

Reducing Damage and Improving Results with Photocoagulation

Use of fluorescein angiogram and indocyanine green imaging combined with subthreshold laser allows greater gains in visual acuity.

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Despite numerous randomized, controlled trials exploring various options for the treatment of diabetic macular edema (DME), the ETDRS guidelines for laser photocoagulation remain the standard of care. Better imaging capability and novel laser techniques may help refine laser treatment protocols, thereby limiting the potential complications and enhancing the beneficial effects of laser.

THE ETDRS PROTOCOL

The ETDRS treatment guidelines recommend focal argon laser, which would visibly whiten the microaneurysms; or to apply “moderately visible” grid laser photocoagulation; or a combination thereof to areas of clinically significant macular edema (as defined by study).¹

Although most patients eventually manifest a positive response to laser therapy over the course of 3 monthly follow-up visits, many report an initial decline in visual acuity lasting for a few months following the treatment. As imaging technology has progressed, the impact of laser treatment has been more closely analyzed. Other laser protocols seem to result in a similar delay in improvement and some actually yield an initial decline in visual acuity after visible laser treatment for DME (which may be significant) that may last up to 1 year before there is an improvement over baseline.² What this demonstrates is that DME can be incited or aggravated by treatment-associated inflammation.

New evidence has emerged suggesting that lower-intensity laser treatment may produce better results.³ Experimental and clinical research has begun to elucidate the mechanism of action behind this theory.

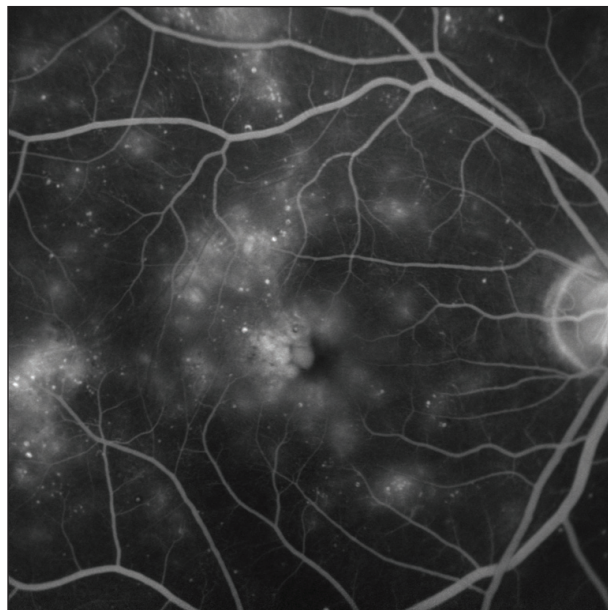


Figure 1. Fluorescein angiography image shows numerous microaneurysms, leakage, and clinically significant macular edema.

Subthreshold laser can stimulate a cell-mediated reparative response that seems to emanate from the level of the retinal pigment epithelium (RPE), essentially modulating the inflammatory and wound healing process. Rather than causing a visible white or mild burn and destroying cells, thermal energy can be applied to induce wanted changes and a reparative cellular response, including modulating numerous cellular mediators, including up-regulation or production of VEGF.⁴

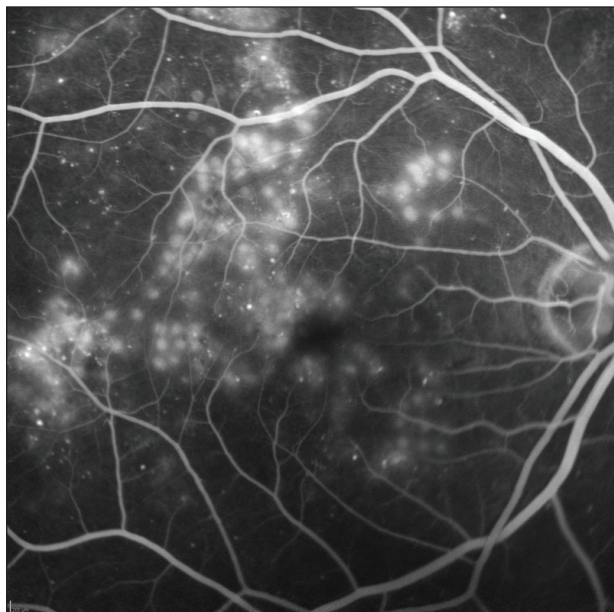


Figure 2. The patient received focal and grid laser photocoagulation at a subvisual threshold power, where no retinal blanching was seen. However, treatment is visually obvious 10 minutes after treatment on angiography.

PATIENT ZERO: CHALLENGING THE PROTOCOL

A patient who was an Asian-Pacific Islander presented to my clinic with comorbid age-related macular degenerative retinal angiomatous proliferation, or RAP, and DME. The complexity of the disease states led me to examine the patient with multiple modalities using the Spectralis (Heidelberg Engineering), whereupon I discovered the utility of indocyanine green angiography (ICGA) in identifying problems of the anomalous retinal vasculature. Indocyanine green has both lipophilic and hydrophilic properties and is 98% protein-bound in vivo. Eighty percent of the indocyanine green molecules actually bind to A1-lipoprotein. Therefore, less of the dye escapes from damaged or fenestrated vasculature. After using the ICGA images to target only these angiographically hot, larger microaneurysms with focal treatment, followed by sub-threshold, reduced-fluence grid laser photocoagulation treatment to the areas of diffuse fluorescein angiographic leakage, this patient had exceptional results, with resolution of DME and involution of the AMD RAP lesions.

SUBTHRESHOLD TREATMENT

Subthreshold laser treatment is not without its potential risks or local consequences. The patient depicted in Figure 1 underwent subthreshold focal and grid laser treatment as guided by fluorescein angiogram (FA) alone. The spots were titrated to a subvisible threshold

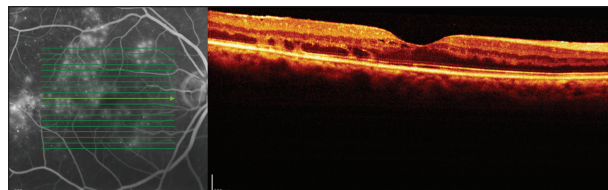


Figure 3. Optical coherence tomography (OCT) imaging 10 minutes after treatment also clearly shows visible laser columns and the occurrence of thermal alteration in the extrafoveal and juxtafoveal regions. It appears that energy absorption occurred predominantly in the outer retinal layers.

and then this power and duration was used for the entire focal and grid treatment. At the conclusion of the laser treatment, with a contact lens in place, no visible spots were present. However, 10 minutes later, the patient underwent a post laser FA to assure that treatment was instilled (Figure 2). The posttreatment OCT clearly shows the laser columns were predominately contained to the outer retina (Figure 3). One month later, the patient returned for follow-up. ETDRS visual acuity remained exactly the same, however the spectral domain OCT now clearly demonstrated a new increased degree of cystoid macular edema that was a presumed inflammatory reaction (Figure 4).

Using less total energy theoretically reduces collateral damage and might minimize the initial decline in visual acuity associated with conventional visible treatment; however, a question remains as to whether this reduced fluence treatment protocol still uses too much energy.

A PROSPECTIVE STUDY

My colleagues and I performed a prospective study designed to validate our clinical experience.⁵ Visual acuity, central macular volume identified with OCT, and ICGA and FA findings were obtained to identify focal leakage from hot spots (retinal microaneurysms, which were then treated selectively with direct bare threshold [light blanching] focal laser). FA findings were used to guide the sub threshold, invisible, grid laser treatment, using a spot size of 100 μm and duration of 10 to 20 ms. Average total fluence was 2720 J/cm².

Visual acuity improved by a mean of 6.1 ± 5.2 , 5.6 ± 5.7 , and 6.3 ± 5.8 ETDRS letters after 3, 6, and 12 months, respectively ($P < .05$ for all points). Macular volume also showed a statistically significant improvement at each period. Minimizing the total energy used in the eye and using ICGA and FA to determine treatment location resulted in less collateral damage and inflammation in the study eyes. This allowed for significant improvements in visual acuity and central macular volume at each of the time points evaluated.

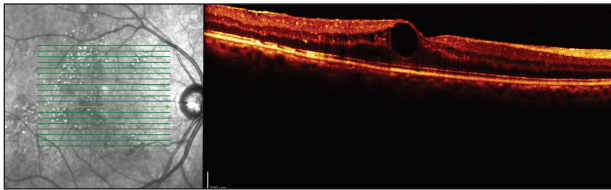


Figure 4. An OCT image 1 month after treatment clearly shows inflammation and cystoid macular edema, with remodeling at the level of the RPE. This patient had clinically significant macular edema at the 1-month follow-up despite a very low level of treatment.

APPLYING NEW THOUGHTS

The spot size of the laser can heavily influence the amount of subjective and objective collateral damage. With a thermal spot size of 100 μm or less applied to the retina, the photoreceptors adjacent to the treatment site will migrate in to fill the thermal treatment gap, resulting in greater photoreceptor continuity, fewer blind spots, and better objective visual function.⁶ However, when the spot size exceeds 100 μm , the retina is sufficiently damaged such that the surrounding photoreceptors are unable to migrate and fill the entire void.⁷ In addition to spot size, the total amount of energy delivered to the eye should also be closely monitored. DME is a vascular disease that is associated with low-grade inflammation, and aggressive laser treatment seemingly incites additional inflammation.

If the collateral and inflammatory damage of laser therapy can be reduced, patients will benefit from the treatment effects, while the potential for treatment-related adverse events will be greatly reduced. Improved imaging capabilities have enabled revolutionary findings regarding the therapeutic mechanism of action of laser therapy, and they should be further studied as they continue to guide patient care. ■

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