TISSUE-SPARING LASER FOR CENTER-INVOLVED DME NOT RESPONSIVE TO ANTI-VEGF TREATMENT

Advantages include improving safety and reducing the burden of injections.

BY VICTOR GONZALEZ, MD

In patients with center-involved diabetic macular edema (DME), treatment with an anti-VEGF agent is my first-line strategy. I administer a minimum of three injections in these individuals and then evaluate their response. For patients who have both improved visual acuity (VA) and reduced edema, I continue with three more injections.

Some patients do not show an improvement of VA or reduction of retinal thickening despite anti-VEGF treatment. If such patients have VA of 20/40 or better, they likely will not respond to a different anti-VEGF agent, as was seen in the Diabetic Retinopathy Clinical Research Network (DRCR.net) Protocol T study.[1,2] Therefore, in patients who gain fewer than 5 letters and experience less than a 20% reduction in macular thickness, I consider adding a steroid or treating with laser.

In my experience, most patients respond to steroids, so I typically take that route first. I introduce laser next, particularly if I do not see dramatic resolution of edema after the use of a sustained-release steroidal agent for 6 to 8 weeks, for example.

DECISION POINT

At the sixth injection, I reach a decision point in my algorithm. If, at any step along their treatment path, patients achieve VA of 20/20 and normalized anatomy, I start them on a treat-and-extend regimen with the anti-VEGF agent. If patients have VA improvement to 20/20 and normalized central macular thickness but persistent edema that satisfies the old ETDRS criteria,[3] I extend the anti-VEGF treatment interval and add laser.

That is, in these cases, I back off the frequency of the anti-VEGF agent but add laser photocoagulation. I use semiautomatic pattern scanning laser photocoagulation technology with the Pascal (Topcon) device's Endpoint Management (EpM) software to treat areas of edema around the fovea. This treatment delivers good efficacy with little to no risk. Every injection carries a risk of infection, however small, which would be devastating to the patient, so use of the laser helps to keep the risk profile low.[4]

There is mounting evidence that standard laser treatment in the macula, even at modified ETDRS levels, has the potential to be toxic. Evidence from the DRCR.net Protocol I study and other work has encouraged a move away from using standard ETDRS photocoagulation as initial treatment in center-involved DME.[5,6] In the phase 2 DA VINCI trial evaluating aflibercept (Eylea; Regeneron), my colleagues and I also saw a decrease in

AT A GLANCE

- In the author's algorithm, patients with center-involved DME who do not respond to anti-VEGF therapy are treated with steroid, then with tissue-sparing laser.
- Adding laser serves to decrease the frequency of anti-VEGF injections while at the same time retaining the effect of the drug.
- Large-scale studies comparing new laser technologies to drugs for DME would be instructive.

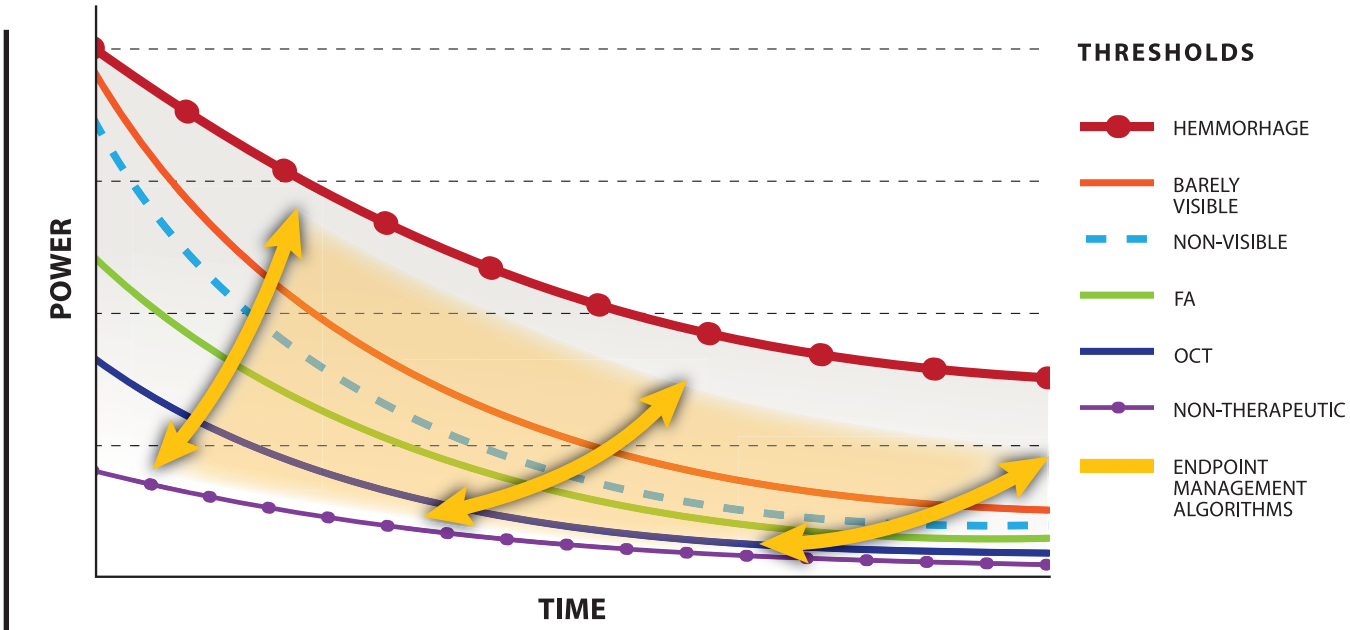

Figure. EpM algorithms adjust power and duration simultaneously, maximizing the ability to safely and accurately control the desired endpoints. Figure courtesy of Topcon.

retinal sensitivity among patients who received macular laser photocoagulation compared with those who received the drug alone.[7]

This evidence led to my adoption of a tissue-sparing laser approach with EpM. The objective of applying laser energy to tissue is to upregulate heat shock protein in the retinal pigment epithelium.[8] There are three ways to do this: with thermal laser, with EpM, or with micropulse technology. I favor EpM over micropulse because the former offers a titration protocol (Figure). Using this algorithm allows application of laser therapy within specific parameters to elicit a cellular response but avoid tissue damage.[9,10]

Some of the factors I consider in applying tissue-sparing laser in patients with center-involved DME are listed in the sidebar "Laser Therapy Retreatment Considerations," below right.

A PLACE FOR LASER

Although new classes of drugs are being developed to treat DME and other retinal pathologies, the use of, or need for, multiple and repeated injected agents will reach a point at which it becomes an obstacle for patients and providers. The efficacy and safety of laser therapy may be underappreciated, and large-scale studies comparing new laser technologies to drugs would be instructive.

In my practice, where 25% of patients have diabetes, laser treatment has been extremely beneficial for DME that is not responsive to anti-VEGF therapy. Adding laser to my treatment algorithm reduces the burden of injections and their associated complications and at the same time preserves the benefit of the drug regimen. Reducing the number of injections is also cost-effective. ■

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LASER THERAPY RETREATMENT CONSIDERATIONS

Factors to contemplate when applying tissue-sparing laser in patients with center-involved DME:

- ▶ Consider laser therapy as an injection
- ▶ Re-treat patients as you would with an injection, using a 3-month interval between laser applications
- ▶ Increase density of treatment area in nonresponders by decreasing space between spots
- ▶ As with treatment using anti-VEGF agents, not all patients respond to therapy