Optimizing Laser Treatment for Diabetic Macular Edema

Micropulse mode and 577-nm wavelength are an effective and safe combination.

By Rohit S. Adyanthaya, MD

Laser photocoagulation continues to play a prominent role in the treatment of diabetic macular edema (DME) despite the introduction of anti-VEGF medications. Although traditional continuous-wave laser mode has proved to be effective for DME, as shown in the Early Treatment for Diabetic Retinopathy Study[1] there are a number of drawbacks including, but not limited to, permanent destruction of the photoreceptors and enlargement of laser scars into the fovea with further deterioration of vision. We are now learning that modified treatment parameters and selective laser wavelengths have the ability to produce a less destructive and more therapeutic effect.

Studies have shown that destruction of cells is not necessary; rather, photostimulation of the RPE can cause a transcriptional activation of cytokines and upregulation of the beneficial intracellular biological factors.

The Conventional Laser's Mechanism of Action

The understood mechanism of action of conventional focal lasers is to induce coagulation necrosis and permanent destruction of the retinal pigment epithelium (RPE) and photoreceptors, which in turn spurs the upregulation of inhibitors and downregulation of causes of inflammation.[2] Studies have shown, however, that destruction of cells is not necessary; rather, *photostimulation* of the RPE can cause a transcriptional activation of cytokines and upregulation of the beneficial intracellular biological factors such as pigment epithelium-derived factor (PEDF) and other potent antiinflammatory factors.[3,4]

How Micropulse Works

An alternative technology to continuous wave laser mode that has been developed is micropulse laser. Micropulse technology effectively chops a conventional mode laser beam into a train of repetitive short bursts. The pauses between the bursts allow the tissue

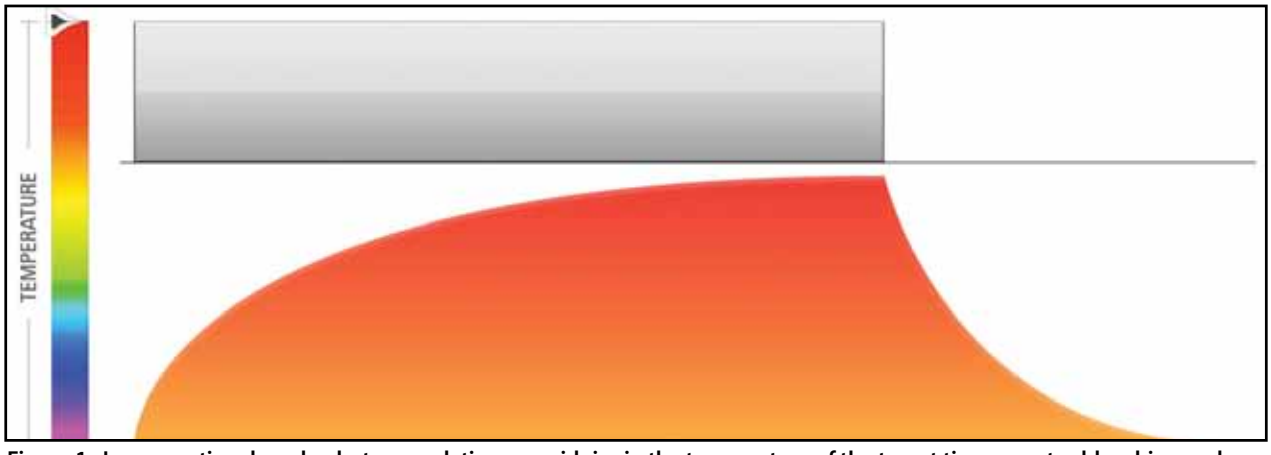

Figure 1. In conventional mode photocoagulation, a rapid rise in the temperature of the target tissue creates blanching and a high thermal spread.

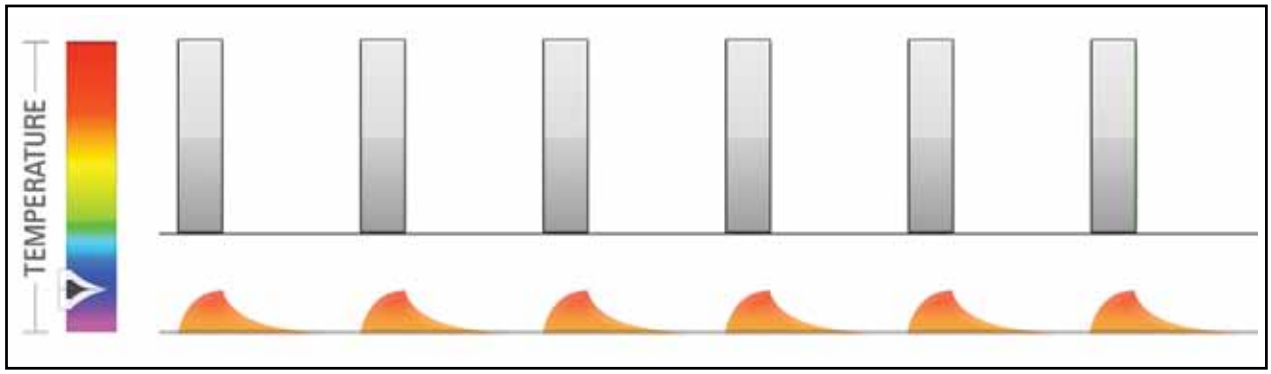

Figure 2. Micropulse technology finely controls the thermal elevation by chopping a conventional mode laser beam into a train of repetitive short pulses, allowing tissue to cool between pulses and reducing thermal buildup.

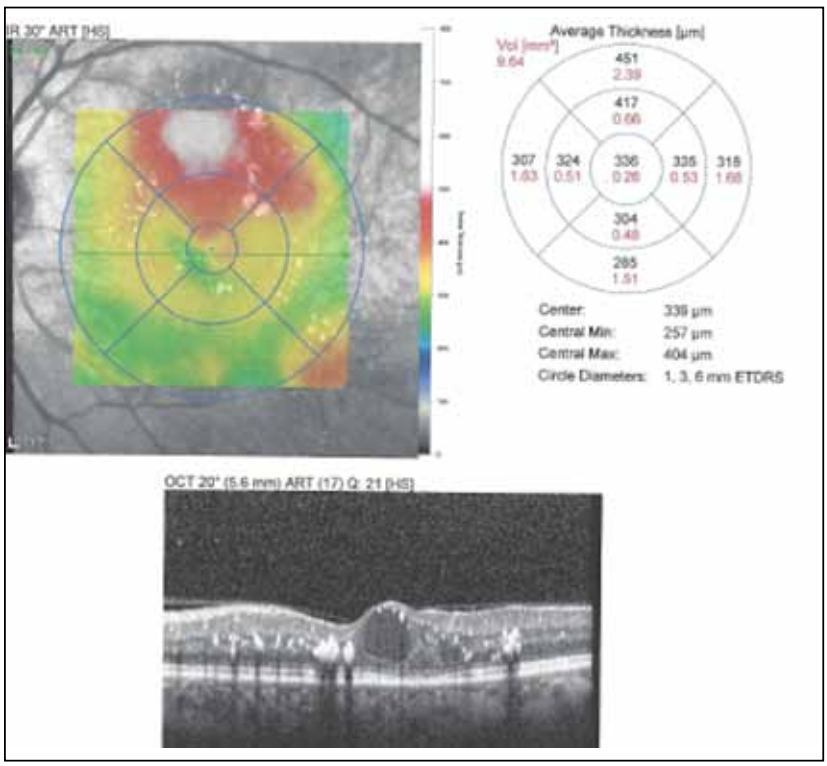

Figure 3. Patient with severe nonproliferative diabetic retinopathy and clinically significant macular edema, prior to undergoing therapy with micropulse laser.

to cool, preventing thermal buildup and collateral damage (Figures 1 and 2). Multiple studies have shown that micropulse laser achieves similar results to conventional laser treatment, with the added benefit of no retinal scarring, as demonstrated by fundus autofluorescence.[5-8] Additionally, microperimetry has demonstrated significant improvement in retinal sensitivity with micropulse laser.[5]

Micropulse Treatment Parameters

As micropulse technology is relatively new, treatment parameters are still to be standardized. My approach is to first perform a test burn with the laser in the micropulse mode itself in a nonthickened area of the retina (usually nasal to the nerve). I start with 5% duty cycle, 600 mW of power, 100 µm spot size and 200-ms duration. Power is then increased by 100 mW, moving to an adjacent area each time, until a barely visible burn appears. Usually, I see a barely visible burn at around 1000 mW of power. Once that threshold has been determined, the power is halved and treatment performed (eg, if a barely visible burn was noticed at 1000 mW of micropulse power, I will treat with 500 mW of micropulse power).

Using the optical coherence tomography map as a guide and the fundus biomicroscopic exam, a confluent grid is placed directly over the areas of thickened retina and microaneurysms, leaving no space between laser applications. Because micropulse exposures limit thermal spread, it calls for the delivery of a greater number of spots with denser spacing than used for traditional conventional wavelength treatment.[6] When placing the test burn, I use 0-ms interval; however, because micropulse requires a confluent pattern over areas of thickened retina, I prefer to treat using an interval of 200 ms, as this speeds up the procedure and also avoids the need to press the foot pedal for every spot. As there is no visible burn, it is important to focus the laser beam accurately on the retina during the treatment.

Understanding the 577-nm Yellow Wavelength

In addition to micropulse treatment mode, selecting the best laser wavelength is an important step in increas-

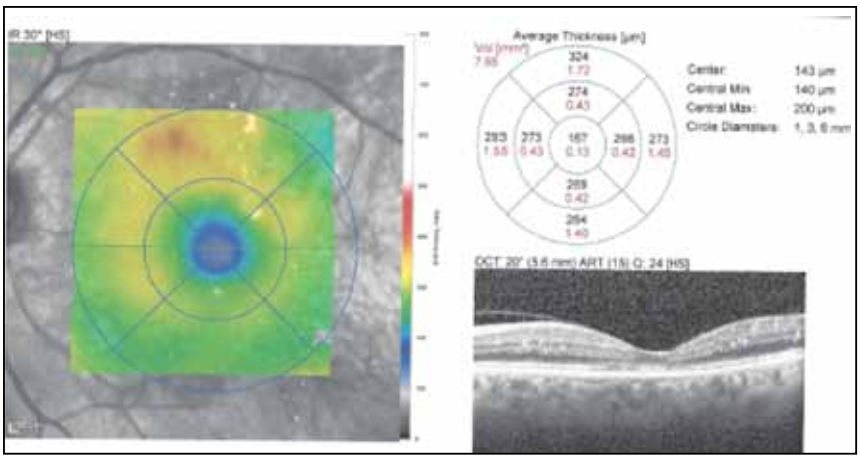

Figure 4. Three months after a second treatment with micropulse laser, edema is resolved and vision is 20/30.

ing efficacy and decreasing collateral damage. The 577-nm wavelength is on the peak of the oxyhemoglobin absorption curve. Greater absorption of laser energy by oxyhemoglobin facilitates efficient closure of microaneurysms, when desired. Additionally, the 577-nm wavelength is negligibly absorbed by xanthophyll in the fovea,[9] which increases its safety profile and permits treatment closer to the fovea. Its high transmission rate through dense media, such as cataracts, allows treatment with low power, increasing patient comfort.

Modifying the Treatment Paradigm

In cases of DME, micropulse laser can be used either as monotherapy or in conjunction with anti-VEGF medications. The absence of detectable focal laser scars is a distinct advantage, allowing patients to be safely retreated in the future if edema returns, with no risk of loss of macular function.

In cases of DME, with central retinal thickness (CRT) of less than 350 µm, micropulse laser can be used as monotherapy without the need for anti-VEGF medications. In cases of DME with CRT of more than 350 µm, I recommend initiating therapy with anti-VEGF medications to reduce the swelling to below 350 µm. Once this is achieved, micropulse can be used to prolong the results of the anti-VEGF injections. This combination reduces the need for repeated intravitreal injections.

In DME patients with CRT of more than 350 µm who refuse intravitreal injections or cannot receive it due to insurance issues, micropulse laser can be performed as monotherapy, after explaining to the patient that he or she may require multiple sessions to resolve the edema.[8] Three months following the first laser treatment, examine the patient again to see if the edema has decreased. If the central retina remains thick, another round of laser treatment can be performed safely, continuing follow-up every 3 months to monitor the edema.

Case Study

A 54-year-old Hispanic male with type 2 diabetes and hypertension for the last 8 years came to me complaining of decreased vision in the left eye. He had no history of eye problems nor any treatments in the past. His right eye had 20/25 vision, with moderate nonproliferative diabetic retinopathy with no clinically significant macular edema. His left eye was 20/80 with severe nonproliferative diabetic retinopathy with clinically significant macular edema. (Figure 3). Due to insurance issues, anti-VEGF treatments could not be initiated, so we decided to perform micropulse laser with the 577-nm laser to the left eye. For the first session, I placed laser spots in a confluent grid over the thickened area using 750 mW of power on the micropulse setting. After 3 months, the edema had significantly reduced but was not completely resolved. To address the residual edema, a second session was performed using the same settings, and after 3 months, the fovea was completely flat, and visual acuity was 20/30 (Figure 4).

Although there have been significant pharmacologic advances for the treatment of DME, laser remains an important treatment modality. As our understanding of wavelengths and treatment modalities increases, we can improve efficacy and decrease unintended collateral damage to the retina. ■

Rohit S. Adyanthaya, MD, is a vitreoretinal consultant at the Valley Retina Institute in McAllen, TX. He states that he has no financial relationships to disclose. He may be reached at (956) 631-8875 or at rohiteyedoctor@gmail.com.

1. Early Treatment Diabetic Retinopathy Study Research Group. Photocoagulation for diabetic macular edema. Early Treatment Diabetic Retinopathy Study report number 1. *Arch Ophthalmol.* 1985;103(12):1796-1806.
2. Wilson AS, Hobbs BG, Shen WY, et al. Argon laser photocoagulation-induced modification of gene expression in the retina. *Invest Ophthalmol Vis Sci.* 2003;44(4):1426-1434.
3. Ogata N, Tombran-Tink, J, Jo N, Mrazek D, Matsumura M. Upregulation of pigment epithelium-derived factor after laser photocoagulation. *Am J Ophthalmol.* 2001;132(3):427-429.
4. Binz, N, Graham, CE, Simpson, K, et al. Long-term effect of therapeutic laser photocoagulation on gene expression in the eye. *FASEB J.* 2006;20(2):383-385.
5. Vujosevic S, Bottega E, Casciano M, Pilotto E, Convento E, Midena E. Microperimetry and fundus autofluorescence in diabetic macular edema: subthreshold micropulse diode laser versus modified early treatment diabetic retinopathy study laser photocoagulation. *Retina.* 2010;30(6):908-916.
6. Luttrull JK, Sramek C, Palanker D, Spink CJ, Musch DC. Long-term safety, high-resolution imaging, and tissue temperature modeling of subvisible diode micropulse photocoagulation for retinovascular macular edema. *Retina.* 2012;32(2):375-386.
7. Lavinsky D, Cardillo JA, Melo LA, et al. Randomized clinical trial evaluating mETDRS versus normal or high-density micropulse photocoagulation for diabetic macular edema. *Invest Ophthalmol Vis Sci.* 2011;52(7):4314-4323.
8. Adyanthaya R, Zavala G, Gonzalez V. Subthreshold micropulse diode laser photocoagulation as monotherapy for mild to moderate diabetic macular edema. *Invest Ophthalmol Vis Sci.* 2013;54(6):E-Abstract 2381.
9. Mainster MA. Wavelength selection in macular photocoagulation. Tissue optics, thermal effects, and laser systems. *Ophthalmology.* 1986;93(7):952-958.