For this Practical Retina column, Sejal Shah, MD, from New York City was asked to comment on the current use of micropulse retina lasers to treat macular diseases.

For more than half a century, laser technology has evolved to become an essential tool in treating a variety of vitreoretinal diseases. The evolution of retina lasers since the 1940s is fascinating. After observing the effects of a solar eclipse on patients’ retinas, Gerhard Meyer-Schwickerath investigated the use of natural sunlight to treat retinal disease in 1949 (Sun Coagulator). Unfortunately, the technique was limited by weather conditions, the lengthy exposure time required, and the constantly changing angle of the sun. To address these shortcomings, Meyer-Schwickerath developed a carbon arc lamp as a more reliable artificial light source. Although considered an advance, the unpredictable retinal burns limited its usefulness. In the 1950s, Carl Zeiss and Meyer-Schwickerath developed the xenon arc lamp, which was a generational leap forward due to its high uniform power output. The Ruby laser in 1960 launched the modern laser era, providing clinicians with a range of wavelengths and pulse durations allowing precise treatments. The coming 40 years saw development of argon lasers, allowing flexibility of treating retinas with either slit lamp or indirect ophthalmoscope delivery. Solid-state lasers were a major advance that reduced cost and size of laser units. Most recently, the NAVILAS laser, integrating imaging, planning, and treatment into one compact platform, was ground-breaking, as well as the PASCAL Pattern laser.

In this article, Dr. Shah will share her vast expertise in using micropulse subthreshold lasers to treat a variety of macular diseases. She will review current thinking and appropriate indications. Furthermore, she will share two illustrative cases from her practice. I am certain that her insights will be most valuable.

Focal/grid macular laser photocoagulation has been the gold standard for treating diabetic macular edema (DME). Argon laser is used in this “conventional” technique to produce a visible treatment endpoint resulting in chorioretinal scarring. This is classified as “suprathreshold” photocoagulation, which is in contrast to “subthreshold” laser that is not visible at the time of treatment.1

In the first Early Treatment Diabetic Retinopathy Study (ETDRS) report, the main clinical benefit of macular photocoagulation was to reduce by 50% the rate of moderate visual loss with clinically significant macular edema.2 Suprathreshold macular photocoagulation can result in pre- and subretinal fibrosis, choroidal neovascularization, visual field loss, loss of color vision, progressive expansion of the laser scars into the fovea, metamorphopsia, central scotomas, and early and late visual loss due to inadvertent foveal photocoagulation. These possible adverse effects induced by the laser limited treatment repeatability and the ability to treat near the fovea safely.2-6

It is believed that laser burns resulting in visible burn endpoints are necessary for successful treatment, but have never been validated.2-7 Conversely, newer hypotheses on the mechanism of action of laser photocoagulation postulate that the therapeutic benefits are not derived from the “burned” area of chorioretinal damage caused by suprathreshold treatment, but rather from the bordering areas affected by a lower, sublethal thermal elevation.8

Subthreshold diode micropulse (SDM) laser uses confluent “painting” of the target retina with large number of small, high-density (HD), short-duration laser spots maximizing head dissipation and minimizing the risk of unintended thermal injury,1 whereas conventional laser photocoagulation applies a steady continuous-wave laser output. The duration of pulses in SDM is typically 100 ms to 300 ms with a spot size of 100 µm to 200 µm and power typically ranging from 200 mW to 800 mW. Each
pulse has an “on” and “off” duration. The duty cycle is defined as the ratio of on to off time. A lower-duty cycle allows the tissue temperature to decrease to the baseline prior to the arrival of the next pulse, therefore diminishing the overall thermal effect without the detectable tissue damage associated with standard photocoagulation.\textsuperscript{1,9-12}

Using SDM, DME may be treated confluenltly up to the edge of the foveal avascular zone 360° as well as transfoveal.\textsuperscript{13} No evidence of SDM-induced retinal injury was noted by funduscopy, red-free fundus photography, or fluorescein angiography (FA), as previously reported. Additionally, there was no evidence of retinal injury noted by Spectralis (Heidelberg Engineering, Heidelberg, Germany) infrared fundus photography, indocyanine green (ICG) angiography, spectral-domain optical coherence tomography, or fundus autofluorescence.\textsuperscript{1,10,14-16} It has also been demonstrated recently that subthreshold micropulse laser wavelengths yellow (577 nm) and infrared (810 nm)

\textbf{Figure 1.} Optical coherence tomography and central retinal thickness (CRT) of a patient with diabetic retinal edema before subthreshold diode micropulse (SDM) laser treatment (A), 6 weeks after treatment (B), and 12 weeks after treatment (C). The decrease in edema and retinal thickness can be seen after SDM laser treatment. Of note, there was no additional treatment given during this time.
Figure 2. Optical coherence tomography and central retinal thickness of a patient who presented with central serous retinopathy (A) and again after 3 months (B) with persistent subretinal fluid (SRF). At this visit, subthreshold diode micropulse laser treatment was applied. Two months later, the central SRF had resolved (C). The patient followed up 4 months later without any central SRF (D), but instead with superior SRF, for which repeat micropulse laser was applied.
delivered at a 5% duty cycle was safe without any visible retinal or choroidal lesions on any imaging modality.\textsuperscript{13,17} Since no adverse effects are observed, it is considered safe to repeat as necessary.\textsuperscript{9,10}

Multiple studies have compared conventional laser photoacoagulation with subthreshold micropulse laser for the treatment of clinically significant DME. Figueira et al. concluded that subthreshold micropulse laser was equally as effective as conventional green laser with no statistically significant differences in best-corrected visual acuity (BCVA), contrast sensitivity, or retinal thickness between the two laser modalities. However, the risk of developing laser scars was 8.9-times higher when using conventional laser than with micropulse laser.\textsuperscript{18}

Laursen et al. conducted a small, randomized study of only 23 eyes, but results of the study showed that SDM laser photoacoagulation showed an equivalent effect on visual acuity as conventional argon laser treatment. In this study, SDM laser showed a stabilizing, if not improving, effect on macular edema.\textsuperscript{11}

In a retrospective study, Luttrull et al. showed decreased edema in 96% and stabilized or improved vision in 85% of treated eyes with a mean follow-up of 12.2 months without any adverse laser events.\textsuperscript{3}

Lavinsky et al. performed a randomized clinical trial evaluating modified ETDRS (mETDRS) versus normal or HD micropulse photoacoagulation for DME. In this study, the HD-SDM group had the most improvement in BCVA at 12 months, followed by the mETDRS group. There was no significant improvement in vision in the ND-SDM group.\textsuperscript{16}

Luttrull et al. explored the safety of transfoveal SDM laser for fovea-involving DME in patients with good visual acuity (at least 20/40 vision). Overall, a significant improvement in visual acuity was noted at 4 months to 7 months postoperatively, especially in eyes presenting with a central foveal thickness (CFT) less than 300 µm. In eyes presenting with CFT greater than 300 µm, there was no significant difference between preoperative and postoperative CFT.\textsuperscript{13} This is similar to the findings by Mansour et al. that showed an average reduction of 55 µm in CFT, along with two lines of visual gain at 12 months in patients who had an initial CFT of less than 400 µm prior to treatment with SDM laser.\textsuperscript{12}

**CENTRAL SEROUS RETINOPATHY**

A large proportion of central serous chorioretinopathy (CSCR) cases resolve without treatment following a period of observation.\textsuperscript{20} In cases of chronic CSCR, focal laser treatment, photodynamic therapy (PDT), and intravitreal anti-vascular endothelial growth factor (VEGF) medications have all been employed as possible treatment options.\textsuperscript{21} Focal laser photoacoagulation at the site of leakage on fluorescein angiography has been shown to promote resolution of the serous detachment, though the burn lesion places the patient at risk for focal scar expansion, scotoma, and choroidal neovascularization. Moreover, certain lesions may not be amenable for focal laser photoacoagulation.\textsuperscript{22} PDT can be applied to juxtafoveal and subfoveal leakage, though there is risk of retinal pigment epithelium (RPE) atrophy, choroidal ischemia, choroidal neovascularization and transient central scotoma.\textsuperscript{23,24} Given the excellent safety profile, subthreshold micropulse laser has been applied to patients with central serous retinopathy with variable success. Some investigators have performed SDM laser over ICG-stained RPE cells to perform selective treatment for the active leaking sites, though most have shown good results with FA-guided treatment.\textsuperscript{25}

In a retrospective case series by Kim et al. involving 10 eyes that underwent subthreshold yellow laser (577-nm) for those with chronic or recurrent central serous retinopathy (CSR), central macular thickness decreased at 3 months ($P = .0009$) and at final follow-up ($P = .0009$), which ranged from 6 months to 24 months. The mean BCVA improved at 3 months ($P = .020$) and at final follow-up ($P = .012$).\textsuperscript{26} Similarly, Elhamid et al. also used subthreshold yellow laser (577-nm) for the treatment of nonresolving CSR in 15 eyes. The mean final BCVA after 6 months compared to the initial visual acuity was statistically significant ($P < .05$), improving in 60% of eyes and stable in 40% of eyes. There was complete resolution of subretinal fluid in eleven (73%) eyes and partial resolution in four eyes (27%) after 3 months. Retreatment in two eyes resulted in complete resolution in 13 (86.6%) eyes after 6 months.\textsuperscript{27}

Malik et al. used an 810-nm subthreshold micropulse laser in patients with symptomatic CSCR of 3 months or greater. The authors used power ranging from 750 mW to 1,000 mW at a duty cycle of 5%. The maximum macular thickness (MMT) was significantly reduced in eight of 11 eyes after a single treatment session ($P = .0046$). The range in the number of laser spots was 85 to 657. It has been mentioned that the only risk of HD-SDM is undertreatment. In this particular study, one patient who had recurrence of fluid on follow-up had repeat treatment with an increase in the number of spots. There was no recurrence after that treatment. Additionally, two cases that did not respond to treatment had the least number of applications. Of note, three eyes had a MMT greater than 400 µm. Those three eyes had a significant reduction in macular edema.\textsuperscript{9,10}
in thickness in contrast to previous studies in patients with diabetes showing a nonsignificant reduction in thickness with pretreatment MMT beyond 300 µm.12,13,28

BRANCH RETINAL VEIN OCCLUSIONS

The use and success of SDM laser treatment for macular edema associated with branch retinal vein occlusions seems to be limited and has found to be most effective in patients with a BCVA greater than 20/40.29,30

In my experience, I have found micropulse to be more effective when treating DME in eyes with macular thicknesses less than 400 µm, similar to the results from Luttrull and Mansouri (Figure 1). If the macular edema is greater than 400 µm, I often start off with anti-VEGF therapy and then add subthreshold micropulse laser as adjunctive therapy. I will then repeat the laser after 3 months if needed. Since I often combine laser treatments with anti-VEGF intravitreal injections as needed, it is hard to isolate the use of micropulse laser alone. It would be interesting to try to standardize the number of shots needed per area of edema being treated since undertreatment is a concern. In the treatment of CSR, results have varied, though most patients have shown some benefit (Figure 2). The use of micropulse does not seem to be effective in those patients who have developed choroidal neovascularization. Given the absence of adverse effects and the repeatability of treatment, subthreshold micropulse laser treatment does play a significant role in adjunctive therapy in diabetics and as first line therapy in patients with central serous retinopathy if the fluid has not resolved spontaneously after 3 months.

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