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LASERS IN DME

Laser Focus

Experts discuss the continued critical role of lasers in the treatment of DME

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As a new retina specialist or fellow, you will see your share of patients with diabetic macular edema (DME). And it's likely you will call on anti-VEGF agents, corticosteroids, and emerging combination approaches to fight many of your battles.

But make no mistake: Today's conventional and micropulse lasers remain potent go-to weapons in the treatment of DME, and it pays to know just when and how to use them most effectively. We tapped several veteran retina specialists for their wisdom and insights.

ABOUT DME

DME is a consequence of diabetic retinopathy that causes swelling in the macula. DME is the most common cause of vision loss among people with diabetic retinopathy. About half of all people with diabetic retinopathy will develop DME. Although it is more likely to occur as diabetic retinopathy worsens, DME can happen at any stage of the disease.¹

As recently as 5 years ago, lasers were considered the gold standard of treatment in most cases. Even today, many specialists still consider laser as a first-line treatment for DME. In recent years, however, numerous studies have demonstrated the efficacy and superiority of other therapies, such as anti-VEGF agents and corticosteroids, in fighting center-involving-DME (CI-DME), the most common type of DME.

LASERS FOR NCI-DME AND NON-RESPONDERS

CI-DME patients don't make up all DME cases; however, and a multitude of studies and practicing retina specialists support the use of lasers in at least two major subtypes of DME cases: non-center-involving-DME (nCI-DME) patients and patients who simply don't respond adequately to anti-VEGF agents or corticosteroids.

"In 2016, laser is still the treatment of choice for [nCI-DME]," says Jay S. Duker, MD, a retina specialist with The New England Eye Center at Tufts Medical Center in Boston. The practice has 35 ophthalmologists and nine optometrists, and treats 50 to 60 cases of DME per month. "For nCI-DME, I

still use the definition and criterion for treatment outlined in the ETDRS, and I apply modified grid laser to those eyes," Dr. Duker adds.

The ETDRS, or Early Treatment Diabetic Retinopathy Study, was a multicenter, randomized clinical trial designed to evaluate argon laser photocoagulation and aspirin treatment in the management of patients with nonproliferative or early proliferative diabetic retinopathy. More than 3,700 patients were recruited and followed for 4 years to provide long-term information on the risks and benefits of treatments for eye conditions, such as clinically significant DME.

Charles Mayron, MD, FACS, a 25-year retina specialist with Capital Retina Associates PLLC in Latham, NY, agrees that laser is often best applied to cases of clinically significant nCI-DME.

"I use focal laser to the center of the circinate rings," Dr. Mayron says. "For the diffuse component, the laser approach I use is PanMacular Photostimulation (PMP), a term that I feel describes the treatment. It is micropulse laser with low intensity/high density (confluent) grid using 100 to 200 um spot with a 5% duty cycle using accepted photostimulative parameters."

According to Dr. Mayron, the treatment area is based on the Heidelberg Spectralis OCT thickness map with the ETDRS overlay using a technique he calls "treating by the colors."

"For nCI-DME (clinically significant macular edema; CSME), if the subfields adjacent to the center are pink or better, I use PMP; if the subfields are red or worse, I will induce with anti-VEGF monotherapy to achieve pink or better, and then use PMP," Dr. Mayron explains. "For CI-DME in patients with good glycemic control and central subfield thickness of 350 um or less (yellow or better in the central subfield), I offer PMP monotherapy. If the central subfield is thicker than that (orange or worse), I will induce with anti-VEGF monotherapy until the central subfield is yellow." Then, the entire area of thickening, including the fovea based on the pre-anti-VEGF induction SD-OCT thickness map, is treated with PMP monotherapy. The goal is a reduced treatment burden without sacrificing the best visual outcome. PMP, if done right, adds durability and fewer planned anti-VEGF injections in select cases of CI-DME. In patients with DME who are in poor glycemic control or have severe non-proliferative diabetic retinopathy or worse, I rely on retinopharmacotherapy," he says.

Like Drs. Duker and Mayron, Victor Chong, MD, a retina specialist at the Oxford Eye Clinic in Oxford, England, agrees that laser is best reserved for nCI-DME. But he also believes it can also be used for CI-DME under certain circumstances. Dr. Chong says these would include cases of "early CI-DME with central subfield thickness of less than 300 microns in TD-OCT (or about 340 microns to 350 microns with SD-OCT), depending on the sex of the patient and the machine used) in treatment-naïve patients."

Dr. Chong and his colleagues at the Oxford Eye Clinic in Oxford have more than 400 DME patients undergoing treatment and another 600 laser patients under follow-up treatment for DME. All told, they see more than 3,000 diabetic retinopathy patients per year. Dr. Chong also indicated he is comfortable combining micropulse laser with anti-VEGF therapy in certain cases.



EXPERT ADVICE

Experts offer a few of their favorite tips on using lasers to treat DME:

Charles Mayron, MD:

- Never start near the fovea. Begin PMP away from the fovea, just in case you are not in the correct mode.
- Make sure you check and double-check all your settings. A treatment that looks invisible can be harmful.
- Make sure the contact lens is the correct magnification. The relationship to spot size is exponential (e.g., the energy of a 100 um spot increased to a 200 um spot is reduced by a quarter, not by a half).
- For added safety, use a 5% duty cycle if doing PMP.
- If you change settings — which is dangerous in the middle of a session — never go back to the fovea. You do not want get confused by what is being applied.
- The downside of under treatment is delay of a better option. Retreatment is common, but be aware that PMP takes time to work. So, if vision is going to be adversely affected by the slower treatment response, choose retinopharmacotherapy. An unacceptable downside of titration in MicroPulse is becoming subvisible (no longer PMP) and not being aware of laser-induced maculopathy. Do no tissue damage if your plan is PMP. Fundus Autofluorescence will memorialize it.

- Take a thorough drug history. PMP must be avoided if photosensitizing medications are listed.
- Pick cases of CI-DME where PMP is likely to work — in patients with good glycemic control and moderate edema. PMP never damages, but we damage it if we delay what has been proven to work.

Victor Chong, MD:

- Get a micropulse laser and learn how to use it.
- If conventional laser is all you have, use only invisible burn, shorter duration, and smaller spot size.
- Consider an angiogram to look for macular ischemia if micropulse laser does not work.

Jay Duker, MD:

- Think about adding laser if anti-VEGF monotherapy response is sub-adequate or delayed, or if your patient cannot continue with the regimen.
- ETDRS was a great study — learn from it.
- Do not expect an immediate effect on macular thickening from laser.

Anat Loewenstein, MD:

- Don't continue to inject if there is no response.
- Consider fluorescein angiography if there is no response.
- Don't do laser burns which are too heavy.

“The main reason is that in the RESTORE² study, the combination [therapy] group showed a slight (not statistically significant) benefit of combination therapy over Lucentis* monotherapy in treatment-naïve patients using conventional laser, so the benefit for micropulse laser might be even more,” Dr. Chong says. “In Protocol I, there is a reduction of the number of injections in year 2 onward for immediate treatment compared with deferred laser treatment, but the visual outcome is slightly worse in the immediate treatment group. However, I believe that if we were using micropulse laser, that would not cause retinal damage, so there is no reason the visual outcome would be poorer. And reducing by even one injection per year would still be worthwhile.”

A retina specialist since 1998, Anat Loewenstein, MD, of Tel Aviv Medical Center, Tel Aviv, Israel, is another retina specialist who uses laser treatment to enhance response in patients who don't initially respond to anti-VEGF agents or other treatments. Dr. Loewenstein chairs the Department of Ophthalmology at the Tel Aviv Medical Center, which sees roughly 30 DME patients a day, about a quarter of its total retina patient volume.

“I perform focal laser in cases which are unresponsive to at least three intravitreal injections of anti-VEGF, usually after also having shown to be unresponsive to Ozurdex* (or not suitable for steroid therapy). At this point, after doing a fluorescein angiography, I determine if the patient has treatable lesions, and, if he does, I perform very mild focal laser therapy to the leaking microaneurysms,” Dr. Loewenstein says. “The reason I use this approach is that it has been shown that deferred laser brings along as good results as prompt laser. On the other hand, even in the most recent protocols, about 40 percent of patients in all treatment groups (for example in protocol T) needed laser treatment at some point.”

Dr. Duker, meanwhile, adds laser treatment to anti-VEGF therapy in unresponsive patients.

“For some patients, anti-VEGF monotherapy alone is not enough. Combining anti-VEGF with laser — either conventional focal/grid and/or micropulse — is a safe alternative,” he says. “I find laser especially useful in eyes with circinate exudates arising from a cluster of microaneurysms that are not near the foveal center.

“Unfortunately,” notes Dr. Duker, “we do not have a well-designed, well-controlled study that precisely describes the timing and pattern of laser therapy in DME eyes that undergo initial treatment with anti-VEGF monotherapy.”

PITFALLS OF LASER TREATMENT

Valuable as they can be to DME treatment, lasers must be handled with care, experts say.

MAJOR PLAYERS

Companies offering ophthalmic lasers:

Ellex • ellex.com

Iridex • iridex.com

Lumenis • lumenis.com

Nidek • nidek.com

OD-OS • od-os.com

Quantel • quantel-medical.com

Topcon • pascalvision.com

Zeiss • zeiss.com

One common mistake is to treat the retina with too much energy, seeking a clear reaction, says Dr. Chong, who notes that the risk in doing so is that the laser scar will expand, leading to extensive retinal damage. Conversely, another common error among new physicians is to undertreat the retina, particularly with micropulse lasers, which don't produce the same reaction as conventional lasers, says Dr. Duker.

"Micropulse laser is not applied to achieve a visible endpoint, but ETDRS-type laser should be," he says. "The endpoint should be a very mild greying of the retinal pigment epithelium in areas of diffuse leakage in the case of a grid laser."

Because the number of laser treatments for DME being performed today is much lower than in the past — due in large part to the success of anti-VEGF and corticosteroid therapies — Dr. Duker also believes many new retina specialists don't have as much confidence in their laser skills. However, "given how safe laser is to perform," he says, "I think the most common mistake would be not employing it at all."

LASERS CONTINUE TO PLAY A ROLE

Indeed, most experts overwhelmingly agree that lasers continue to play a major role in the treatment of patients with DME, especially in those with nCI-DME and in those who fail to respond adequately to anti-VEGF agents and/or corticosteroids. Clearly identifying such patients, and knowing precisely how and when to target them with the right laser treatment, can put DME treatment success well within your sights. **NRP**

REFERENCES

1. National Eye Institute website. Facts about diabetic eye disease. Available at: <https://nei.nih.gov/health/diabetic/retinopathy>; accessed June 16, 2016.
2. Mitchell P, Bandello F, Schmidt-Erfurth U, Lang GE, Massin P, et al.; RESTORE study group. The RESTORE study: ranibizumab monotherapy or combined with laser versus laser monotherapy for diabetic macular edema. *Ophthalmology*. 2011;118(4):615-625.

*Lucentis (ranibizumab, Genentech); Ozurdex (dexamethasone intravitreal implant, Allergan)

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