The Evolution of Posterior Segment Laser Surgery

The gentle art of destruction.

BY NANCY M. HOLEKAMP, MD

Posterior segment laser surgery dates back to the 1960s, when German ophthalmologist Gerd Meyer-Schwickerath observed the effects of a solar eclipse on the retina and began looking for a way to use light to purposely scar retinal tissue. He experimented with natural sunlight, heliostat, and then a carbon arc lamp before Carl Zeiss Meditec developed the xenon photocoagulator for him. The ophthalmic argon laser would eventually replace xenon arc photocoagulation.

In recent years, dual-frequency Nd:YAG diode lasers have become the standard for retinal treatment. Newer developments have brought to light the benefits of multiple-impact lasers. The expected technological advancements over time notwithstanding, Meyer-Schwickerath’s invention of photocoagulation revolutionized the treatment of retinal tears, diabetic retinopathy, and other diseases of the retina and macula.

THE PURPOSE OF LASER PHOTOCOAGULATION

From the beginning, the purpose of retinal laser photocoagulation has been to destroy retinal tissue. The process of burning retinal tissue creates a permanent chorioretinal scar that has proven useful for treating retinal disease. For example, a laser scar will adhere the edges of a retinal tear to the underlying tissues, thereby preventing retinal detachment. Likewise, a chorioretinal scar will decrease the vascular endothelial growth factor (VEGF) stimulus for proliferative diabetic retinopathy (PDR) by killing the ischemic retina that is eluting VEGF, killing the healthy retina that is consuming the otherwise available oxygen, and increasing intraocular oxygen tension when oxygen from the choriocapillaris diffuses through the scar. (Oxygen is a naturally occurring potent anti-VEGF agent.)

The process of burning retinal tissue has been the most important advance in treating PDR. After more than 40 years, it remains the standard of care. Thus, posterior segment laser photocoagulation is the gentle art of destruction—destroying unimportant parts of the retina while preserving vision. The original tool, xenon arc photocoagulation, was a blunt instrument that left large posterior scars on the retina. After treatment, eyes with PDR remained stable for decades due to the permanent effect the large chorioretinal scars had on intraocular oxygen tension (Figure 1); however,
the treatment was performed in the operating room and was quite cumbersome for both physician and patient.

After the advent of argon laser photocoagulation and dual-frequency Nd:YAG diode lasers, the procedure moved to the office setting. In severe cases, 5,000 or more laser spots can be required to control disease, resulting in debilitating loss of peripheral and night vision (Figure 2).

SAME PURPOSE, GENTLER TECHNIQUE

Newer methods of laser photocoagulation for PDR have retained the need to destroy retinal tissue, but the art of destruction has become gentler and kinder with the evolution of newer platforms for laser delivery. Emphasis has been placed on shorter and less painful treatments as well as production of small, portable, versatile, and reliable laser delivery systems. There has never been a better time to be either the patient receiving or the retinal physician performing laser photocoagulation for a variety of disease states.

One word about laser wavelength: If the goal of laser photocoagulation is retinal destruction, then wavelength (red, yellow, green, etc.) does not matter. In fact, the national Canadian collaborative trial of argon green versus krypton red laser photocoagulation for treatment of choroidal neovascularization for age-related macular degeneration (AMD) showed no appreciable difference in outcomes based on laser wavelength.\(^1\)

There has yet to be impressive and conclusive evidence that laser wavelength makes more than a theoretical difference (ie, a clinically meaningful difference) when treating patients: Laser destruction is laser destruction.

LASER PHOTOCOAGULATION FOR RETINAL TEARS

Peripheral retinal tears identified by indirect ophthalmoscopy can be treated easily with either cryosurgery or indirect laser photocoagulation. With the latter, three confluent rows of chorioretinal scars must be created around the entire extent of the retinal tear (not just the posterior borders). The procedure is performed in the office with only topical anesthesia, and, in general, there is minimal pain for the patient. In pseudophakic eyes with an opacified peripheral capsule, it can prove challenging to achieve a small, well-focused laser delivery. Nevertheless, indirect laser photocoagulation for retinal tears is generally a simple and effective 5-minute procedure.

Posterior retinal tears identified by slit-lamp biomicroscopy are amenable to slit-lamp delivery of laser photocoagulation. Again, three confluent rows of chorioretinal scars must be created around the entire extent of the retinal defect. These can be performed in the office with only topical anesthesia, and there is minimal pain for the patient.

Conventional laser photocoagulation requires the individual placement of laser spots. Newer platforms of pattern-scanning laser delivery systems allow the laser surgeon to choose a pattern of spots with which to surround the tear. This can work well for small and large retinal tears due to the variety of patterns available.

LASER PHOTOCOAGULATION FOR PDR

The goal of laser panretinal photocoagulation (PRP) is destruction of peripheral ischemic retinal tissues to preserve central vision. The therapeutic dose for PRP is hundreds if not thousands of laser spots. With previous laser systems, treatment might be limited to 250 to 500 laser spots at a time because of patient discomfort. Thus, a full PRP treatment would require multiple office visits or a retrobulbar block. The multispot laser platform offers quick and painless treatment for the patient, allowing a 1,000-spot PRP pattern in the peripheral fundus to be performed in the office.
under topical anesthesia in less than 10 minutes.

A multispot laser delivery system works with settings that are fairly high powered but of very short duration. It is common to start with a 200-µm spot size with a 0.01-second duration, as opposed to the traditional 0.1-second duration. The shorter duration is key to making laser surgery painless for patients; however, when the exposure to the laser is so brief, it is necessary to have sufficient power to destroy the retina and reduce intraocular VEGF (Figure 3). Laser power settings up to 1 W may be needed to reach the desired endpoint of a detectable retinal color change. With the short spot duration settings, this amount of laser intensity is well tolerated by the patient despite the fact that 9 to 25 burns are applied rapidly and sequentially.

Commercially available lasers offer multiple laser patterns, varying from a single spot to 25 spots at a time. The shape and angle of the patterns can be changed, allowing treatment to be tailored to the patient’s fundus. Although the impacts in a 9- to 25-spot grid are not simultaneous, the time lapse from the first to the last spot is approximately 0.5 seconds. For PRP, it is common to use a 9- or 16-spot grid pattern.

**LASER PHOTOCOAGULATION FOR DME**

For every rule, there is an exception. The purpose of laser photocoagulation for diabetic macular edema (DME) or other forms of macular edema is likely not retinal destruction. The therapeutic effect of macular laser treatment for edema is thought to be the stimulation of cytokines that lead to reabsorption of fluid in the macula. The Early Treatment Diabetic Retinopathy Study (ETDRS) established laser photocoagulation as the primary therapy for clinically significant DME, and the Diabetic Retinopathy Clinical Research Network (DRCR.net) confirmed that focal/modeled grid photocoagulation should be the benchmark against which other treatments are compared.

In the past, the clinical endpoint of focal laser photocoagulation was turning the diabetic microaneurysm white. Contemporary mainstream focal laser photocoagulation, however, involves a kinder application of thermal laser, leaving a grey-white (almost imperceptible) lesion, as described in DRCR.net clinical trials. The parameters for state-of-the-art modified ETDRS laser treatment are shown in Figures 4 and 5.

Outside of mainstream retinal practice is the concept of micropulse grid laser photocoagulation for DME. Because the benefit of focal laser photocoagulation may simply be the stimulation of therapeutic cytokines, the theory behind micropulse grid laser is photostimulation without creating retinal lesions (rather than thermal photocoagulation with associated retinal damage). Theoretically, this technique allows finer control of the laser thermal effects by using a train of extremely short laser pulses. Sample treatment parameters would be an 80-µm spot size, 0.004-second duration, and 20 mW power. The laser impacts are painted over the thickened retina, but, due to the short impulse duration and low energy, there are no visible burns. Newer laser delivery platforms can offer micropulse laser settings defined by duty cycle (usually 200 ms) divided by the interval between pulses (usually 2,000 ms) plus the micropulse duration. Duty cycle can vary between 5% and 15%, with a typical duty cycle for clinical use being 9% (Figure 6).

This form of treatment requires a laser platform with
micropulse capabilities, but it is imperative to point out that this therapeutic approach is new and requires validation in a scientifically rigorous study.

CONCLUSION

With the advent of injections of anti-VEGF therapy for a variety of retinal diseases, in 2012 it may seem that laser photocoagulation of the retina is fading into the past as a modern treatment modality. Nothing could be further from the truth. Laser photocoagulation remains the standard of care for retinal tears and PDR. It remains an important tool for managing DME and retinal edema due to other causes. Thankfully, the platforms by which laser is delivered to patients with retinal disease in the office continue to evolve, making the gentle art of destruction better than ever.

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Retinal Laser: A Flexible Approach

A multicolor scan laser can be used in all clinical scenarios in the posterior segment.

By Evangelia Papavasileiou, MD, FEOphthalm; and Som Prasad, MS, FRCSeD, FRCOphthalm, FACS

Retinal laser is a valuable treatment modality for a variety of posterior segment diseases. Despite the advent of pharmacotherapy for some retinal conditions such as wet AMD, retinal photocoagulation remains the mainstay of therapy for diseases such as PDR. The argon green laser has traditionally been the main retinal laser modality.

Applying more than 1,000 laser burns used to be a time-consuming and laborious process that was uncomfortable for the patient, especially when repeat treatment was necessary. The advent of pattern-repeating technology in the form of the PASCAL laser (Topcon Corp.) in 2006 revolutionized retinal laser treatment and improved the safety, precision, comfort, and speed of photocoagulation procedures for eye diseases.1 More recently, the MC-500 Vixi Multicolor Pattern Scan Laser (Nidek Co. Ltd.), a second-generation multiwavelength laser system, has become available. This is the first pattern scan laser available with a customizable choice of three wavelengths: 532-nm green, 577-nm yellow, and 647-nm red. In clinical use we find this to be a versatile platform enabling quick and comfortable treatment.

YELLOW LIGHT

The 532-nm green is the most common wavelength for treating retinal pathology with PRP. In the presence of a cataract, however, better penetration is achieved with the 577-nm yellow wavelength compared with the green wavelength.2 The Vixi laser allows the physician to switch to the yellow wavelength to perform efficient photocoagulation through the opaque media.

Yellow is also the color of choice for laser application in the macula. Hemoglobin absorbs yellow light more precisely than other colors, and the 577-nm wavelength is more effective than any other for sealing abnormal blood vessels while doing minimal damage to the macula. This is because yellow is safer in locations where the inner choroid is heavily pigmented, such as over a large choroidal vessel, avoiding the risk of hemorrhage. Joondeph et al3 used 577-nm yellow to treat retinal macroaneurysms and reported resolution of hemorrhage, exudate, edema, or serous macular detachment.

Figure 6. Micropulse duty cycle is an expression of the energy delivered to retinal tissues.
Translating Short Pulse Duration Laser Therapy Into Your Retinal Practice
Subthreshold treatments minimize damage to the sensory retina and RPE.

By Mark R. Wieland, MD

The PASCAL 532-nanometer laser platform (Topcon Corp.) was developed with the goal of making photo-coagulation less time-consuming while improving patient outcomes. Pulse duration was decreased from the traditional 50 to 100 ms to 20 to 30 ms, resulting in decreased thermal diffusion of laser energy. Decreasing the thermal diffusion of laser energy into the retinal pigment epithelium (RPE) minimizes laser RPE creep, the enlargement of laser scars that occurs after focal laser photoacoagulation. With less energy diffusion into the choroid, there is also less pain for the patient during treatment.

Because the initial price tag of $110,000 was more than our seven-member retinal group wanted to pay for, the initial price tag of $110,000 was more than our seven-member retinal group wanted to pay for. The initial price tag of $110,000 was more than our seven-member retinal group wanted to pay for.

Clinical trials have shown that the yellow laser wavelength is less destructive than green because it causes less temperature elevation; it can achieve therapeutic goals but still preserve visual sensitivity as measured by micro-perimetry. Yellow 577-nm laser light provides excellent lesion visibility, low intraocular light scattering, and high choriocapillaris absorption for more uniform effects in patients with light or irregular fundus pigmentation. It also causes little pain for the patient.

RED LIGHT

Krypton lasers have historically supplied the 647-nm red wavelength for posterior segment treatments. This wavelength is used for photoacoagulation of deep choroidal pathology. In eyes with retinal hemorrhage, better penetration is achieved with the red 647-nm wavelength. With the Vixi multiwavelength laser, in the event of accidental hemorrhage during treatment the clinician can switch rapidly to the red wavelength and cauterize a bleeding vessel. This wavelength can also be used in retinal vascular proliferative diseases and chorioretinal diseases associated with exudative manifestations.35

The red laser (647 nm) is not absorbed by the hemoglobin in retinal hemorrhages or by the macular luteal pigment xanthophyll, and it is transmitted into the choroid, allowing treatment within the macular zone with less damage to the internal retinal elements than would be seen with green laser. Therefore, in cases of subretinal neovascular membrane, the red wavelength is the treatment of choice.36

Even in this era of anti-VEGF pharmacotherapy, selected cases such as stage 3 retinal angiomatous proliferation can be treated with this laser wavelength. The red laser could be the potential treatment of choice in these cases, leading to anatomic closure of the vascular complex and eliminating the risk of development of tears in the retinal pigment epithelium.8

CONCLUSION

Each wavelength has a unique absorption and transmission characteristic that makes it desirable for a particular option. With a multicolor scan laser such as the MC-500 Vixi, we can start treatment with one color and continue it with another. This laser is flexible enough to be used in all clinical scenarios in the posterior segment.

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for a pattern scan laser in 2006, we integrated short pulse duration therapy into our practice with the Nidek, Iridex, and Ellex lasers that we already owned. This was accomplished by decreasing the duration setting to 20 to 30 µs and increasing energy as needed to achieve minimally visible burns.

With short pulse duration there is rarely a need for anything more than topical anesthesia. In clinical studies asking patients to compare traditional longer pulse laser photocoagulation treatment with pattern-scanning technology and associated short pulse treatment, pain scores were significantly lower with the shorter pulse duration.1 Additionally, with short pulse duration we have seen much less laser RPE creep. The laser RPE creep seen with longer pulse duration may result in laser scars two to three times the original diameter of the spot size delivered.

**SUBTHRESHOLD TREATMENT**

The historical belief that laser therapy had to destroy oxygen-consuming photoreceptors or RPE cells in order to be effective has been disproven. Numerous clinical trials have shown that less destructive laser therapy can achieve therapeutic goals with minimal damage to the photoreceptors and RPE cells.2,3 Studies have demonstrated that photocoagulation upregulates pigment epithelium-derived factor, a powerful inhibitor of angiogenesis, and downregulates inducers of VEGF, once again decreasing angiogenesis.4

Newer laser technologies may limit tissue damage by subthreshold treatment endpoints. The term *subthreshold* clinically translates to subvisible, but one might also say sublethal or subtoxic.

**ENDPOINT MANAGEMENT**

The PASCAL Streamline 577 laser offers scanning technology and tissue-sparing subthreshold treatment options. This so-called *endpoint management* includes landmark treatment options that are used to give reference marks for subthreshold treatment (Figure 1). Titration to a barely visible endpoint is first done with the laser to establish a baseline. After titration is set, the landmark option is used to mark the pattern boundaries. The energy levels are controlled by algorithms the physician can set to various levels that do not produce visible lesions, such as 25%, 50%, or 75% of the barely visible endpoint (Figure 2). Imaging techniques such as optical coherence tomography and fluorescein angiography have demonstrated the effects of subvisible laser treatments. The strategy is to apply a subvisible treatment while achieving the desired therapeutic effect, sparing damage to the photoreceptor and RPE (Table 1).

There is some peripheral and night vision loss associated with conventional PRP treatment; however, this

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**TABLE 1. ENDPOINT MANAGEMENT**

| • 4 X 4 spot grid |
| • 200-µm spots with 0.75-mm spacing |
| • 250 mW/20 ms exposure |
| • Corner landmark markers: 100% dose |
| • Interior endpoint applications: 75%, 65%, 50% |
Cover Story

May be minimized with the PASCAL endpoint management through preservation of the peripheral neural retina. Subthreshold treatment, much like micropulse photocoagulation, may be effective for treating macular edema.

The Future

In addition to pharmacologic therapies, laser treatment remains an integral part of our retinal treatment for diabetic retinopathy, branch vein occlusion, peripheral retinal tears, and a host of other retinal diseases. Visible photocoagulation is certainly effective but has numerous possible side effects. In the future, we will be able to maximize our therapeutic effects from laser and minimize the damage to the sensory retina and RPE.

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Recent years have seen great advances in our understanding of the pathogenesis and treatment of retinal vascular disease. The role of cytokines elaborated by the RPE, such as VEGF and others known and unknown, is increasingly understood to be paramount. Pharmacologic therapies designed to target and modulate these factors have revolutionized patient care and improved clinical outcomes. At the same time, thermal retinal photocoagulation remains an important if not essential clinical tool and the benchmark against which other treatments are compared. This modality remains remarkably unchanged since the days of the Diabetic Retinopathy Study and intracapsular cataract surgery 40 years ago. 1-3

Traditional theories of the mechanism of conventional thermal retinal photocoagulation for retinal vascular disease were based on the circumstantial association of clinical improvement with laser-induced retinal scarring. What is not circumstantial is the association between the risks and limitations of conventional photocoagulation and the thermal retinal damage it causes. Recent advances in retinal laser treatment suggest that the mechanistic theories of retinal photocoagulation involving laser-induced retinal damage are incorrect, and that thermal retinal damage and subsequent scarring actually represent unnecessary and undesirable side effects of treatment. 4 We know this because invisible laser applications that do not produce a treatment burn endpoint or laser-induced lesions discernable by any method at any time postoperatively have been found to be at least as effective as conventional thermal retinal photocoagu-

Take-Home Message

• Decreasing the thermal diffusion of energy into the RPE minimizes RPE creep.
• The PASCAL Streamline 577 laser offers scanning technology and tissue-sparing subthreshold treatment options.
• The PASCAL endpoint management preserves the peripheral neural retina.

Invisible Retinal Laser Phototherapy for Retinal Vascular Disease

Subvisible treatment appears to be as effective as thermal laser.

By Jeffrey K. Luttrull, MD

Recent years have seen great advances in our understanding of the pathogenesis and treatment of retinal vascular disease. The role of cytokines elaborated by the RPE, such as VEGF and others known and unknown, is increasingly understood to be paramount. Pharmacologic therapies designed to target and modulate these factors have revolutionized patient care and improved clinical outcomes. At the same time, thermal retinal photocoagulation remains an important if not essential clinical tool and the benchmark against which other treatments are compared. This modality remains remarkably unchanged since the days of the Diabetic Retinopathy Study and intracapsular cataract surgery 40 years ago. 1-3

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![Figure 1. Spectral-domain optical coherence tomography of diffuse center-involving DME resolved following low-intensity/high-density subthreshold diode micropulsed laser. Note absence of laser-induced retinal damage.](image-url)
NEW TREATMENT PARADIGM

Invisible retinal laser phototherapy for retinal vascular disease is a new treatment paradigm currently epitomized by low-intensity/high-density subthreshold diode laser micropulsed photocoagulation (SDM). Low-intensity means that, by design, no evidence of laser-induced retinal damage is detectable by any means during or at any point following treatment. Treatment is thus entirely harmless. The absence of laser-induced tissue injury permits a second fundamental change, that of confluent (ie, high-density) treatment of all areas of retinal pathology to maximize the treatment effect.

Since the pilot study of SDM reported in 2005, subsequent investigators have found subthreshold diode micropulsed laser for treatment of macular edema due to diabetic retinopathy to be at least as effective as conventional photocoagulation: SDM reduced macular edema (Figures 1 through 3) and has resulted in comparable or better visual acuity results, as well as improved macular function by microperimetry and focal electroretinograms, compared with conventional photocoagulation. SDM has also been reported to be effective for treatment of macular edema due to branch retinal vein occlusion, PDR and central serous chorioretinopathy. The safety of SDM permits earlier treatment, which may improve long-term outcomes, and treatment may be repeated as necessary—alone or in combination with drug therapy.

HOW SDM WORKS

How does SDM work in the absence of laser burns? SDM is actually in step with our current understanding of the pathogenesis of retinal vascular disease.

First, low power laser exposure, such as SDM, is known to reduce inflammation and normalize
cytokine expression in many cell types. Common sense suggests that the dead and deranged tissue at the heart of conventional laser burns is no longer biologically active.

Laboratory studies suggest that the benefits of conventional photocoagulation for retinal vascular disease derive from cells surviving at the margins of conventional laser burns, not from the burns themselves. Thus, SDM would appear to modulate or reprogram RPE cytokine expression toward normal without damaging the cell. In the absence of tissue damage, all areas of RPE exposed to SDM—not just the spot margins—are therapeutically affected. Second, the destructive nature of conventional laser treatment limits treatment density. With SDM, however, all areas of retinal pathology, such as macular thickening or ischemia, can be completely and conflently treated without risk, amplifying the therapeutic effect. The lack of retinal damage and high-density treatment application thus maximizes the therapeutically affected and effective retinal surface area.

Third, the clinical effect of cytokines may follow a U-shaped curve, with small changes sometimes eliciting large effects. At the left end of the curve, at which SDM may be operating, cytokine expression may approximate an on-and-off phenomenon rather than dose-response. This is supported by the observation of SDM effectiveness at the lowest reported irradiances. Thus, higher laser energies may increase retinal burn risk without improving the therapeutic response.

Finally, there is no loss of functional tissue or inflammatory reaction. The retinal damage and inflammation associated with conventional photocoagulation may explain the poorer outcomes observed in studies combining conventional laser and drug therapy, compared with drug therapy alone. Thus, it may be that conventional retinal photocoagulation (an iatrogenic laser-induced multifocal chorioretinitis) and SDM (as invisible retinal laser phototherapy) work essentially the same way.

CONCLUSION

The obituary for laser treatment of retinal vascular disease may indeed have been written prematurely. SDM is ushering in a new era for laser treatment of retinal vascular disease.

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TAKE-HOME MESSAGE

- Invisible retinal laser phototherapy for retinal vascular disease is epitomized by low intensity/high density SDM.
- It may be that conventional retinal photocoagulation and SDM work essentially the same way, except that the detrimental and unnecessary destructive effects of conventional photocoagulation are eliminated by SDM.