

Laser for BRVO: History and Current Practice

Subthreshold diode micropulse laser therapy avoids thermal injury.

BY JEFFREY K. LUTTRULL, MD

Branch retinal vein occlusion (BRVO) is the second most common retinal vascular disease after diabetic retinopathy, affecting approximately 180,000 people in the United States each year. Risk factors for retinal vein occlusions (RVOs) include glaucoma, older age, and systemic conditions such as diabetes, hypertension, systemic vascular disease, and smoking status.^{1,2}

Although many treatments for BRVO have been tried, none was found to be effective before the Branch Vein Occlusion study was begun in 1977. That study, after a mean follow-up 3.1 years in 139 eyes randomized to argon laser photocoagulation or control, found a statistically significant improvement in visual acuity from baseline in treated eyes ($P=.0005$).³

The BVOS investigators in 1984 recommended argon laser photocoagulation for treatment of macular edema due to BRVO, and to this day laser photocoagulation remains the standard care for the condition.

In recent years, there has been increasing interest in addressing macular edema due to BRVO pharmacologically. Several case reports and small series suggested that intravitreal injection of triamcinolone acetonide could be effective in reducing edema in patients with BRVO. However, a large-scale, controlled clinical trial⁴ failed to show an advantage of triamcinolone injection over standard laser treatment.

The SCORE-BRVO study⁴ compared the safety and efficacy of intravitreal injection of 1 mg or 4 mg triamci-

nolone to standard care with grid photocoagulation in eyes with macular edema secondary to BRVO. In 411 patients randomized to one of three treatment groups, there were no significant differences between the groups in the primary outcome measure of gain in visual acuity of 15 or more letters at 1 year. However, the rates of adverse events, particularly elevated intraocular pressure (IOP) and cataract development, were higher in the 4-mg triamcinolone treatment group than in the other two groups.

The SCORE-BRVO investigators concluded that grid photocoagulation remains the standard of care for patients with visual acuity loss associated with macular edema secondary to BRVO, and that laser photocoagulation should still be the benchmark against which other treatments for BRVO are evaluated.

Recently it was recognized that vascular endothelial growth factor (VEGF) is an important stimulus of macular edema in RVOs,⁵ and as a result there has been increased interest in the use of VEGF inhibitors for the treatment of BRVO. The BRAVO trial⁶ showed promising safety and efficacy results at its 6-month primary endpoint, with visual improvements seen in patients treated monthly with intravitreal injection of ranibizumab (Lucentis, Genentech). However, although rescue laser was allowed in the trial, the design did not include a laser-alone arm for comparison. This, along with the need for longer-term results with VEGF inhibition, still leaves us with laser photocoagulation as the standard of care for BRVO.

SUBTHRESHOLD (SUBVISIBLE) DIODE MICROPULSE LASER

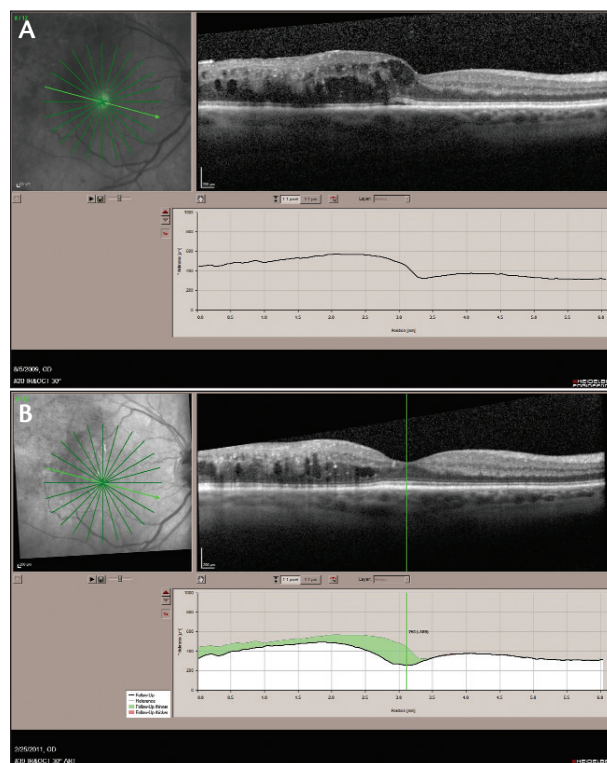
The studies cited above each employed conventional suprathermal laser photocoagulation, the principles of which have remained remarkably unchanged since the days of the Diabetic Retinopathy Study⁷ and the Early Treatment Diabetic Retinopathy Study.⁸ In these landmark studies it was noted that, in general, treatment efficacy increased with treatment density, while treatment complications increased with treatment intensity. In subsequent years, practitioners have modified these classic photocoagulation techniques hoping to improve the safety of treatment, primarily by reducing treatment intensity. The micropulsed diode laser, developed in the 1990s, is one tool that has been employed to this end.

However, when micropulse diode lasers became available, most practitioners continued using these instruments with the same mindset: The aim of the therapy was still to make burns—albeit less intense—in the retina, as it was assumed that thermal retinal destruction was necessary to achieve the desired therapeutic effect. The persistence of thermal chorioretinal damage dictated continued use of traditional grid and modified-grid treatment techniques to minimize the risk of treatment-associated visual loss.

In 2000, when I started using this technology (IQ 810 laser, Iridex Corporation, Mountain View, CA), I took a different approach. My intent was avoid any burns, to perform an effective treatment that caused no thermal retinal damage. To this end I developed a new treatment technique aimed at maximizing the potential benefits of the micropulsed diode laser for retinal vascular disease, termed low-intensity/high-density treatment. With reports beginning in 2005, my colleagues and I were able to show that this new approach to subthreshold (subvisible) diode micropulse laser photocoagulation (SDM) was effective in the treatment of clinically significant diabetic macular edema (DME) and proliferative diabetic retinopathy without any detectable laser-induced retinal damage.⁹⁻¹³ Subsequent randomized clinical trials have confirmed our findings in the treatment of diabetic macular edema.¹⁴⁻¹⁶

SDM offers a number of advantages over conventional thermal laser. Because of its unique safety profile, SDM can be used to treat patients earlier because there is no risk, possibly improving treatment outcomes. Due to the absence of retinal damage, retreatment can be performed as necessary without limit.

Additionally, SDM can be combined with pharmacologic therapy, such as steroid or anti-VEGF agents, for retina-sparing disease management. The optimal timing and sequencing of drug and laser treatments to achieve



Figures 1. Spectral-domain OCT of an eye before (A) and after (B) SDM treatment for BRVO. Note reduction in macular edema without laser-induced retinal damage.

complementary and/or synergistic action and avoid inadvertent inhibition of either treatment is likely important, but unknown. In the absence of thermal retinal injury, SDM appears to work by altering retinal pigment epithelial (RPE) cytokine production. Thus, I generally wait at least 1 month between SDM and drug administration to minimize the risk of the drug “cancelling out” the effect of laser treatment.

Unlike conventional argon laser, the diode laser, operating at 810 nm in the infrared, easily penetrates the retina and retinal blood while targeting the RPE. This difference in wavelength and retinal penetration provides a number of clinical advantages over conventional laser. SDM treatment can be performed without waiting for retinal hemorrhage to clear, a common challenge in BRVO. It also means that treatment intensity does not have to be increased to penetrate a markedly thickened macula. For macular SDM treatment, I use exactly the same parameters on every patient regardless of retinal thickness or fundus coloration.

CLINICAL OBSERVATIONS: SDM FOR BRVO

I now have 11 years experience with SDM as my exclusive laser treatment modality for treatment of

retinal vascular disease, including treatment of BRVO (Figure 1).

SDM can be effective for the treatment of macular edema and neovascularization due to BRVO. While the response to retinal ischemia in BRVO is likely the same as in diabetic retinopathy (increased RPE VEGF production, for instance) the cause is different. Thus, in my experience, macular edema due to BRVO is more likely to wax and wane with more frequent recurrences over a long period of time compared with DME. In addition, because SDM induces a drug-like effect, in some cases it can seemingly wear off. Thus, I find that SDM retreatment and combination therapy are more commonly needed in the management of BRVO than DME. Once again, however, at the end of the day SDM allows me to effectively manage the complications of BRVO without any retinal damage.

Early in my experience with SDM I tended to retreat in 8 to 12 weeks if the macular edema was not completely resolved. Now I follow with spectral-domain optical coherence tomography and re-treat only if there is no response or actual worsening. It is common to observe progressive resolution of macular edema from diabetes or BRVO for as long as 2 years following a single SDM treatment session. Like many others, I tend to use combination therapy more often in eyes with severe center-involving macular edema and/or poor visual acuity in an attempt to accelerate visual recovery.

Finally, high-density/low-intensity SDM may possibly be superior to conventional laser for treatment of BRVO. This may in part be due to the absence of thermal tissue damage and subsequent inflammation that can compromise the effectiveness of treatment. In addition, Parodi and colleagues¹⁷ compared the effects of standard grid subthreshold micropulse diode laser to standard grid conventional laser treatment in patients with BRVO. They found that resolution of macular edema and visual acuity were similar with the two techniques, but the subthreshold technique was not associated with biomicroscopic or angiographic signs. However, subsequent studies of high-density/low-density SDM for DME have found SDM superior to conventional modified ETDRS and normal density micropulsed diode laser treatment.¹⁴⁻¹⁶ I suspect this may hold true in the treatment of macular edema due to BRVO as well.

CONCLUSIONS

It cannot be overstated how the safety and unique clinical characteristics of SDM change one's approach to patient management and conception of photocoagulation for retinal vascular disease, including the treatment of macular edema due to BRVO. SDM offers a perfect

first-line treatment because it does no harm. Treatment can thus be initiated earlier and does not have to be delayed waiting for clearance of retinal hemorrhage. Therapy can subsequently be escalated, depending on how the patient responds, by repeating SDM and/or adding a pharmacologic therapy. Mounting evidence for the safety and efficacy of subvisible retinal phototherapy for retinal vascular disease, such as SDM, challenges the continued use of conventional retina-destructive laser techniques. This is an exciting time in the evolution of laser therapy for retinal vascular disease for both retinal surgeons and their patients. ■

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Dr. Luttrull discloses that he has no financial interest in any device or technique described.

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