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Laser Remains An Effective Treatment Option for DME

The 577 nm SubLiminal laser is a safe and cost-effective option for treatment of diabetic macular edema and central serous retinopathy.

BY KENNETH FONG, MD

As the worldwide population ages, diabetic macular edema (DME) and associated retinal conditions represent an increasingly significant burden to the health care system. Cost and treatment burden are two of the critical factors that influence the viability of available treatment options. In Asia Pacific, where I practice, neither patients nor insurers can justify the high cost of monthly anti-VEGF injections, and monthly visits are a burden to both patients and their caregivers who have to accompany them for the visits.

Conversely, laser therapy reduces both cost and treatment burden for patients who have DME and ancillary conditions, such as central serous retinopathy (CSR).

While anti-VEGF therapy is an important tool in the retinal disease treatment armamentarium, lasers continue to play a critical role as we know from a 2010 Diabetic Retinopathy Clinical Research Network study, which showed that even after 6 months of intensive anti-VEGF therapy, patients still required laser therapy.[1] It is important to bear in mind that the patients in the study were treated with traditional focal lasers, and a large proportion of them, even after treatment with ranibizumab (Lucentis; Genentech/Novartis) or even triamcinolone, still required laser treatment (Figure 1).

The viability of laser therapy for DME is enhancing. Today's modern subthreshold lasers employ multispot technology and improved software—a combination that provides safety, efficacy and patient comfort that is far greater than was possible with early retinal lasers.

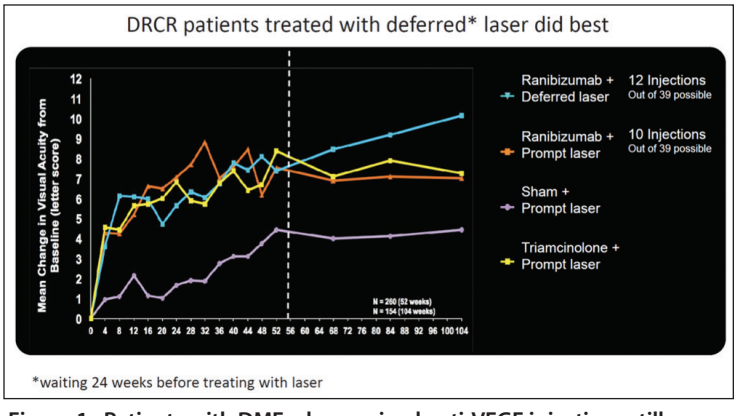


Figure 1. Patients with DME who received anti-VEGF injections still required laser treatment.

These newer subthreshold lasers are known by a variety of names. While their names are different, they share several other important characteristics: they are safer than the rudimentary retinal lasers that preceded them; they offer patients a more comfortable and cost-effective alternative to intravitreal injections; and they are becoming the new standard of care in the laser treatment of macular disease.

The term "subthreshold" has become part of the laser lexicon, but not everyone is clear on exactly what it is. I personally use a 577 nm SubLiminal laser. Essentially, SubLiminal laser refers to when a laser beam is broken into small pockets of pulses, and these small shots are controlled with a mechanism known as duty cycle. Duty cycle is the percentage of time that the laser is on compared to the percentage of time that the laser is off. The "off time" is essential because these momentary power lapses help cool the retinal pigment epithelium and prevent the formation of pigmented scars on the retina itself (Figure 2).

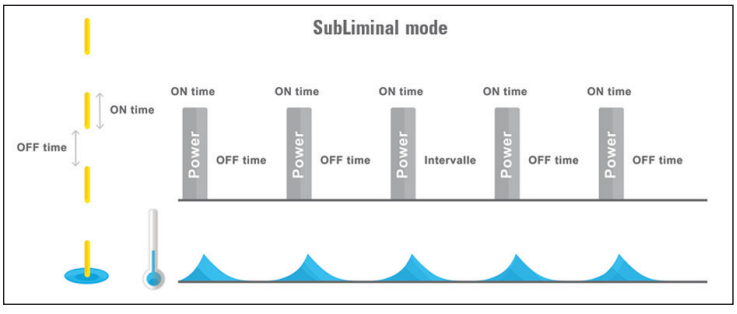


Figure 2. SubLiminal laser refers to when a laser beam is broken into small pockets of pulses, and these small shots are controlled with a mechanism known as duty cycle.

Looking Back: Retinal Laser Review

While subthreshold laser technology is relatively new, it actually has a long enough history to have acquired substantial support in the literature. In the 1990s, the laser physicist, Mr. Vladislav Pankatrov, introduced the concept of chopping up a continuous

laser beam into small pockets of pulses to reduce the heat on the retina.[2] In 2005, Jeffrey K. Luttrull, MD, published his first paper using the diode 810 nm subthreshold laser.[3] Three years later, 532 green and 577 yellow subthreshold lasers were made available, and within the past 5 to 10 years they have become widely available. In 2011, a randomized controlled trial (that did not include anti-VEGF treatment) showed that subthreshold diode laser was more effective than conventional laser for treatment of DME.[4]

In 2009, I became one of the first ophthalmic surgeons in Asia Pacific to use a SubLiminal laser to treat DME. I performed a randomized controlled trial comparing the conventional 532 nm green laser with the SubLiminal 577 nm yellow laser.[5] This study took place before anti-VEGF treatment results were available, so we performed a laser-to-laser comparison. The results showed that the improvement in the best corrected vision from baseline was equivalent in both groups (Figure 3). This finding was proof of concept that the 577 nm SubLiminal laser was as safe as a conventional laser.

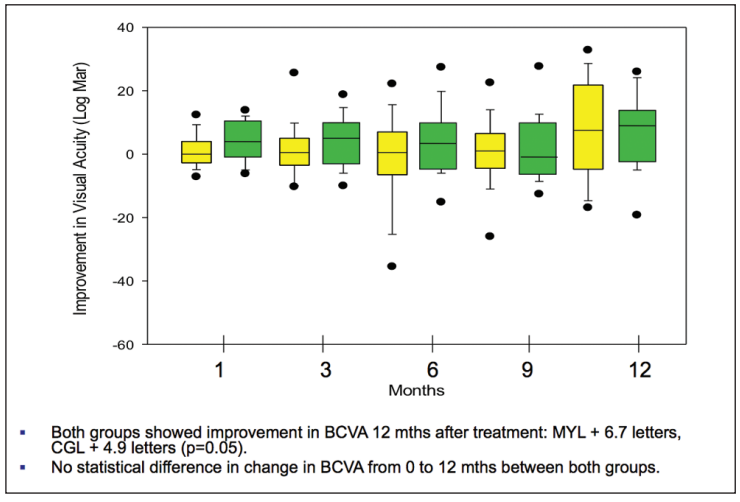


Figure 3. Improvement in BCVA from baseline.

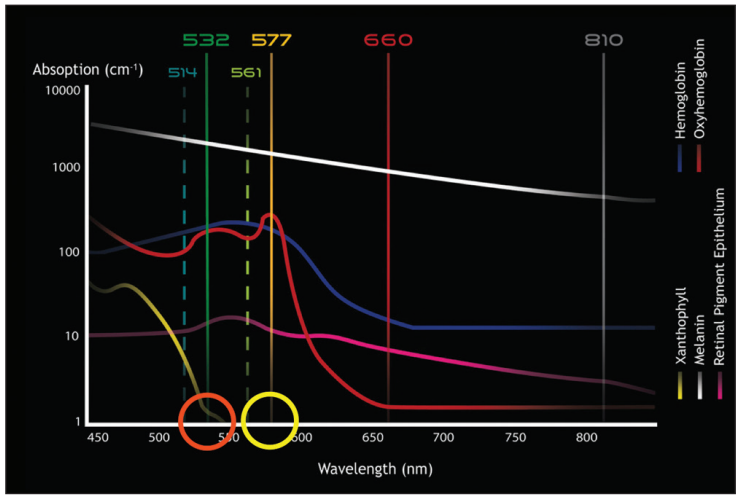


Figure 4. The yellow 577 nm wavelength causes less scatter and requires the use of a lower energy level compared to green 532 nm and other yellow.

> "One of the keypoints where Quantel's 577 nm EasyRet laser distinguishes itself among subthreshold lasers is that it allows combination of the Multispot and the SubLiminal technologies."
>
> *— Kenneth Fong, MD*

In addition to being as safe as the conventional green laser, the SubLiminal 577 nm yellow laser has many benefits. In the literature, the yellow 577 nm wavelength has been described as a safe and versatile wavelength.[6-10] Thanks to its absorption characteristics (Figure 4), the yellow 577 nm wavelength causes less scatter and requires the use of a lower energy level compared to green 532 nm and other yellow—561 to 568 nm wavelengths. It is minimally absorbed by macular xanthophylls, potentially allowing for treatments close to the fovea. It has a very good penetration for patients with cataract, and it is highly absorbed by the oxyhemoglobin.

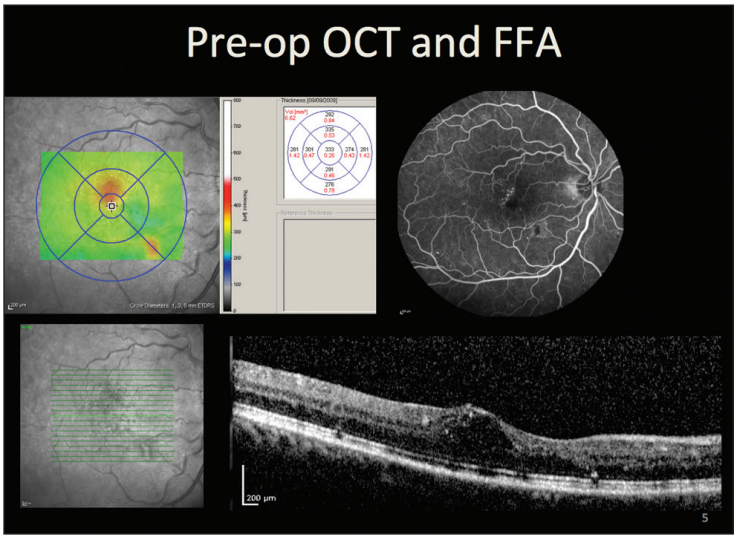
SubLiminal Treatment Parameters

As more information about the safety, efficacy, and comfort of SubLiminal laser therapy becomes known, treatment parameters are crystalizing. For the best effect, we recommend very dense treatment: the laser spots should be touching each other. To achieve this, we use a spot size of 160 microns, a pulse duration of 200 ms and a duty cycle of 5%. Some companies that market subthreshold lasers advocate using a fixed power for every patient. I, on the other hand, believe that it is important to titrate the power because every patient has different pigmentation in the retinal pigment epithelium.

My treatment strategy entails titrating outside the macula area; first testing with a 5% duty cycle until seeing a barely visible effect (not a burn); then reducing the power by 50%; and then lasering over the macula in the thickened area. You can be assured that this is a safe protocol for treating the macula. You will not see any burns or laser marks, but you will definitely achieve treatment effect.

The use of optical coherence tomography (OCT) enables you to guide your treatment. You can review the OCT scan and locate the exudates, then look at the 3D stereoscopic vision on the contact lens and proceed from there (Figures 5 and 6).

One of the keypoints where Quantel's 577 nm EasyRet laser distinguishes itself among subthreshold lasers is that it allows combination of the Multispot and the SubLiminal technologies.



Figures 5. Preoperative OCT scan shows the exudates.

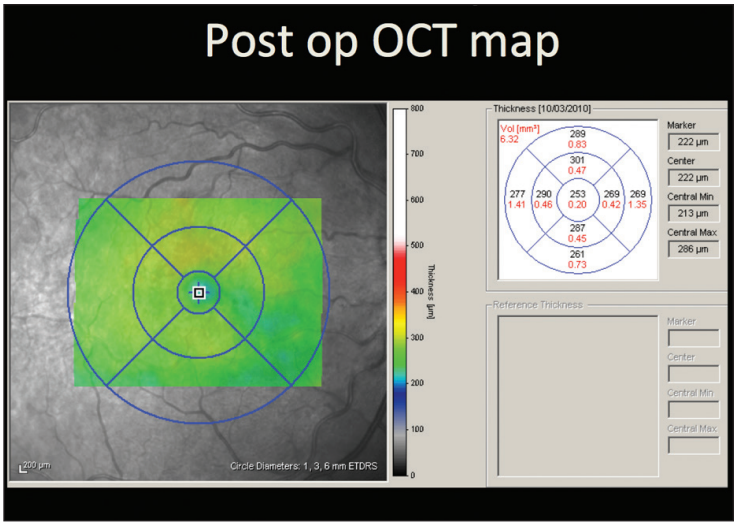


Figure 6. Postoperative OCT scan.

Indeed, the EasyRet laser features a customizable macular grid enabling the surgeon to customize the treatment to the area of edema on the macula. You press your foot down on the pedal and treat the entire area in under 1 minute. If the patient moves, you lift up the pedal, and the laser will stop in the middle of the pattern. When you resume treatment, the laser treats the remaining portion of the pattern. There is a center fixation that allows the surgeon to ensure that the patient is not moving during the treatment.

Patient Selection

If you decide to treat your patients with DME and CSR with SubLiminal Yellow Laser, consider the following recommendations with respect to ideal patients on whom to start: choose patients with good vision who have extra-foveal clinically significant DME; choose patients who have not had a durable response to anti-VEGF therapy or have failed on steroids; choose patients who refuse to or cannot tolerate ocular injections; choose patients who have CSME that is limited to the fovea, and therefore, too minimal to start injection; and finally, choose patients who want to avoid laser scars around the fovea.

When you identify appropriate patients and give them the option of treatment with the SubLiminal laser, you must alert them that the full effect may take up 3 months, which is also the case with focal laser treatment. They should also be aware that even though the response might take a while to completely reveal itself, the effect is long-term. Also, similar to focal laser treatment, if the patient has persisting macular edema after 3 months of SubLiminal laser treatment, you can repeat the treatment on the areas of thickening seen on the OCT. Furthermore, you and the patient should be aware that there are often subjective improvements in vision even when thickening is still visible on the OCT.

In conclusion, DME is a huge burden to our health care system. In the part of the world where I practice, it is not feasible to do monthly anti-VEGF injections for our patients. They cannot afford it, our governments cannot afford it, and insurance companies cannot afford it. The SubLiminal laser therapy is a safe and effective option. It can reduce the treatment burden of injections, and now that we have the latest machines with upgraded software combining Multispot and SubLiminal technologies all in one, we are experiencing a very exciting era in retinal laser therapy. ■

1. The Diabetic Retinopathy Clinical Research Network. Elman MJ, Aiello LP, Beck RW, et al. Randomized trial evaluating ranibizumab plus prompt or deferred laser or triamcinolone plus prompt laser for diabetic macular edema. *Ophthalmology*. 2010;117:1064-1077.
2. Pankratov MM, Pulsed delivery of laser energy in experimental thermal retinal photocoagulation. *Proc Soc Photo Opt Instrum Eng*, 1202 (1990), pp. 205–213.
3. Luttrull JK, Musch MC, Mainster MA, Subthreshold diode micropulse photocoagulation for the treatment of clinically significant diabetic macular edema. *Br J Ophthalmol*. 2005; 89 (1): 74–80.
4. Lavinsky D, Cardillo JA, Melo LA Jr, et al. Randomized clinical trial evaluating ETDRS versus normal or high-density micropulse photocoagulation for diabetic macular edema. *Invest Ophthalmol Vis Sci*. 2011;52:4314-4323.
5. Fong KCS, Ong SL, Iqbal T, et al. RCT comparing Subthreshold 577nm yellow laser and conventional 532nm green laser for diabetic macular oedema. (YELL-1 STUDY7). ClinicalTrials.gov Identifier: NCT01045239.
6. Mainster, MA, Wavelength selection in macular photocoagulation. *Ophthalmology*. 1988;93:952-958.
7. Mainster MA, Decreasing retinal photocoagulation damage: P*rinciples and Techniques. Semin Ophthalmol.* 1999;14:200-209.
8. Trempe CL, Mainster MA, Pomerantzeff O, et al, Macular photocoagulation: optimal wavelength selection. *Ophthalmology*. 1982; 9:721-728.
9. Vogel M, Schafer FP, Stuke M, et al. Animal experiments for the determination of an optimal wavelength for retinal coagulations. *Graefes Arch Clin Exp Ophthalmol*. 1989;227:227-280.
10. Kwon YH, Lee DK, Kwon OW. The short-term efficacy of subLiminal micropulse yellow (577-nm) laser photocoagulation for diabetic macular edema. K*orean J. Ophthalmol*. 2014;28(5):379-385.

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