Supplement to RETINA TODAY May/June 2012

Fovea-friendly MicroPulse Laser

The reviews are in.

"I no longer have to 'tiptoe' through the region of the fovea…"
– Sam E. Mansour, MSc, MD, FRCS(C), FACS

"…MicroPulse is an ideal 'repeatable' therapy."
– Victor Chong, MD, FRCS, FRCOphth

"…with MPLT, it is now possible to address foveal leakage in a safer and more effective manner with subclinical invisible laser treatment."
– José Augusto Cardillo, MD

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MicroPulse Laser Therapy for DME

BY NEELAKSHI BHAGAT, MD, MPH AND MARCO ZARBIN, MD, PHD, FACS

As the epidemic of diabetes mellitus continues throughout the developed world, diabetic macular edema (DME) will remain one of the pathologies most frequently seen by retina specialists.

Laser photocoagulation has been the gold standard of treatment for DME since the ETDRS. The anatomical and visual benefits have been shown to be sustainable over the long term; however, the treatment is associated with risks and side effects due to the iatrogenic damage to retinal tissue.

A major advancement to laser photocoagulation is subthreshold MicroPulse Laser Therapy (MPLT). MPLT is therapeutically effective without producing discernible signs of laser-induced damage during treatment or at any time postoperatively, offering a more attractive option for patients and specialists.

In more recent years, pharmacotherapy has been advocated for the treatment of DME. Its widespread adoption, largely prompted by compelling acute effects, has been tempered by the realizations that its benefits require multiple intraocular injections and many patients do not respond adequately.

In selected cases, the addition of laser treatment to anti-VEGF therapy can achieve a sustained therapeutic effect while reducing the need for injections. MicroPulse laser appears to be the most logical choice for laser therapy because it has been shown to be less destructive to tissue while achieving the desired biological effect. Recently, Vujosevic et al[1] showed that MicroPulse laser treatment appears to be as effective as modified-ETDRS laser photocoagulation for treating DME, but it causes far less damage to the retinal pigment epithelium, as judged by microperimetry and fundus autofluorescence. Having the option of a laser therapy that produces little to no collateral damage is quite attractive in the setting of patients with severe disease and difficult access to ophthalmic care. We believe that combination therapy of pharmacotherapy and non-damaging laser is a particularly useful approach for DME in these cases.

OUR EXPERIENCE

UMDNJ-University Hospital in Newark, NJ is a tertiary referral center. As a result, we care for many patients in whom the severity of diabetic retinopathy is high. We first started using subthreshold MPLT for these patients with clinically significant macular edema. MPLT protocols employ low intensity/high density laser applications in envelopes of repetitive short pulses to induce beneficial intracellular antiangiogenic and restorative biological factors without photodestruction.

We performed a study over 10 years ago to evaluate whether diode MPLT reduced the side effects that have been noted with argon thermal laser for macular edema. We started the study in 2001 and followed patients through to 2004, and in that time period, we noted that the edema was reduced for patients treated with MPLT with less visual loss, fewer retinal scars, less subretinal fibrosis, and lower risk of choroidal neovascular membranes and scotomata, as compared to conventional continuous-wave laser photocoagulation.[2]

PAIRING MPLT WITH 577 NM

Our MicroPulse experience has been with 810 nm lasers. This same technology has been paired with the new 577 nm lasers, providing similar tissue-sparing capabilities and clinical outcomes. In the following pages, 3 retina specialists who have used 577 nm MPLT for treating disease, including DME and central serous chorioretinopathy, will discuss the effects of MPLT on achieving successful clinical outcomes, increasing patient satisfaction, and its positive impact to their practices. ■

Neelakshi Bhagat, MD, MPH, is Associate Professor of Ophthalmology at UMDNJ and Director, Vitreoretinal and Macular Surgery at Institute of Ophthalmology and Visual Science at University of Medicine and Dentistry (UMDNJ). Dr. Bhagat may be reached at bhagatne@umdnj.edu.

Marco A. Zarbin, MD, PhD, FACS, is Professor and Chair at the Institute of Ophthalmology and Visual Science and Professor of Neurosciences at UMDNJ. He is also Chief of the Department of Ophthalmology at University Hospital in Newark, NJ. Dr. Zarbin may be reached at zarbin@earthlink.net.

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Tissue-sparing MicroPulse 577 nm Laser Therapy: The "Aha" Moment from the Ultimate Skeptic

BY SAM E. MANSOUR, MSc, MD, FRCS(C), FACS

I previously was very reluctant about using subthreshold laser for the treatment of retinal disorders. I considered it somewhat of a "homeopathic laser" because of the lack of a visible endpoint. Conversely, I had never enjoyed performing conventional laser therapy for macular edema because I felt it to be a very destructive procedure. However necessary conventional laser has been, I still view it as a form of "retinal amputation," causing irretrievable tissue loss. When I first performed subthreshold laser therapy for macular edema in the early 1990s, I was pleasantly surprised with the limited tissue response in the absence of visible photocoagulative damage. MicroPulse Laser Therapy (MPLT) takes subthreshold to even safer levels, allowing a phototherapeutic treatment without any photodestruction. I believe that the 577 nm laser used with MPLT settings is the safest laser to use in the sensitive area of the fovea—not only around the fovea, but when treating refractory edema over the fovea.

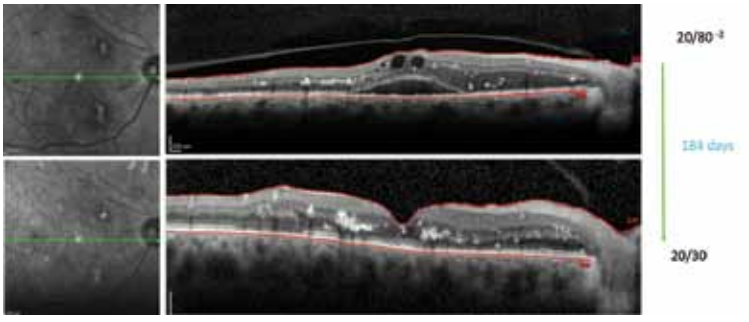

Figure 1. Top: SD-OCT of right eye of a patient with DME who had previously received a single intravitreal triamcinolone injection 4 months prior to the scan showing persistent edema. Bottom: 6 weeks following MPLT, there is a significant resolution of the retinal edema as well as a concomitant increase in visual acuity.

One of my first cases was treating a patient with diabetic macular edema (DME) and cataracts, with no prior pharmacotherapy. The patient's vision was 20/30-1, largely due to diffuse foveal thickening and hard exudate formation. I did a single grid application of 577 nm MPLT and was amazed at the fact that the vision improved to 20/20-2 in less than 2 months with no visible signs of laser treatment, neither clinically nor on fluorescein angiography or spectral-domain optical coherence tomography (SD-OCT).

As I became more comfortable performing MPLT, I found that it gives me a large safety margin. I no longer have to "tiptoe" through the region of the fovea because I am not concerned about photocoagulative damage. I am able to treat quickly in an almost preset format, and my laser sessions take half the time than with a conventional focal and grid laser session. MPLT has significantly boosted my efficiency in the clinic.

> "I no longer have to 'tiptoe' through the region of the fovea because I am not concerned about photocoagulative damage."

MY COMBINATION TREATMENT ALGORITHMS

I have found that using 577 nm MPLT in combination with pharmacotherapy is an option that works well for my patients with DME. I use MPLT to confluently cover all areas of retinal edema.

For mild DME with a central subfield mean thickness (CSMT) of ≤250 µm as determined by SD-OCT, I primarily use MPLT (See *Parameters for Treating DME Using the IQ 577 Laser System*).

For moderate macular edema, CSMT 251-400 µm, I typically start with 2 monthly intravitreal anti-VEGF injections and, if 30 days after the second injection there is no significant reduction in the edema, I proceed to MPLT. If there is a response to the initial 2 injections, I will continue to a maximum of 3 additional injections before proceeding to laser treatment.

For severe macular edema, CSMT >400 µm, I start with 3 monthly injections of an anti-VEGF agent and if the patient responds, I will continue to a maximum of 3 additional injections. If, following the anti-VEGF injections the CSMT on OCT is reduced to less than 400 µm, I proceed to MPLT. If there is an insufficient response following the anti-VEGF (CSMT >400 µm), I will then consider the option of intravitreal corticosteroids with the patient weighing the risks and benefits of that therapy, and if I choose to inject intravitreal triamcinolone acetonide, 30 days later I will apply MPLT again.

POSITIVE IMPACT TO MY PRACTICE AND PATIENTS

In my practice, tissue-sparing MicroPulse has now completely replaced conventional continuous-wave (CW) laser for macular edema resulting from diabetes or retinal vein occlusion. I have used more laser therapy in comparison to pharmacotherapy alone on patients with macular edema in the last year than I have for the past 3 years due to the success that I have had with MPLT.

One consideration on which the patient should be advised is that with MPLT, there will probably not just be a single session. Typically, 2-3 sessions, 3-4 months apart will be required. MPLT is repeatable because it does not induce thermal damage. And, because this is the safest way to reduce edema, it is plausible it will take longer than conventional laser to achieve the desired result. As a result, MPLT has definitely increased our practice revenue because I am performing more laser treatments.

Additionally, I am performing more laser therapy because the indications for MPLT are wide. DME represents the bulk of my cases (Figure 1), but I also use MPLT to treat macular edema secondary to retinal vein occlusion, chronic uveitis, and in rarer cases, even pseudophakic macular edema. MPLT has proved to be very versatile.

> "…MPLT has definitely increased our practice revenue because I am performing more laser treatments."

When treating refractory edema, I have found that MPLT has helped me significantly. We all have those patients for whom pharmacotherapy with anti-VEGF agents and steroids fail to completely resolve the macular edema. These patients plateau to a point where the edema just fails to resolve or keeps recurring. It is very likely that if a patient does not respond after 3 consecutive injections with an anti-VEGF agent or steroid, they will not respond any better to subsequent injections. For these patients, I can use MPLT to shrink the residual edema without injecting again.

> "When treating refractory edema, I have found that MPLT has helped me significantly."

Given a choice between MPLT and pharmacotherapy for my patients who have mild to moderate DME, I have found that my younger working patients opt for MPLT. Their work and family obligations keep their schedule very busy and they typically don't have time for monthly visits. Patients who are confined to wheelchairs also find this a more convenient option.

One of the interesting findings with MPLT is that most of my patients have experienced a subjective improvement in their vision, typically within 2-3 weeks after treatment.

SAM MANSOUR, MD, FRCS (C), FACS PARAMETERS FOR TREATING DME USING THE IQ 577 LASER SYSTEM

Pre-Treatment Test Burn

Mode: CW
Spot Size (Adapter): 200 µm
Lens: Mainster Focal Grid
Duration: 200 ms
Power: Start at 50 mW
Test Spot Technique: Perform test spot in mildly edematous region >2 disc diameters from foveal center; titrate power upwards by 10 mW increments (each time, moving to an adjacent spot) until a barely visible tissue reaction develops.

Subthreshold MicroPulse Laser Therapy

Mode: MicroPulse
Spot Size (Adapter): 200 µm
Lens: Mainster Focal Grid
Duration: 200 ms
Power: 4x power achieved from test burn
Duty Cycle: 5%
Technique: Dense, confluent grid pattern application; OCT-guided coverage area. I never recommend a higher than 5% duty cycle with the yellow laser for macular application.

WATCH IT NOW ON THE RETINA SURGERY CHANNEL AT WWW.EYETUBE.NET!

MicroPulse IQ577: Practical Applications for DME
By Sam E. Mansour, MSc, MD, FRCS(C), FACS

direct link to video:
http://bcove.me/vdyysc18

eyetube Ophthalmic Video Resource

SUMMARY

The ideal goal with any therapy for DME is to achieve the greatest reduction in macular thickness in the shortest time, with the least amount of side effects, and with the longest duration. Although pharmacotherapy is playing a larger role, laser therapy is still a key factor in treatment. In my practice, subthreshold MPLT has proven to be as effective as conventional laser, but with a greatly reduced risk of iatrogenic, nontherapeutic effects, and has improved my options to better manage patients with DME and other retinal disorders. ■

Sam E. Mansour, MSc, MD, FRCS(C), FACS, is Clinical Professor in the Department of Ophthalmology at George Washington University in Washington, DC, and is Medical Director of the Virginia Retina Center with 3 locations in Northern Virginia. Dr. Mansour states that he is a consultant to Iridex and QLT. He may be reached via email at SM@virginiaretina.com.

Laser for DME in the Anti-VEGF Era

BY VICTOR CHONG, MD, FRCS, FRCOPHTH

Since the ETDRS, laser photocoagulation has been the gold standard for the treatment of diabetic macular edema (DME). In recent years, there have been interesting developments in regards to pharmacologic options, particularly anti-VEGF agents, and these are positive advancements to expanding the treatment options for our patients. One important point to note about the clinical trials with anti-VEGF is that only patients with foveal involvement were included in these studies. So, for DME that does not involve the fovea, laser photocoagulation may continue to be the gold standard for treatment.

Anti-VEGF has shown good results for DME. The Diabetic Retinopathy Clinical Research Network (DRCR.net) Protocol I study in the United States and the RESTORE study in the United Kingdom and Europe both showed ranibizumab to be effective, both alone and in combination with laser.[1,2]

Even if we shift our treatment paradigm for DME to injecting anti-VEGF, I do not believe that we will discontinue our use of laser. After all, do we truly want to commit our patients to monthly, or even more frequent, injections for an extended period of time? Particularly for our younger patients, this could mean decades of injections. Just as having anti-VEGF agents as another option for patients is an advantage, so is having laser as an option. Considering that some of our patients may find it incredibly inconvenient to have multiple injections along with the burden that costly injections could place on health care systems, having more options, such as laser, may represent a good compromise.

LASER REDUCES FREQUENCY OF INJECTIONS

In reviewing the DRCR.net 2-year expanded study, I did not find any significant difference in the number of injections in the ranibizumab with prompt laser vs ranibizumab with deferred laser, but over the course of the study, 80% of all patients had received laser treatment.[1] The READ-2 study, however, did find that when laser was added to ranibizumab, patients required far fewer injections (4.9) over 24 months than with ranibizumab alone (9.3) with similar visual acuity results (6.80 letter gain and 7.70 letter gain, respectively).[3]

In addition, combining laser with pharmacotherapy can offer benefits of reduced chair time, cost, and inconvenience to the patient in regard to frequent injections.

DOES SCARRING THE RETINA MATTER?

Some people would say that scarring the retina doesn't matter because it's the fovea that actually matters. Our understanding of how laser photocoagulation

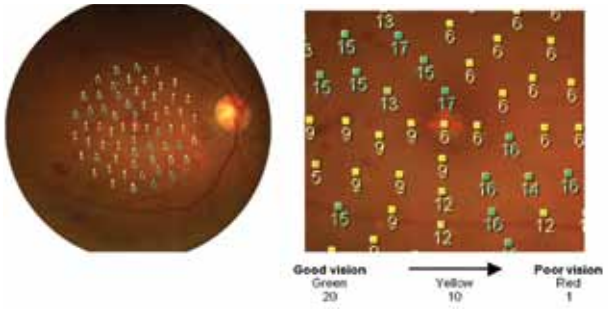

Figure 1. Microperimetry map. Microperimetry measures retinal sensitivity and visual function.

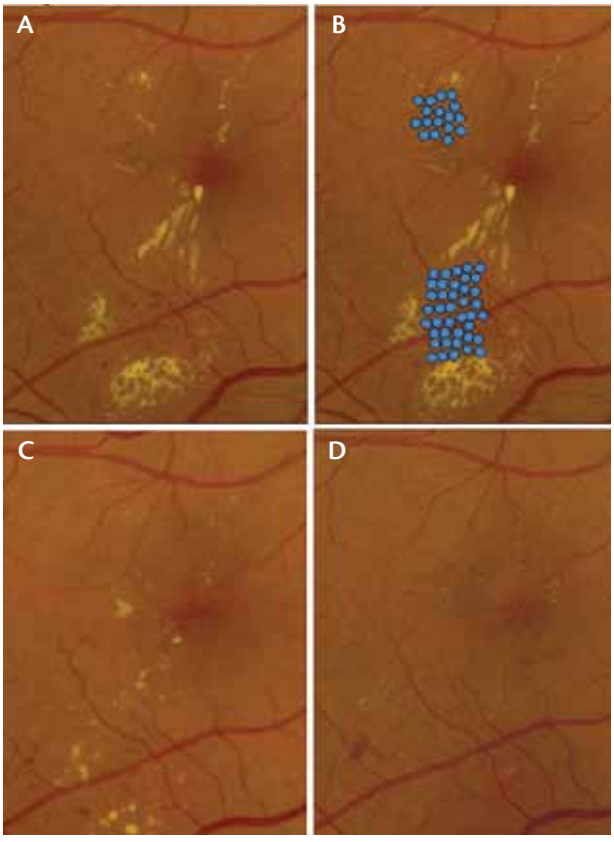

Figure 2. 810 nm MPLT for DME. Pre-treatment (A); High density 810 nm MPLT (B); 4 months post-treatment (C); 1 year posttreatment; note that there are no laser scars (D).

"… combining laser with pharmacotherapy can offer benefits of reduced chair time, cost, and inconvenience to the patient in regard to frequent injections."

works has evolved from direct coagulation of leakage in the retina as the main mechanism of action to learning that laser energy is absorbed by the retinal pigment epithelium (RPE), which changes the microenvironment, leading to the closure of microaneurysms and reduction of macular edema.

One of the long-standing issues with conventional laser is the concomitant damage and scarring that spreads over time, leading to future scotomas. Although 20/20 results can be achieved with conventional laser, what about overall retinal function? In addition to optical coherence tomography (OCT), fundus photography, and fluorescein angiography (FA), we now have microperimetry available to see deeper into how laser affects retinal sensitivity (Figure 1).

Based on microperimetry, we carried out a study on reading ability in patients who have DME. It's common for patients with DME who appear to have good visual acuity say that they cannot read. In our study, we found that patients with slower reading speeds had a reduction of contrast sensitivities, a reducing microperimetry, and a loss of fixation. Therefore, one can postulate that when there's scarring, there can be a reduction of retinal sensitivities. Quite often very faint scars in the beginning enlarge over time. After a year, they could be quite large; after 5 years the scars can be even more horrendous.

CONTINUOUS-WAVE PATTERN SCANNING IS NOT MICROPULSE

The subthreshold MicroPulse Laser Therapy (MPLT) technique delivers laser energy in pulses resulting in no visible scarring compared to conventional continuous-wave (CW) laser treatment. According to Topcon, the PASCAL pattern laser system is able to deliver multiple spots at 50% of the visible threshold power to achieve similar subthreshold effects as MPLT. In my opinion, however, 50% PASCAL is not the same as MPLT. With 50% PASCAL—but not with MPLT—scarring can still be observed on fundus autofluorescence (FAF).

With MPLT, the laser energy is delivered in a train of repetitive microsecond pulses with adequate cooling time in between. The resulting total energy can be higher but no lethal photothermal effects are produced and no laser lesions are discernible on FA and FAF as reported by Vujosevic et al[4] (See *MicroPulse Technology: It's Not Your Classic Laser*, page 15).

BENEFITS OF 577 NM MICROPULSE IN PRACTICE

In addition to Vujosevic et al,[4] other authors have shown 810 nm MPLT effective in the treatment of DME[5-7] (See Table 1) as well as other vascular disorders, such as macular edema due to branch retinal vein occlusion[8] and central serous chorioretinopathy,[9] with minimal or no collateral effects.

One of the more recent developments is the incorporation of MicroPulse laser technology in a 577 nm yellow laser system, such as the IQ 577 (Iridex) laser system, which offers both CW and MicroPulse modes. In my experience, I have found similar outcomes using 577 nm MPLT as with 810 nm MPLT for the treatment of DME. With 577 nm MPLT, I use a 5% duty cycle:

TABLE 1. CLINICAL OUTCOMES OF 810 NM MPLT FOR DME

Author	Authors' Conclusions	Follow-up
Figueira et al. *Br J Ophthalmol.* 2009[5]	MPLT is equally as effective as conventional green laser (CGL) treatment for clinically significant macular edema. There was less scarring in the MPLT group than in the CGL group. This is an important finding, as spread of retinal atrophy around conventional laser scars occurs over the years and is a frequent complication, particularly for macular laser.	1 year
Vujosevic et al. *Retina.* 2010[4]	MPLT is 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 et al. *Invest Ophthalmol Vis Sci.* 2011[6]	MPLT is superior to the mETDRS based on BCVA improvement and CMT reduction.	1 year
Luttrull et al. *Retina.* 2011[7]	MPLT can effectively treat retinovascular macular edema without laser-induced retinal damage.	Up to 10 years

laser on for 0.1 ms and off for 1.9 ms (See *MicroPulse Laser Therapy: Parameters for Treating DME Using the IQ 577 Laser System*). After I perform a test burn, I reduce power by 70%. These settings appear to be effective and do not produce scarring at any time post-treatment, which make subthreshold MPLT an ideal "repeatable" therapy (Figure 2). Similar to my experience using 810 nm MicroPulse, with 577 nm MicroPulse, I use a dense treatment pattern that is OCT-guided, so I do not specifically treat microaneurysms. Dense treatment means that we use confluent laser applications with overlapping spots. The entire edematous area is treated based on OCT.

PATIENT SELECTION CONSIDERATIONS

In my practice, MPLT is our routine practice for treating patients with DME. We also use it for treating macular edema due to retinal vein occlusions, and central serous chorioretinopathy. Recently, I have started treating small foveal cysts, which can cause mild visual loss but can get worse over time. These cysts are commonly associated with microaneurysms within 100 µm of the foveola, which is too close to be treated by conventional laser. Because MPLT does not scar, this is an ideal treatment.

When patients realize that there is no scarring and a much better safety margin with MPLT (than with conventional laser treatment), they are very accepting of the procedure, particularly if they've had prior conventional laser treatment. They are reassured that even if they move during treatment, it is actually very unlikely to be a problem.

577 NM MPLT CASE REPORT

A 65-year-old white man was referred to me by his optometrist, who noted reduced vision OD in a routine examination. The patient had been on medication for type 2 diabetes for 15 years, his HBA1c level was 7.0, and his blood pressure was 140/70 with medication. His cholesterol was 4.8 mmol/l and he was taking a statin. His ocular status was mild nuclear sclerosis cataract and best corrected visual acuity of 20/40 OD and 20/20 OS. Figure 3 shows the OCT of the patient's right eye, preoperative (top) vs postoperative (bottom). Note the reduced macular edema 4 months postoperatively after a single treatment with MPLT.

SUMMARY

Laser is still required in the majority of patients with DME, particularly those who do not have foveal involvement. Subthreshold MPLT, in my opinion, can be safely applied without producing retinal scarring at any time posttreatment, even in the treatment of cysts that are within 100 µm from the fovea. Further, in combination with anti-VEGF agents, MPLT can reduce the number of

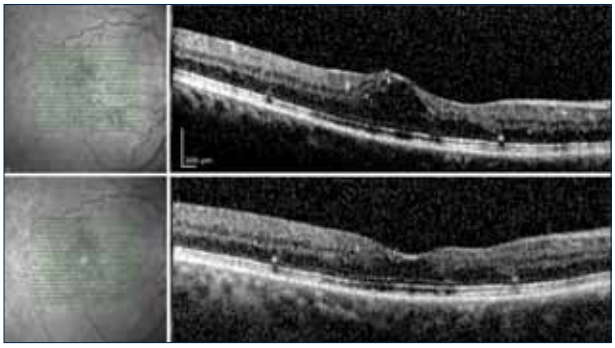

Figure 3. 577 nm MPLT for DME. Top: Pretreatment, central macular thickness (CRT): 333 µm, VA 20/40. Bottom: 4 months post a single treatment of 577 nm MPLT, CRT 253 µm, VA 20/25.

VICTOR CHONG, MD, FRCS, FRCOPHTH

MICROPULSE LASER THERAPY: PARAMETERS FOR TREATING DME USING THE IQ 577 LASER SYSTEM

Pre-Treatment Test Burn

Mode: MicroPulse
Spot size (Adapter): 100 µm
Lens: Area Centralis
Duration: 200 ms
Duty cycle: 5%
Power: ~700 mW
Technique: We pick an area of normal retina near the edge of the edematous area. Depending on the skin color of the patients, we usually start with about 500 mW in Caucasians and then moving up by 100 mW steps until a just visible tissue reaction is noted, if unsure, place another spot with the same energy.

Subthreshold MicroPulse Treatment

Mode: MicroPulse
Spot size (Adapter): 100 µm
Lens: Area Centralis
Duration: 200 ms
Duty cycle: 5%
Power: Reduce 70% from MicroPulse test burn (ie, 700 mw gives just visible burns, cut to 490 mW to treat)
Technique & Treatment Pearls: Dense treatment guided by OCT. Contiguous pattern with the laser over the edematous area based on OCT. Microaneurysms are not deliberately treated, but will be hit with the pattern. It's most important to focus during the entire treatment because there is no color change. An extra safety margin exists with the MicroPulse technique, allowing the spots to be closer to one another.

injections in the management of patients with DME, and without scarring, might get a better visual outcome. ■

Victor Chong, MD, FRCS, FRCOphth, is Consultant and Head of Department, Oxford Eye Hospital, University of Oxford, UK. He states that he is a consultant to Novartis, Pfizer, Allergan, Bayer, Regeneron, Iridex, and Alimera Sciences; a speaker for Heidelberg and Quantel; receives departmental research funding from Novartis, Pfizer, Alcon, Allergan, and Bayer; and has received equipment donation from Optos, Quantel, Iridex, and Carl Zeiss Meditec. Dr. Chong may be reached via email at victor.chong@eye.ox.ac.uk.

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577 nm MicroPulse Laser Therapy: Addressing the Immediate Need of Our Patients With DME

BY JOSÉ AUGUSTO CARDILLO, MD

I have a long background in ocular pharmacology and began researching drugs for the treatment of diabetic macular edema (DME) many years ago. Over the course of several years, my colleagues and I have tested several agents, including anti-VEGF agents and steroids, with a particular interest in sustained-release steroids. After 1 or 2 years, however, we noted several deleterious side effects, ie, 50% of patients required surgical intervention for glaucoma. We have now largely shifted gears to new laser treatments for DME to address the immediate need of our patients.

Laser was established as the gold standard for treating DME almost 30 years ago in the ETDRS[1]; however, comparing the laser treatments that we were using 30 years ago to what we have available currently is like comparing a 30-year old generic type of car to a brand new Ferrari. That said, in 30 years, there has been no accurate algorithm for laser treatments. The rationale for using a modified-ETDRS laser technique is based largely on surveys. For example, in the recent Diabetic Retinopathy Clinical Research Network's (DRCR.net) study comparing anti-VEGF plus prompt or deferred laser to steroids plus prompt laser for DME, they chose the modified-ETDRS technique based on a survey,[2] which is not a scientific-based decision but rather an observations-based decision. The fact is that there is no evidence in the scientific literature to support the idea that a modified-ETDRS laser technique is better than the standard ETDRS laser technique. The idea that modified-ETDRS laser is superior was born from a few different individual studies using this technique, not direct head-to-head comparisons.[3-5]

In my opinion, laser has not been explored to its full potential, particularly now that we have newer technologies available, such as subthreshold MicroPulse Laser Therapy (MPLT) with the IQ 577 laser (Iridex). In fact, we are misjudging and proposing an immediate DME therapy paradigm shift to pharmacotherapy without fully exploring the maximal clinical potential of laser. For instance, I have had colleagues refer patients to me who they had identified as "laser failures." Upon examination, I found they were not laser failures at all, but simply failures in the techniques used to administer the laser.

DENSE TREATMENT FOR MAXIMUM EFFECT

We know that density of laser treatment patterns matters. The DRCR.net published data from a study showing that increased density of the laser burns is

TABLE 1. 1-YEAR OUTCOMES: HIGH-DENSITY MPLT PROVED SUPERIOR THAN NORMAL-DENSITY MPLT AND MODIFIED-ETDRS FOR THE TREATMENT OF DME

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

*Indicates significant improvement vs mETDRS and MPLT normal density $P < .05$.

more effective in reducing retinal thickening caused by DME than using a lower density mild macular grid pattern as evaluated by optical coherence tomography (OCT).[6] A mild macular grid is a spot titrated to a barely clinically visible lesion, but the DRCR.net also increased the spacing between the spots, which, in my opinion, makes no sense. When I use low intensity, subthreshold MPLT, I increase the density of my spots to achieve the maximal effect.

We performed a prospective, double-masked, controlled clinical trial evaluating the anatomical effects using 532 nm modified-ETDRS treatment (direct and grid photocoagulation technique) vs 810 nm MPLT using normal-density laser (mild macular grid placed at the macula without direct treatment of microaneurysms) or high-density (increased number of spots to enhance the area of retinal pigment epithelium [RPE] activation) for DME in 123 eyes. We found that at 1 year, the high-density MPLT proved superior to the other 2 treatments (Table 1).[7] Vujosevic et al[8] also conducted a study comparing modified-ETDRS treatment to MPLT. Their findings at 1 year were that high-density MPLT was as effective as modified-ETDRS treatment, but without any changes or damage to the RPE detectable by fundus autofluorescence, and with increased retinal sensitivity as measured by microperimetry. Recently, Luttrull et al[9] confirmed that over the long-term (eyes in this study were treated as early as 2000) high-density MPLT was effective in reducing edema without causing retinal damage.

SANDWICH TECHNIQUE–MPLT DELIVERED OVER FOVEAL CENTER

Another important consideration is how and where the laser is delivered. According to ETDRS guidelines, initial burns must be placed 500 µm from the foveal center. For retreatments, the ETDRS protocol specifies placing burns 300 µm from the foveal center. Realistically, how can a destructive treatment be applied this close to the foveal center? Using conventional lasers, this would, in some cases, do more harm than good.

Our subthreshold MPLT experience shows that intense burns are definitely not necessary and a comparable outcome can be reached with no visible lesions. Based on the idea that we want to maximize tissue response while minimizing side effects, we currently use a *Sandwich Technique* for the treatment of DME (See *577 nm* Sandwich Grid *Treatment Technique for DME With Foveal Leakage*).

Figure 1 shows a patient with a difficult case of diffuse DME who received 7 monthly injections of bevacizumab (Avastin, Genentech) with no results. I treated her with a single treatment of 577 nm laser using the Sandwich Technique. At 6 months follow-up, the patient's central macular thickness (CRT) reduced from 736 µm to 353 µm. Visual acuity improved from 20/320 to 20/63.

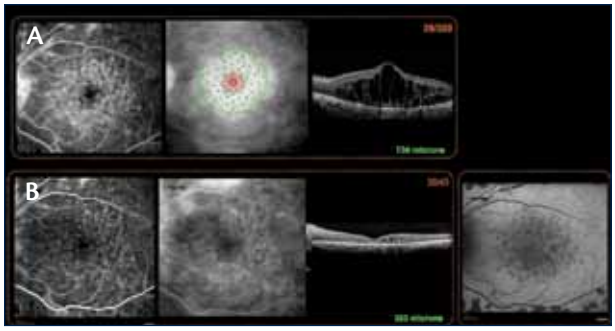

Figure 1. 577 nm Sandwich Technique for the treatment of diffuse DME. Pretreatment. CRT: 736 µm. Visual acuity: 20/320 (A). Six months post-treatment. CRT: 353 µm. Visual acuity: 20/63 (B).

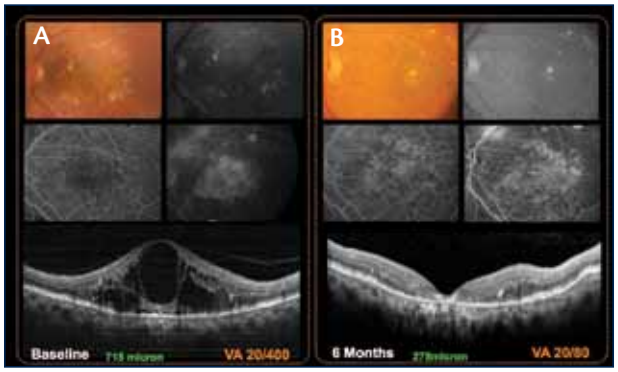

Figure 2. 577 nm Sandwich Technique for the treatment of refractory edema. Pretreatment. CRT: 715 µm. Visual acuity: 20/400 (A). Six months post-treatment. CRT: 278 µm. Visual acuity: 20/80 (B).

Figure 2 shows a patient with diffuse DME who received 6 monthly injections of bevacizumab with no results. After a single 577 nm laser treatment using the Sandwich Technique with the IQ 577 laser system, the patient's CRT reduced from 715 µm to 278 µm, and visual acuity improved from 20/400 to 20/80 at 6-months follow-up.

I use continuous-wave (CW) 577 nm laser to produce barely visible lesions that will be only detectable on FA, 1 spot apart in a grid pattern 360° around the fovea, up to 500 µm from the center of the foveal avascular zone (FAZ). Then, I switch from CW to MicroPulse emission to paint contiguously with subvisible MPLT in all areas with foveal leakage within 500 µm from the center of the FAZ.

A WIDE RANGE OF INDICATIONS FOR MPLT

Studies using 810 nm subthreshold MPLT have shown clinical efficacy in the treatment of central serous chorioretinopathy (CSC) (Table 2). I also have found 577 nm subthreshold MPLT is effective and an ideal therapy for the treatment of chronic CSC.

My colleagues and I conducted a trial using 577-nm MPLT in 10 patients with chronic CSC with

TABLE 2. CLINICAL OUTCOMES OF 810 NM MPLT FOR CSC		
Author	**Authors' Conclusions**	**Follow-up**
Lanzetta et al. *Eur J Ophthalmol.* 2008[10]	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 3-36 months)
Gupta et al. *Clin Exp Ophth.* 2009[11]	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 6-24 months)
Koss et al. *Eye.* 2012[12]	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

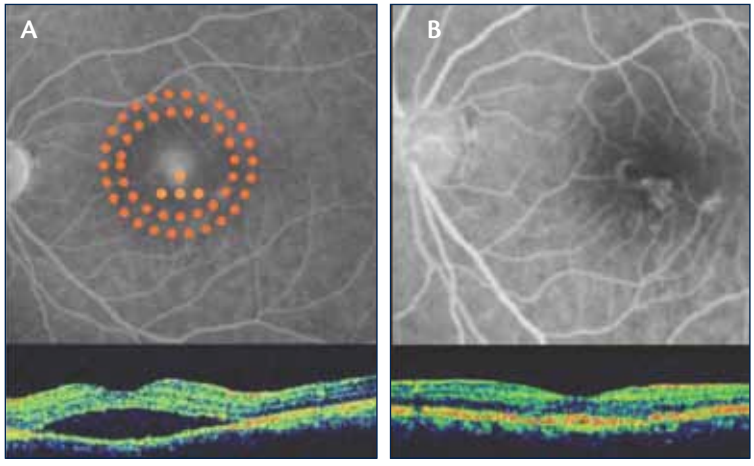

Figure 3. 577 nm MPLT for chronic CSC. Pre MPLT. VA 20/200 (A); 6 months post MPLT. Visual acuity: 20/32 (B).

foveal and juxtafoveal leakage.[13] High-density MPLT was delivered targeting all areas of angiographic leakage including the foveal center as well as adjacent normal retina (Figure 3). At 6 months follow-up, visual acuity improved 3 or more lines in 6 (60%) of the eyes, 9 eyes (90%) required only 1 treatment. Point source and diffuse leakage cases had an equal anatomic response, and complete fluid resolution in 10 eyes (100%) was achieved 15-30 days posttreatment. No visible clinical signs of treatment could be detected on FA, and microperimetry showed no laser-related damage to the treatment area.

MPLT PROVIDES SUSTAINABLE RESULTS

Our experiences with anti-VEGF injections and steroids for DME show that patients often experience an immediate response in terms of reduced edema; however, these results are not sustained over the long term, and in most cases patients require monthly or even more frequent injections. This is not a sustainable model for management of a long-term disease. In our trial with MPLT, we are seeing clinical results lasting over 1, 2, or more years. This is comparable to observations reported by the DRCR.net.[14]

Using combination therapy with anti-VEGF and MPLT would benefit patients by offering an initial boost of effect with the injection and then adding laser to help sustain the effect and reduce the need for frequent injections.

> "…with MPLT, it is now possible to address foveal leakage in a safer and more effective manner with subclinical invisible laser treatment."

SUMMARY

What do I envision for the future? I certainly see a combined laser and drug treatment using a refined and optimized laser technique. I also see laser remaining the gold standard treatment for DME, provided that we adopt new techniques that can maximize benefits while minimizing retinal damage. When treating DME

with laser, there is a need to enhance selectivity around the fovea as to not cause harm to this sensitive region. There is no way to do this using the standard ETDRS laser protocol, but with MPLT, it is now possible to address foveal leakage in a safer, more effective manner with subclinical, invisible laser treatment. ■

José Augusto Cardillo, MD, is Research Coordinator, Department of Retina and Ocular Pharmacology Federal University of São Paulo, Brazil, and Chief of the Retina Department at the Hospital de Olhos de Araraquara.

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JOSÉ AUGUSTO CARDILLO, MD 577 NM *SANDWICH GRID* TREATMENT TECHNIQUE FOR DME WITH FOVEAL LEAKAGE

Step 1: Barely Visible Low Energy/Short Pulse Duration

Mode: CW
Spot Size (Adapter): 100 µm
Lens: Area Centralis
Power: Adjusted to show a barely visible lesion
Duration: 10 ms
Duty Cycle: 100 % (CW)
Technique: Deliver barely visible lesions 1 burn apart in a grid pattern 360º around the fovea, up to 500 µm from the center of the FAZ.
Evidence of laser treatment on FA: Yes

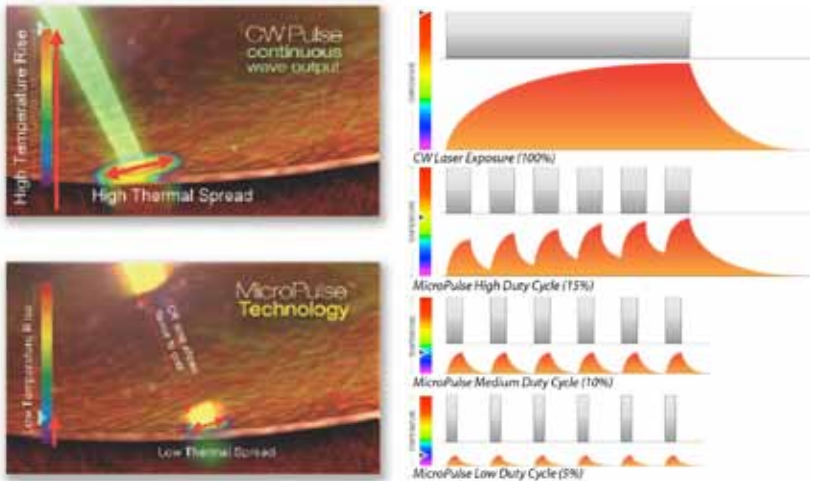
Step 2: Subvisible MicroPulse Laser Therapy

Mode: MicroPulse
Spot Size (Adapter): 100 µm
Lens: Area Centralis
Power: 20% increase from power used in CW mode (Step 1)
Duration: 200 ms
Duty Cycle: 10% or less
Technique: Paint contiguously all areas of leakage within 500 µm from the FAZ's center.
Evidence of laser treatment on FA: No

MicroPulse Technology

It's more than your classic laser.

With conventional (classic) laser, the treatment endpoint is a readily visible burn. This implies a high and lethal thermal gradient (>30 ºC) in the tissue directly targeted by the laser, as well as in the adjacent tissue reached by the equilibrating and decaying thermal wave at a still lethal temperature. The enlarged burn becomes visible some time after treatment and progresses in an atrophic scar, which expands over time. Surrounding tissue reached by the equilibrating and decaying thermal wave at a sublethal temperature, remains viable and capable of reacting to the thermal injury with stress responses which induce beneficial intracellular biological factors that are antiangiogenic and restorative.[1]



In conventional, continuous-wave (CW) photocoagulation, a rapid temperature rise in the target tissue creates blanching and a high thermal spread. MicroPulse technology finely controls thermal elevation by "chopping" a CW beam into a train of repetitive short pulses allowing tissue to cool between pulses and reduce thermal buildup.

With modified (classic) laser, the lighter treatment endpoint of a barely visible burn is sought. Directly targeted tissue is still destroyed, with scar enlarging and expanding over time, but the effects, although similar as with conventional laser, are confined to a smaller region surrounding each burn.

With MicroPulse Laser Therapy (MPLT), the temperature rise induced in the directly targeted tissue remains sublethal and no visible lesion is produced (subvisible-threshold). Because of this, both directly targeted and surrounding tissues remain viable and capable of creating a stress response which induces beneficial intracellular biological factors that are antiangiogenic and restorative.

In MPLT, the low temperature gradient reequilibrates to baseline temperature within a short spreading distance, limiting and confining the therapeutic photothermal effect around the tissue directly targeted by the laser. For this reason, and conversely to conventional (classic) laser that must be applied in grids with spaced burns, MPLT is normally performed with the high-density placement of confluent applications, a novel laser treatment paradigm that is made possible by the absence of chorioretinal laser damage and risk of iatrogenic scotoma. ■

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NEW DME PATIENT EDUCATION WEBSITE

Supports patient awareness and education on MicroPulse technology for DME.

direct link to website:
http://treatmydme.com

Why Should Physicians Consider MicroPulse?

MPLT users share their opinions.

Sam E. Mansour, MSc, MD, FRCS(C), FACS: "…as I was one of the biggest skeptics … when this first came up—but after several patients, it was pretty impressive…" [scan QR code at right to hear more or follow this direct link: http://j.mp/JfBZdh]

Victor Chong, MD, FRCS, FRCOphth: "… they will find that MicroPulse is extremely easy to do and they just need to try it…" [scan QR code at right to hear more or follow this direct link: http://eyetube.net/video/micropulse-laser-in-dme-snippet]

José Augusto Cardillo, MD: "… it's not going to harm their patients, so there is no risk. It's a very, very selective treatment… safer treatment over our current standard of care, in terms of laser treatment." [scan QR code at right to hear more or follow this direct link: http://j.mp/JCz2av]