CHAPTER 18

Laser Therapy and Cryotherapy for Posterior Segment Diseases

This chapter includes a related video. Go to www.aao.org/bcscvideo_section12 or scan the QR code in the text to access this content.

Highlights

- Laser setting parameters, including wavelength, power, duration, and spot size, are chosen with the goal of the laser treatment and the targeted tissue in mind.
- Although anti–vascular endothelial growth factor injections have replaced laser photocoagulation as the treatment of choice for several diseases, laser photocoagulation remains a useful treatment for proliferative retinopathies and ablation of retinal vascular lesions.
- Photodynamic therapy is effective for selective diseases, including idiopathic polypoidal choroidal vasculopathy and central serous chorioretinopathy.

Basic Principles of Photocoagulation

Photocoagulation uses light energy to coagulate tissue. After light energy is applied to the target tissue, it converts into thermal energy and the tissue temperature rises above 65°C, causing denaturation of tissue proteins and coagulative necrosis.

Current posterior segment laser delivery systems span the visible light spectrum of 400–700 nm (green, yellow, red) and venture into the infrared wavelengths (>700 nm). Delivery systems may use a transpupillary approach with slit-lamp or indirect ophthalmoscopic delivery, endophotocoagulation during vitrectomy, or transscleral application with a contact probe.

The effectiveness of photocoagulation depends on the transmission of light through ocular media and the absorption of that light by pigment in the target tissue. Light is absorbed principally by ocular tissues that contain melanin, xanthophyll, or hemoglobin. Figure 18-1 illustrates the absorption spectra of the key pigments found in ocular tissues:

- Melanin is an effective absorber of green, yellow, red, and infrared wavelengths.
- Macular xanthophyll readily absorbs blue wavelengths but minimally absorbs yellow and red wavelengths.
- Hemoglobin easily absorbs blue, green, and yellow wavelengths but has minimal absorption of red wavelength.

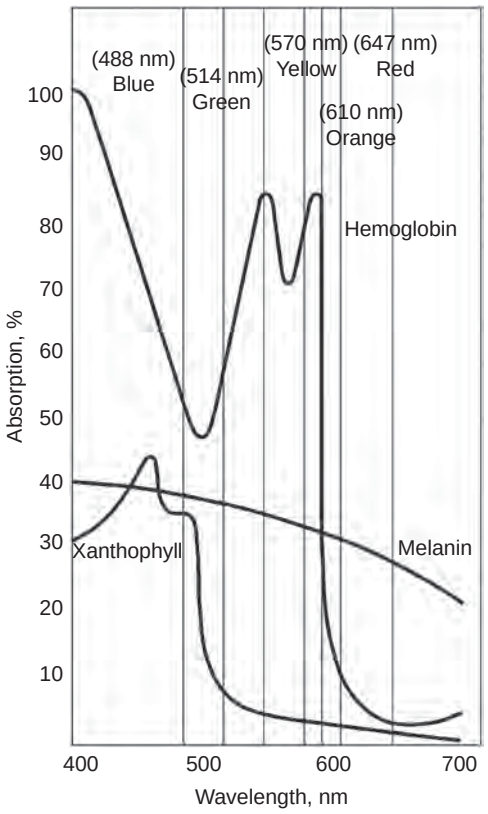

Figure 18-1 Absorption spectra of xanthophyll, hemoglobin, and melanin. *(From Folk JC, Pulido JS.* Laser Photocoagulation of the Retina and Choroid. *Ophthalmology Monograph 11. American Academy of Ophthalmology; 1997:9.)*

Choice of Laser Wavelength

Laser wavelength selection depends on the specific goals of treatment and the degree to which the photocoagulation must be targeted to the particular tissue while sparing adjacent healthy tissue. The *area* (depth and diameter) of effective coagulation is directly related to the *intensity* and *duration* of irradiation. For a specific set of laser parameters (spot size, duration, and power), the intensity of the burn obtained depends on the clarity of the ocular media and the degree of pigmentation.

The green laser produces light that is absorbed well by melanin and hemoglobin and less completely by xanthophyll. Because of these characteristics and the absence of undesirable short (blue) wavelengths, the green laser has replaced the blue-green laser for treatment of retinal vascular abnormalities and choroidal neovascularization (CNV).

The red laser penetrates through nuclear sclerotic cataracts and moderate vitreous hemorrhages better than lasers with other wavelengths do. In addition, it is minimally absorbed by xanthophyll and thus may be useful in treatments near the fovea. However, the red laser causes deeper burns with a higher rate of patient discomfort than other wavelengths and inhomogeneous absorption at the level of the choroid. The infrared laser has characteristics similar to those of the red laser with even deeper tissue penetration.

The advantages of the yellow laser include minimal scatter through nuclear sclerotic lenses, low xanthophyll absorption, and little potential for photochemical damage.

It appears to be useful for destroying vascular structures while minimizing damage to adjacent pigmented tissue; thus, it may be valuable for treating retinal vascular and CNV lesions.

Laser effects on posterior segment tissues include photochemical and thermal effects and vaporization. Photochemical reactions can be induced by ultraviolet or visible light that is absorbed by tissue molecules or by molecules of a photosensitizing medication (eg, verteporfin), producing cytotoxic reactive oxygen species (eg, free radicals). Absorption of laser energy by pigment results in a temperature rise by tens of degrees and subsequent protein denaturation; the exact temperature rise depends on laser wavelength, laser power, duration of laser application, and spot size. Vaporization is generated by the rise in water temperature above the boiling point, which causes microexplosions, as can occur in overly intense burns. For further discussion of laser light characteristics and light–tissue interactions, see BCSC Section 3, *Clinical Optics and Vision Rehabilitation,* Chapter 2.

Atebara NH, Thall EH. Principles of lasers. In: Yanoff M, Duker JS. *Ophthalmology*. 4th ed. Elsevier/Saunders; 2014:32–37.

Palanker D, Blumenkranz MS. Retinal laser therapy: biophysical basis and applications. In: Schachat AP, Wilkinson CP, Hinton DR, Sadda SR, Wiedemann P, eds. *Ryan's Retina;* vol 1. 6th ed. Elsevier/Saunders; 2018:chap 41.

Practical Aspects of Laser Photocoagulation

Anesthesia

Topical, peribulbar, or retrobulbar anesthesia may be necessary to facilitate delivery of laser photocoagulation.

Lenses

Two types of contact lenses are available to assist in slit-lamp delivery of photocoagulation: negative-power planoconcave lenses and high-plus-power lenses. Planoconcave lenses provide an upright image with superior resolution of a small retinal area, and most clinicians favor their use for macular treatments. Mirrored planoconcave lenses facilitate viewing and photocoagulation of more peripheral retina. In general, planoconcave lenses provide the same retinal spot size as that selected on the slit-lamp setting.

High-plus-power lenses provide an inverted image with some loss of fine resolution, but they offer a wide field of view, which facilitates efficient treatment over a broad area. High-plus-power lenses provide a spot size that is magnified over the laser setting size; the magnification factor depends on the lens used (Table 18-1).

Parameters and indications

Selection of laser setting parameters depends on the treatment goals, the clarity of the ocular media, and the fundus pigmentation. As a rule, smaller spot sizes require less energy than larger spot sizes, and longer-duration exposures require less energy than shorter-duration exposures to achieve the same intensity effects.

Macular laser Although intravitreal anti-vascular endothelial growth factor injections have replaced laser as the treatment of choice for many etiologies of macular edema and

Table 18-1 Magnification Factors for Common Laser Lenses

Lens	Magnification	Laser Spot Magnification
Panretinal photocoagulation lenses		
Ocular Mainster PRP 165	0.51×	1.96×
Ocular Mainster Wide Field PDT	0.68×	1.5×
Ocular Pro Retina	0.5×	2.0×
Rodenstock Panfunduscope	0.7×	1.43×
Volk Equator Plus	0.44×	2.27×
Volk HR Wide Field	0.5×	2.0×
Volk QuadrAspheric	0.51×	1.97×
Volk SuperQuad 160	0.5×	2.0×
Focal laser lenses		
Goldmann 3-mirror (central)	0.93×	1.08×
Ocular Fundus Laser	0.93×	1.08×
Ocular Mainster High Magnification	1.25×	0.8×
Ocular PDT 1.6×	0.63×	1.6×
Ocular Reichel-Mainster 1× Retina	0.95×	1.05×
Ocular Reichel-Mainster 2× Retina	0.5×	2.0×
Ocular Yannuzzi Fundus	0.93×	1.08×
Volk Area Centralis	1.06×	0.94×
Volk Centralis Direct	0.9×	1.11×
Volk Fundus 20	1.44×	0.7×
Volk Fundus Laser	1.25×	0.8×
Volk HR Centralis	1.08×	0.93×
Volk HR Wide Field	0.5×	2.0×
Volk PDT Lens	0.66×	1.5×
Volk Super Macula 2.2	1.49×	0.67×

CNV, laser photocoagulation still has a role in the management of some forms of macular edema, extrafoveal CNV, and focal retinal pigment epithelium (RPE) abnormalities with leakage, such as those seen in central serous chorioretinopathy and around retinal arterial macroaneurysms. To avoid central scotomata, treatment should not be administered within 500 μm of the foveal center. Macular laser treatment for edema generally uses a small spot size (50–200 μm) and short duration (≤0.1 second) to achieve smaller, less-intense burns. For diabetic macular edema, green or yellow direct laser therapy is typically applied to all leaking microaneurysms located between 500 μm and 3000 μm from the center of the macula. For zones of capillary nonperfusion and diffuse leakage more than 500 μm from the center of the macula and 500 μm from the temporal margin of the optic nerve head, a light-intensity grid pattern is applied using a green or yellow laser. A similar strategy is used to treat macular edema caused by branch retinal vein occlusion. In the treatment of CNV or RPE leakage spots, the aim is to achieve a more intense burn of the entire lesion or area of leakage.

Peripheral retinal photocoagulation Peripheral retinal photocoagulation may be performed with either a slit-lamp or indirect ophthalmoscopic delivery system. In panretinal photocoagulation (PRP) or laser retinopexy, spot size typically is 200–500 μm and laser power is adjusted to achieve gray or light-cream burns. For PRP, burns are usually one-half to one burn width apart (see Chapter 5, Fig 5-10) and should spare the macula. For milder retinopathy,

one can leave approximately 1–2 disc diameters of retina outside the macula and optic nerve head untreated, whereas more severe retinopathy may require treatment up to the arcade vessels and closer to the optic nerve (Fig 18-2). Initial treatment should be concentrated in the inferior retina in case of subsequent vitreous hemorrhage and to preserve the temporal, nasal, and inferior visual field. The posterior ciliary nerves in the 3 and 9 o'clock meridians should be avoided, and any coexisting macular edema should be treated beforehand to avoid exacerbation. Typically, 1200–1400 laser applications of 500-μm spot size, or the equivalent of smaller burns, are placed.

Laser retinopexy is used to create a chorioretinal adhesion around retinal tears or for demarcation of a (small) retinal detachment. Usually, 2 or 3 rows of photocoagulation around the break are sufficient.

Laser ablation of retinal vascular lesions Vascular lesions, such as retinal arterial macroaneurysms, are often treated using a large spot size (≥500 μm), low power, and long duration so each lesion slowly heats up and coagulates "from the inside out." High-intensity burns whiten the surface of retinal vascular lesions, after which visible-light laser does not penetrate well, making it difficult to achieve the treatment goal.

Alternative laser delivery systems and strategies

Recent innovations in slit-lamp delivery systems include pattern scanners that deliver an entire array of laser applications with each foot-pedal depression; the high-intensity laser pulses are ultrashort (20–50 milliseconds) and are delivered in rapid succession. This approach may increase the efficiency of treatment, but it may not achieve an effect equivalent to that of traditional laser treatment on a spot number–to–spot number comparison.

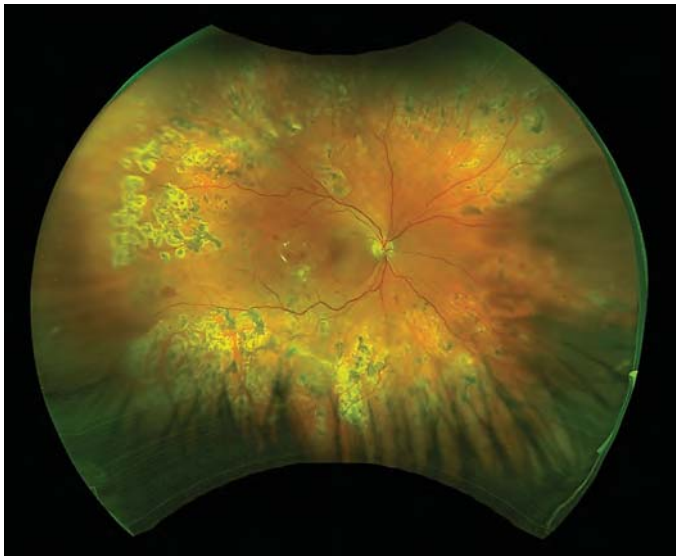

Figure 18-2 Illustration of the posterior extent of full panretinal photocoagulation showing sparing of the 3 and 9 o'clock meridians to avoid damage to the posterior ciliary nerves. *(Courtesy of Gaurav K. Shah, MD.)*

Some laser delivery systems incorporate real-time retinal image overlay and registration. This configuration allows for computer-assisted planning and precise targeting of the retinal lesions during treatments.

Delivery systems that apply subthreshold (ie, barely visible to invisible) laser spots administer micropulses (≤0.1 millisecond) that confine heat conduction to the RPE while limiting thermal damage to the photoreceptors and choriocapillaris. These systems have been effective in treating diabetic macular edema and may reduce the number and size of scotomata. Titration of burn intensity and monitoring of the area of placement of invisible laser spots during laser delivery is facilitated by commercial laser systems using endpoint software technology.

Baumal CR, Ip M, Puliafito CA. Light and laser injury. In: Yanoff M, Duker JS. *Ophthalmology*. 4th ed. Saunders/Elsevier; 2013:461–466.

Chappelow AV, Tan K, Waheed NK, Kaiser PK. Panretinal photocoagulation for proliferative diabetic retinopathy: pattern scan laser versus argon laser. *Am J Ophthalmol.* 2012;153(1):137–142.e2.

Complications of Photocoagulation

The most serious complications of photocoagulation are caused by the use of excessive energy or misdirected light. These complications include inadvertent corneal and iris burns, which can lead to corneal opacities, and iritis and zones of iris atrophy, respectively. Thermal damage to the posterior ciliary nerves in the suprachoroidal space and/or the iris sphincter muscle can lead to persistent mydriasis, loss of accommodation, and corneal anesthesia with subsequent dry eye, whereas absorption by lens pigments may create lenticular burns and resultant opacities. Optic neuropathy may occur from treatment directly to or adjacent to the optic nerve head, and nerve fiber damage may follow intense absorption in zones of intraretinal hemorrhage, increased pigmentation, or retinal thinning. Chorioretinal complications include foveal burns, Bruch membrane ruptures, creation of retinal or choroidal lesions, and exudative choroidal or retinal detachment. When the retinal nerve fiber layer is damaged during laser treatment, visual field loss may extend beyond the local area.

Accidental foveal burns

Great care should be taken to identify the fovea by means of biomicroscopy. To maintain orientation, frequent reference to the foveal center throughout the procedure is helpful. In some instances, the risk of foveal burns may be reduced by immobilizing the globe with peribulbar or retrobulbar anesthesia.

Bruch membrane ruptures

Small spot size, high power, and short duration of laser applications all increase the risk of a rupture in Bruch membrane, which may subsequently give rise to hemorrhage from the choriocapillaris and development of CNV.

Retinal lesions

Intense photocoagulation may cause full-thickness retinal holes. Similarly, intense treatment may lead to fibrous proliferation, striae, and foveal distortion, with resultant meta-

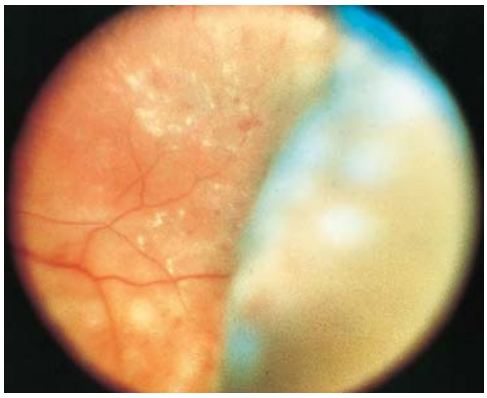

Figure 18-3 Color fundus photograph shows choroidal detachment that occurred after panretinal scatter photocoagulation for diabetic retinopathy. *(Courtesy of M. Gilbert Grand, MD.)*

morphopsia or diplopia. Focal treatment with small-diameter, high-intensity burns may cause vascular occlusion or perforate blood vessels, leading to preretinal or vitreous hemorrhage. In addition, extensive panretinal treatment may induce or exacerbate macular edema, particularly in patients with diabetes.

Choroidal lesions

Treatment of CNV may be complicated by subretinal hemorrhage, choroidal ischemia, and additional CNV or chorioretinal anastomosis. Progressive atrophy of the RPE may occur at the margin of photocoagulation scars, resulting in enlarged scotomata. Also, photocoagulation may precipitate tears of the pigment epithelium.

Exudative retinal and choroidal detachment

Extensive, intense photocoagulation may lead to massive chorioretinal edema and resultant serous retinal and choroidal detachment (Fig 18-3). In turn, the latter may lead to narrowing of the anterior chamber angle from forward rotation of the ciliary body, elevated intraocular pressure, and in rare cases, aqueous misdirection. Limiting the extent of the laser burns delivered in one session of PRP may prevent this complication.

Palanker D, Lavinsky D, Blumenkranz MS, Marcellino G. The impact of pulse duration and burn grade on size of retinal photocoagulation lesion: implications for pattern density. *Retina.* 2011;31(8):1664–1669.

Transpupillary Thermotherapy

Transpupillary thermotherapy (TTT) acts in a subthreshold manner by slightly raising the choroidal temperature, thus causing minimal thermal damage to the RPE and overlying retina. TTT is administered with an infrared laser (810 nm) using beam sizes from 0.8 mm to 3.0 mm, power settings between 250 mW and 750 mW, and a 1-minute exposure time. For choroidal melanoma, TTT may be considered as a stand-alone treatment for tumors less than 4 mm thick; however, for thicker tumors, a combination of TTT and plaque radiotherapy provides better local tumor control than TTT alone.

Photodynamic Therapy

Photodynamic therapy (PDT) using the photosensitizing drug verteporfin is approved by the US Food and Drug Administration for treating certain types of subfoveal CNV in age-related macular degeneration and secondary to ocular histoplasmosis syndrome and myopia. Because more effective treatments have become available, PDT has generally fallen out of favor; however, it is still a valuable option for the treatment of leaking polyps in idiopathic polypoidal choroidal vasculopathy. It is also useful in central serous chorioretinopathy and some ocular tumors.

PDT is a 2-step procedure:

1. intravenous administration of the photosensitizing drug, which localizes to endothelial cells of vessels present in CNV and tumors
2. local activation of the drug by a laser wavelength preferentially absorbed by the sensitizing drug

The low-intensity laser energy induces a photochemical reaction, leading to the formation of reactive oxygen species, including free radicals. These radicals cause endothelial cell damage, platelet adherence, vascular thrombosis, and capillary closure.

Complications of Photodynamic Therapy

The most serious adverse effects of PDT are photosensitivity reactions that range from mild to second-degree burns of sun-exposed skin. These can be avoided by having the patient minimize exposure to sunlight for 5 days after treatment. Severe vision loss may occur in approximately 4% of patients after standard-fluence PDT of subfoveal lesions. To minimize choriocapillaris nonperfusion, treatment using half-fluence PDT (25 J/cm^2 energy; 300 mW/cm^2 light intensity) has become more common. Another method to approximate (but not duplicate) half-fluence is to use full fluence for 41–42 seconds, or half the typical time of 83 seconds.

Cryotherapy

Cryotherapy involves the freezing and thawing of tissue, resulting in cell injury and death. In practice, cryotherapy is most often used to treat retinal breaks (cryopexy), either as a stand-alone procedure or as part of retinal detachment repair. When media opacity, light pigmentation, far peripheral breaks, and subretinal fluid around the tear could impede laser uptake, cryopexy may be preferable over laser retinopexy. Cryotherapy is also used to treat retinal vascular tumors and pars planitis.

Cryotherapy freezes the tissue that is in direct contact with a handheld probe. The freezing interface progresses in an outward direction, resulting in a temperature distribution that is coldest at the point of contact with the probe. After reaching a temperature below −40°C, cells at the center of the cryoablated tissue die from the disruptive process of extracellular and intracellular ice formation. Peripheral cells that do not reach −40°C die primarily from apoptosis and necrosis. Cryotherapy also induces ischemia by causing

vascular stasis and disruption of small-caliber vessels and may lead to breakdown of the blood–ocular barrier. Subsequent chorioretinal scarring produces a firm adhesion between the retina and choroid.

Cryopexy Technique

Before cryotherapy is applied to the eye, the surgeon should confirm that the cryoprobe tip is cooling properly. When the cryoprobe is initially applied to the conjunctiva or sclera, however, the tip should be at room temperature. Using indirect ophthalmoscopy or a surgical microscope for visualization, the surgeon begins by positioning the cryopexy probe tip near the retinal tear and pressing down gently, creating an indentation. Typically, a footswitch is depressed to allow coolant to flow to the tip, causing an ice ball to form and turning the tissue a whitish color. Because strong adhesion is created with freezing, the probe should not be moved at this time to avoid tearing the tissue. Once the probe has been allowed to thaw, it can be repositioned for another application. This sequence continues until the entire tear has been completely surrounded by cryopexy. See Video 18-1 for an example of cryopexy used to treat a retinal break.

VIDEO 18-1 Intraoperative cryopexy for a peripheral retinal break.
Courtesy of Franco M. Recchia, MD.

Inadvertent freezing of the macula may occur if indentation of the shaft of the cryotherapy probe is mistaken for the tip. Other treatment complications include eyelid damage from inadvertent freezing from the probe shaft, transitory uveitis, temporary chemosis, and subconjunctival hemorrhage.