What is the Current Role of Laser Therapy in the Management of DME?

Subthreshold laser may provide a viable adjunct to pharmacologic therapy in selected patients.

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

Diabetic macular edema (DME) is a leading cause of vision loss among individuals with diabetes mellitus (DM), occurring in approximately 3.8% of the diabetic population.[1] Currently, 21 million Americans, 7% of the population, have DM; this translates to approximately 798 000 individuals with DME.

The Diabetic Retinopathy Clinical Research Network (DRCR.net) defined clinically significant DME (CSME) as having the following characteristics:[2]

- Definite retinal thickening due to DME based on clinical examination at or within 500 µm of the macular center.
- A thickness of 250 µm or more in the central subfield or a thickness of 300 µm or more in any one of the four subfields directly adjacent to the central subfield on optical coherence tomography (OCT).
- Hard exudates within 500 µm of the center of the macula with adjacent retinal thickening.

TREATMENT OPTIONS FOR DME

As recently as 5 years ago, the standard of care of CSME was macular focal and grid laser therapy according to a modified Early Treatment Diabetic Retinopathy Study (mETDRS) protocol. Although the mETDRS protocol was an attempt to provide laser therapy that would minimize retinal scarring while still providing the required efficacy, the resultant scarring and accompanying scotomas still produced loss of macular function.

Over the past few years, pharmacotherapy has come to the forefront in the management of DME, particularly with the success of intravitreal anti-VEGF injections for this indication. However, many retina specialists recognize that there is still a role for laser therapy. According to the 2014 American Society of Retina Specialists Preferences and Trends Membership Survey, 12.9% of US respondents would use focal laser as first-line therapy for a new DME patient with visual acuity of 20/50 and phakic status.[3] In addition, 32.7% would manage a CSME patient with visual acuity of 20/25 and fluid visible on OCT with macular laser treatment, and 55.5% would perform panretinal photocoagulation in patients with any form of proliferative diabetic retinopathy (PDR), even if early in the disease.

Additionally, although there are ample data from clinical trials for the use of pharmacologic agents for treatment of center-involved DME, there are not similar data on the use of anti-VEGF or corticosteroid agents in non–center-involved DME. Intuitively, it might seem there would be a role for laser in these patients, especially among those with leaking vasculature. Anecdotally, it appears to be the case that many retina specialists follow a protocol of using laser in selected patients with non–center-involved DME.

A ROLE FOR SUBTHRESHOLD LASER THERAPY

Rationale For Subthreshold Laser

As automated macular microperimetry (MP) has gained ground as a reliable method of assessing overall macular function, the ability to diagnose and treat CSME has greatly improved. Although BCVA as determined by Snellen chart remains the gold standard for measuring visual function, it is widely recognized that this conventional test underestimates the actual level of visual impairment. With modern MP systems, which utilize fundus image registration and autotracking systems, more accurate measurements of retinal sensitivity within

the central visual field can be obtained, even in patients with unstable or extrafoveal fixation. These systems also allow automated follow-up examinations at the same retinal loci and can readily show whether a specific treatment reduces or increases overall macular sensitivity.

Recent MP studies have demonstrated that, while the mETDRS laser protocol can improve central vision, it decreases overall macular function compared with subthreshold laser therapy.[4] Subthreshold laser therapy employs energy parameters much lower than those of mETDRS. One such subthreshold laser modality is the MicroPulse laser therapy (MPLT) system developed by the Iridex Corporation.

In this system, a continuous wave laser beam is separated into a chain of microbursts interspersed with much longer pauses than conventional or continuous wave systems. These "off" intervals allow the surrounding tissue to cool, preventing thermal buildup and thus collateral damage. The MPLT modality has been shown to have similar efficacy to mETDRS laser without causing detectable retinal damage or other laser-associated adverse effects (Figure).[4,5]

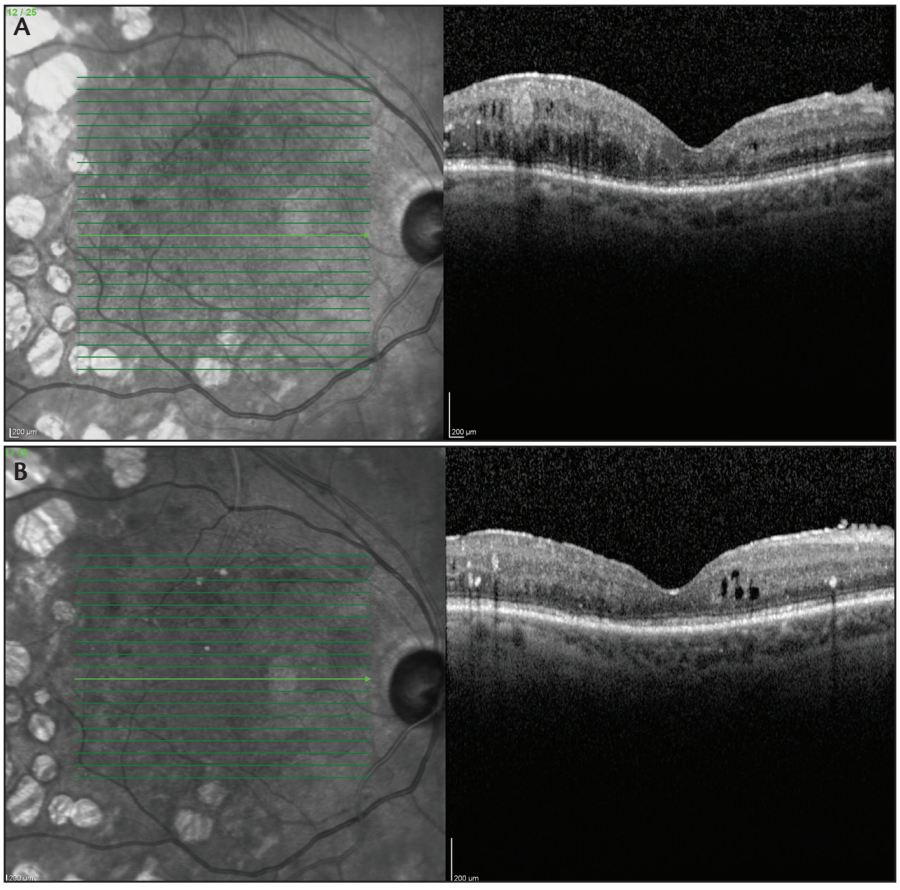

Figure. Patient with CSME that was nonresponsive to serial intravitreal bevacizumab (Avastin, Genentech) injections (top) and 49 days after a single session of MPLT macular grid (bottom) showing significant reduction in foveal retinal thickening.

Animal studies have demonstrated that anti-VEGF agents can significantly compromise retinal pigment epithelial cells and choroidal tissues.[6] In disease states such as macular degeneration and diabetic retinopathy, in which these tissues are already compromised, the delivery of minimal laser energy to these structures becomes paramount.

PERSONAL PROTOCOL

Although recent improvements in laser therapy have been significant, the role of laser in DME management must be considered in context with recent study data from pharmacotherapy trials. The latest update from the VIBRANT study, for example, shows greater gains in vision with anti-VEGF injections than with laser therapy.[7] In addition, recently published data from the Protocol T study by the DRCR.net demonstrated a significant role for anti-VEGF agents, particularly aflibercept (Eylea, Regeneron), in the reduction of DME.[8]

My own experience coincides with that of many of my retina colleagues, in that laser therapy continues to play a significant role in the management of DME. MPLT provides a long-lasting effect that complements pharmacotherapy, potentially reducing the number of anti-VEGF injections required. My current treatment protocols for DME involve both MPLT and pharmacotherapy.

I begin by dividing patients into three categories of DME severity based on OCT scans. Individuals with mild DME—less than 250 µm central retinal thickness (CRT)—are treated initially with MPLT alone. I follow this with pharmacotherapy as needed, based on the response of their DME and the state of their diabetic retinopathy.

For patients with moderate DME—CRT between 250 and 400 µm—I start with monthly anti-VEGF injections for at least 3 months. The goal is to achieve at minimum a 10% decrease in CRT and an improvement of 1 line of

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BCVA. I continue to give anti-VEGF injections until the patient reaches a steady state at which there is no further reduction in DME. I then apply MPLT in a nearly confluent grid pattern to try to achieve a long-term response.

For severe DME patients—CRT greater than 400 µm—I start with three consecutive monthly injections of aflibercept. If the CRT does not get below 400 µm after three injections, I consider the addition of a corticosteroid. Once CRT has been reduced below 400 µm, I move to MPLT with additional pharmacotherapy on an as-needed basis.

CONCLUSION

The treatment of DME has changed significantly in the past decade, and there currently is not a gold standard applicable to all DME patients. Recently there have been excellent advances in both laser therapy and pharmacotherapy for this condition; what remains lacking is the development of an optimal integration strategy for these treatment modalities. I have no doubt, however, that this will be better elucidated in the next few years. ■

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