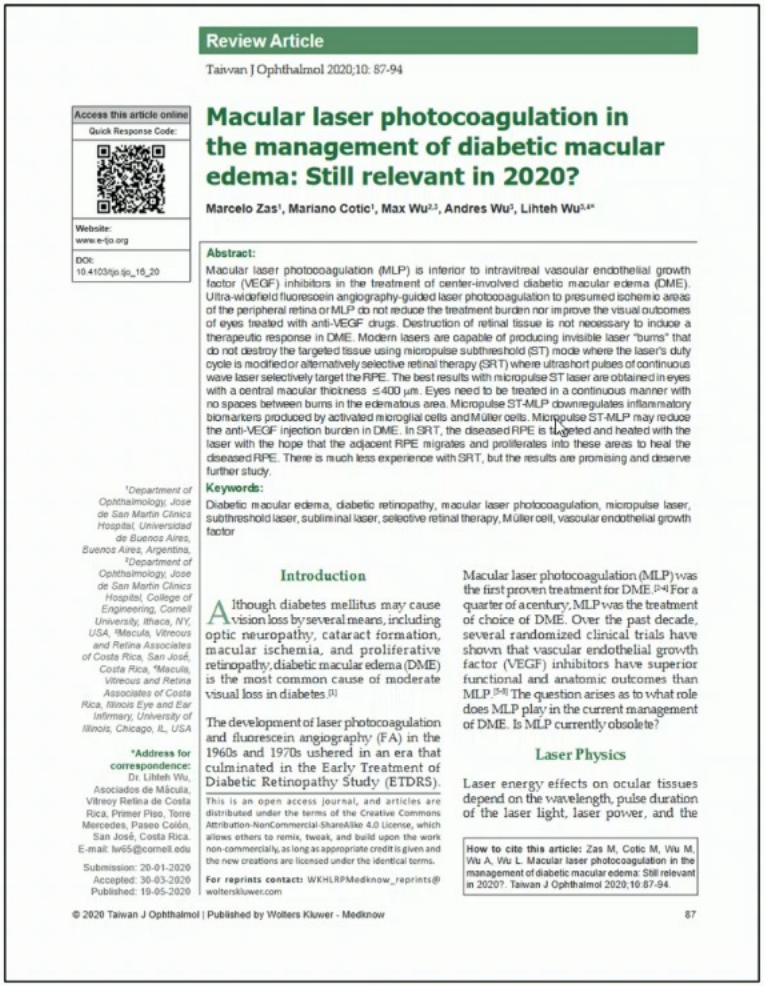

Review Article

Taiwan J Ophthalmol 2020;10: 87-94

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DOI: 10.4103/tjo.tjo_16_20

Macular laser photocoagulation in the management of diabetic macular edema: Still relevant in 2020?

Marcelo Zas[1], Mariano Cotic[1], Max Wu[2,3], Andres Wu[3], Lihteh Wu[3,4*]

Abstract:

Macular laser photocoagulation (MLP) is inferior to intravitreal vascular endothelial growth factor (VEGF) inhibitors in the treatment of center-involved diabetic macular edema (DME). Ultra-widefield fluoresoein angiography-guided laser photocoagulation to presumed ischemic areas of the peripheral retina or MLP do not reduce the treatment burden nor improve the visual outcomes of eyes treated with anti-VEGF drugs. Destruction of retinal tissue is not necessary to induce a therapeutic response in DME. Modern lasers are capable of producing invisible laser "burns" that do not destroy the targeted tissue using micropulse subthreshold (ST) mode where the laser's duty cycle is modified or alternatively selective retinal therapy (SRT) where ultrashort pulses of continuous wave laser selectively target the RPE. The best results with micropulse ST laser are obtained in eyes with a central macular thickness ≤400 μm. Eyes need to be treated in a continuous manner with no spaces between burns in the edematous area. Micropulse ST-MLP downregulates inflammatory biomarkers produced by activated microglial cells and Müller cells. Micropulse ST-MLP may reduce the anti-VEGF injection burden in DME. In SRT, the diseased RPE is targeted and heated with the laser with the hope that the adjacent RPE migrates and proliferates into these areas to heal the diseased RPE. There is much less experience with SRT, but the results are promising and deserve further study.

Keywords:

Diabetic macular edema, diabetic retinopathy, macular laser photocoagulation, micropulse laser, subthreshold laser, subliminal laser, selective retinal therapy, Müller cell, vascular endothelial growth factor

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Introduction

Although diabetes mellitus may cause vision loss by several means, including optic neuropathy, cataract formation, macular ischemia, and proliferative retinopathy, diabetic macular edema (DME) is the most common cause of moderate visual loss in diabetes.[1]

The development of laser photocoagulation and fluorescein angiography (FA) in the 1960s and 1970s ushered in an era that culminated in the Early Treatment of Diabetic Retinopathy Study (ETDRS).

Macular laser photocoagulation (MLP) was the first proven treatment for DME.[2-4] For a quarter of a century, MLP was the treatment of choice of DME. Over the past decade, several randomized clinical trials have shown that vascular endothelial growth factor (VEGF) inhibitors have superior functional and anatomic outcomes than MLP.[5-8] The question arises as to what role does MLP play in the current management of DME. Is MLP currently obsolete?

Laser Physics

Laser energy effects on ocular tissues depend on the wavelength, pulse duration of the laser light, laser power, and the

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OASISEYE SPECIALISTS

CSC: Current evidences for SubLiminal Laser

- Since the first report by Friberg and Karatza in 1997, several studies have concluded that subthreshold laser is **effective in improving visual acuity and reducing DME**.[9-10]
- A meta-analysis of six randomized clinical trials compared the outcomes of eyes treated with subthreshold laser to those treated with standard laser.[15] At 12 months, the **visual outcomes were superior with subthreshold laser** even though there were no changes in the resolution of DME between the two groups.[48] The better visual outcomes with subthreshold laser were not related to a greater resolution of DME but rather to **decreased iatrogenic macular damage as evidenced by microperimetry**.[11,12]
- The DIAMONDS trial showed that subthreshold laser had **comparable efficacy and cost to standard laser**, suggesting that either treatment could be offered to patients with central-involved DME < 400 mm suitable for macular laser therapy.
- Lavinsky et al.[13] demonstrated the importance of the spacing between burns when using subthreshold laser. They found that at 12 months of follow-up, the group with the greatest improvement in visual acuity and the greatest reduction in central macular thickness was the **subthreshold laser with no spacing** between burns group.
- Since subthreshold laser impacts are invisible, this implies that lasers need to have an **automatic pattern scan technology** in order to provide the best results.[13]
- **Baseline macular thickness** is another variable to take into account. Mansouri et al.[14] compared the outcomes following subthreshold laser in eyes with a baseline central macular thickness >400 µm to eyes with a baseline central macular thickness <400 µm. The eyes with a baseline central macular thickness <400 µm had reduction in CMT, visual gain, and none of the eyes required rescue treatment with intravitreal bevacizumab. In contrast, none of eyes with a baseline CMT ≥400 µm had an improvement in visual acuity or significant reduction in CMT. Furthermore, all the eyes required rescue treatment with intravitreal bevacizumab.[14]

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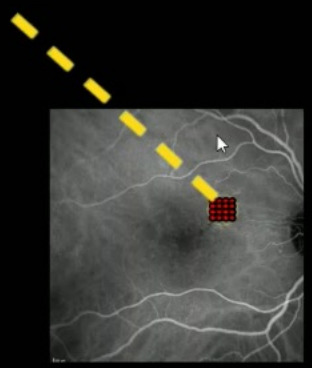
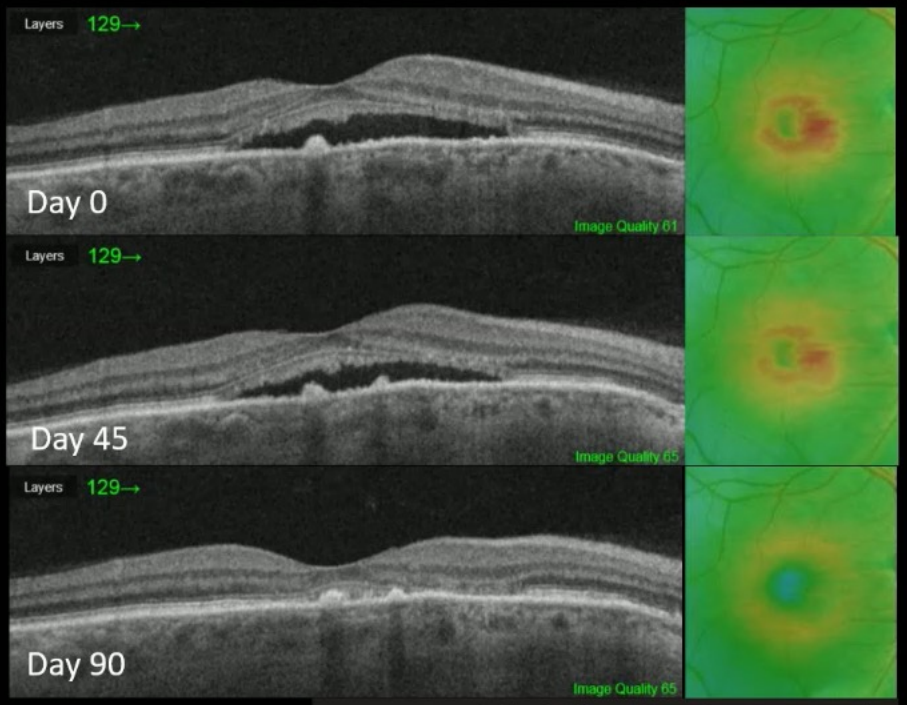
Central Serous Chorioretinopathy (CSC)

FA or ICGA guided treatment





Images courtesy of Alejandro Filloy Rius, MD. Ph.D - Tarragona, Spain

Acta Ophthalmologica

Acta Ophthalmologica 2022

Perspective

Clinical impact of the worldwide shortage of verteporfin (Visudyne®) on ophthalmic care

Marc J. Sirks,[1] Elon H.C. van Dijk,[2] Noa Rosenberg,[3,4] Carla E.M. Hollak,[3,4,5] Stamatios Aslanis,[6] Chui Ming Gemmy Cheung,[7,8] Itay Chowers,[9,10] Chiara M. Eandi,[11,12] K. Bailey Freund,[13,14] Frank G. Holz,[15] Peter K. Kaiser,[16] Andrew J. Lotery,[17] Kyoko Ohno-Matsui,[18] Giuseppe Querques,[19] Yousif Subhi,[20,21] Ramin Tadayoni,[22,23,24] Charles C. Wykoff,[25,26] Dinah Zur,[27,28] Roselie M.H. Diederen,[1] Camiel J.F. Boon[1,2,†] and Reinier O. Schlingemann[1,11,†]

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ABSTRACT.

Introduction: **Since July 2021, a worldwide shortage of verteporfin (Visudyne®) occurred: an essential medicine required for photodynamic therapy (PDT). PDT with verteporfin has a broad range of indications in ophthalmology, including chronic central serous chorioretinopathy, polypoidal choroidal vasculopathy and choroidal haemangioma. For these disorders, PDT is either the first-choice treatment or regarded as a major treatment option.**

Materials and methods: **A questionnaire was sent to key opinion leaders in the field of medical retina throughout the world, to assess the role of PDT in their country and the effects of the shortage of verteporfin. In addition, information on the application of alternative treatments during shortage of verteporfin was obtained, to further assess the impact of the shortage.**

Results: **Our questionnaire indicated that the shortage of verteporfin had a major impact on ophthalmic care worldwide and was regarded to be a serious problem by most of our respondents. However, even though there is ample evidence to**

Visudyne Shortage

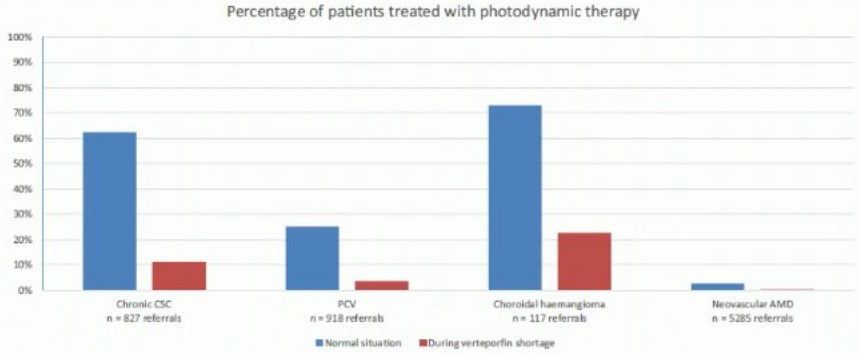

Fig. 1. Percentage of patients treated with photodynamic therapy per disease, both in the normal situation and during the verteporfin shortage. These values were calculated by dividing the number of PDT-treated patients by the number of referred patients per clinic and averaging these percentages. The absolute number of referrals is noted below the bars. AMD = age-related macular degeneration; CSC = central serous chorioretinopathy; PCV = polypoidal choroidal vasculopathy; PDT = photodynamic therapy.

Conclusion: The shortage of verteporfin has had a large effect on the care of ophthalmic patients across the world and may have resulted in significant and irreversible vision loss.

OASISEYE SPECIALISTS

Conclusion

Although intravitreal injections have become the first line of treatment of macular pathologies such as diabetic macular edema (DME), laser application within clinical settings continues to prove efficacious in macular conditions.

SOLS members warmly invite you to join the society to investigate deeper into subtreshold laser treatment options.

Subthreshold laser.

Wether under the name Subliminal or other commercial denominations, STL works under two principles:

- Eliciting a response from the targeted tissue in the form of production of antiinflammatory/restorative molecules.
- Must be invisible at any given moment, except for its results.

Subthreshold laser.

It is a surgical procedure, so:

- Operator dependent (experience)
- Standardization makes it safer, more reproducible and quicker to learn.

Subthreshold laser.

Subthreshold laser.

The ROYAL COLLEGE of OPHTHALMOLOGISTS

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COMMENT

Check for updates

Subthreshold laser therapy guidelines for retinal diseases

Jay Chhablani [1]✉ and SOLS (Subthreshold Laser Ophthalmic Society) writing committee*

Table 1. Subthreshold laser consensus guideline settings for diabetic macular oedema and central serous chorioretinopathy by the Subthreshold Ophthalmic Laser Society (SOLS).

Subthreshold laser settings	Diabetic macular oedema	Central serous chorioretinopathy
Duty cycle	5%	5%
Pulse duration	200 ms	200 ms
Spot size	150–200 µm	100–200 µm
Spacing between spots	No	No
Titration	Yes	Yes
Titration power	50% of threshold power	50% of threshold power

Subthreshold laser. SOLS guidelines.

Parameters.

- Duty cycle: 5%
- Pulse duration: 200ms (effective laser time: 10ms)

Subthreshold laser. SOLS guidelines.

Parameters.

- Spot size: 100-200 microns
- Dense pattern (without spacing between spots)

Subthreshold laser. SOLS guidelines.

Parameters.

Power individually titrated at 50%

- **A-Prevents variability beween patients.**
- **B-Takes into account weakening of the laser cavity with time.**

Subthreshold laser. SOLS guidelines. DME

Center and non-center involving.

In combination with IV drugs.

Treat all over the edematous area.

Check after 6-8 weeks, consider retreatment after 12 weeks.

Subthreshold laser. SOLS guidelines. CSCR

Both for chronic and acute (after 1 month) forms

First line treatment.

Treat over and widely around the leakage point.

Check after 6-8 weeks. Consider retreatment then.

Subthreshold laser. SOLS guidelines. Safety points.

Transfoveal treatment is not encouraged alghough it is considered safe in expert hands.

After treatment: Funduscopy, AF and OCT will determine the abscence of visible changes.

Extra point.

From the mathematical combination of parameters, an "energy density" results, named Fluence. Useful also as a security measure.

12 J/cm2 12-20 J/cm2 20 J/cm2

Subthreshold laser. SOLS guidelines. Safety points.

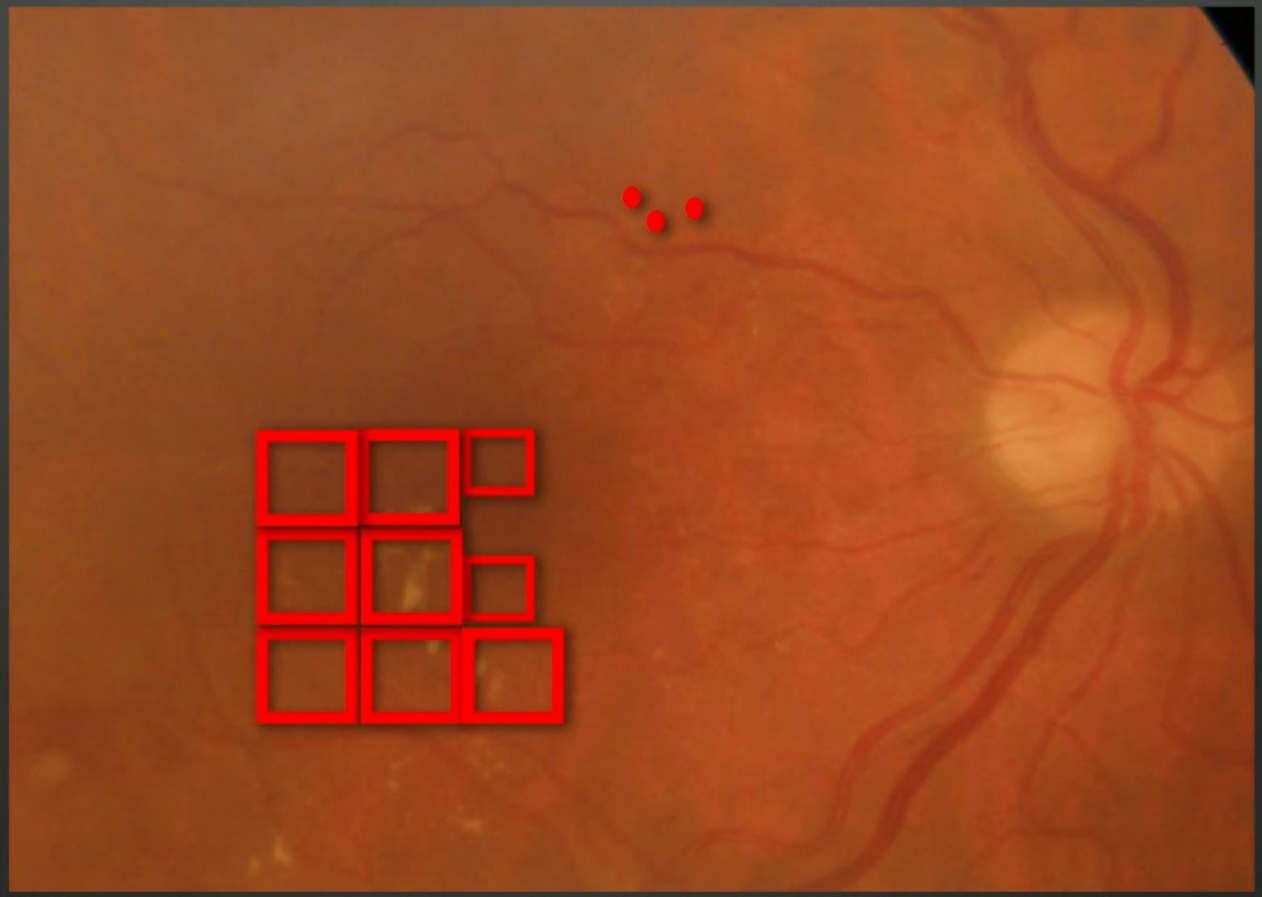
12 J/cm2 12-20 J/cm2 20 J/cm2

Subthreshold laser. SOLS guidelines. Safety points.

12 J/cm2 12-20 J/cm2 20 J/cm2

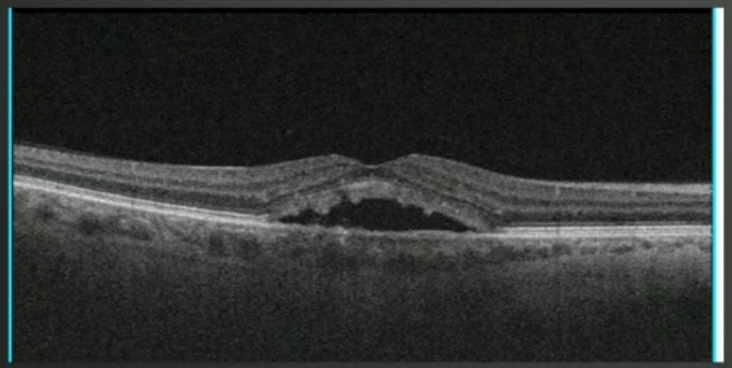
Step by step technique.

- 100-200 microns
- Titrate
- Quick Fluence check
- Treatment delivery.



Step by step technique.

Planning a case example: CSCR

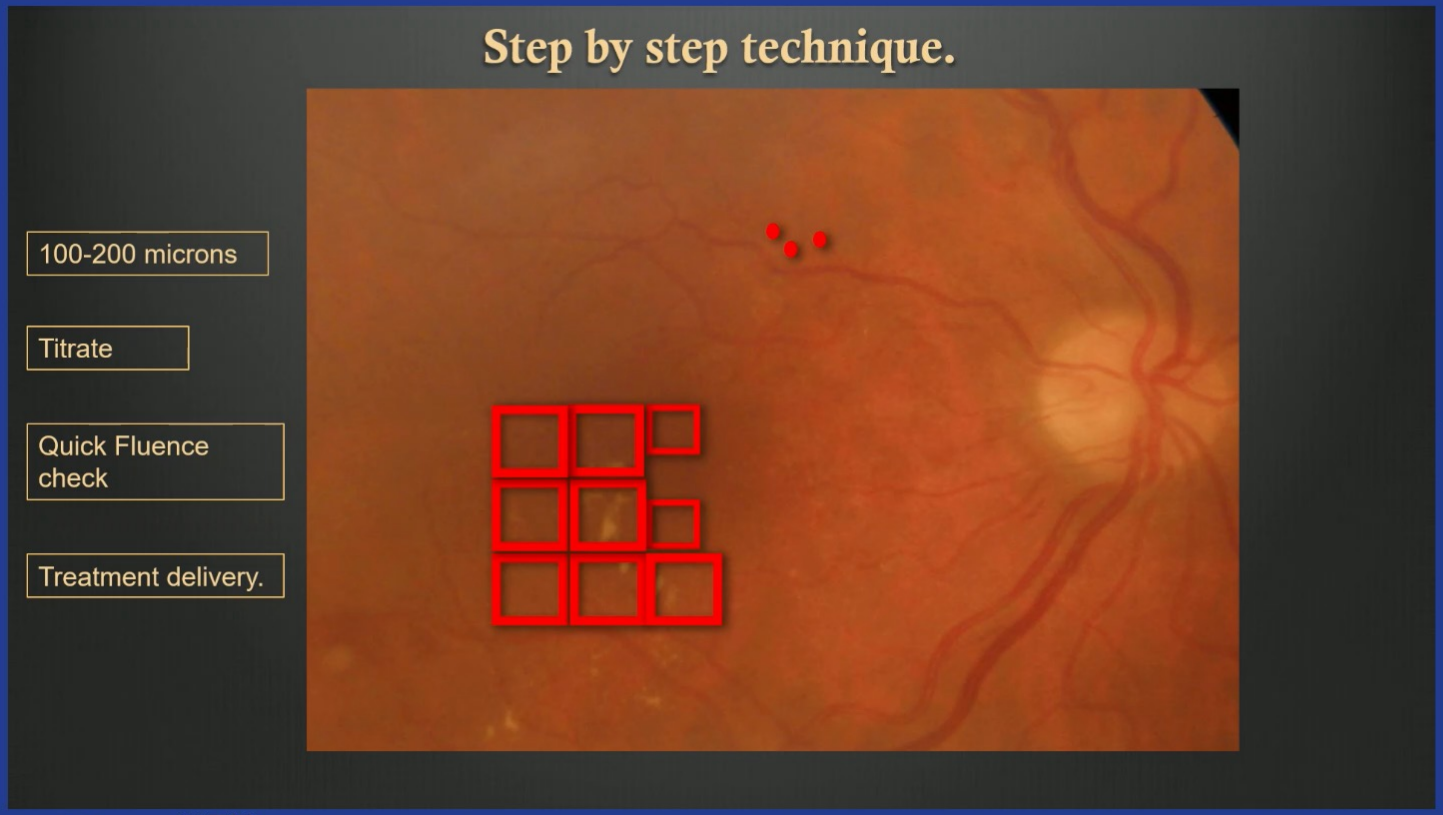


Conclusions

- Guidelines and consensus are key to provide reproducibility and soundness to any therapeutical technique.
- Its many contributors provide great value to the SOLS guidelines.
- A step-by-step technique is the safest approach both for the beginner and the expert.

10:15 - 11:15 Laser for retina and vitreous: All you need to know in 2023.

CHAIR : VICTOR CHONG



Alejandro Filloy

Recommended video treatment guidelines.

OASISEYE SPECIALISTS

SOLS
SUBTHRESHOLD OPHTHALMIC LASER SOCIETY

Thank you