

PROCEDURES IN COSMETIC DERMATOLOGY
Series editor Jeffrey S Dover
Associate editor Murad Alam



Lasers and Lights

Volume I

Vascular – Pigmentation – Hair – Scars
– Medical Applications

Edited by **David J Goldberg**

DVD editor **Thomas E Rohrer**

2ND EDITION

2



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PROCEDURES
IN COSMETIC
DERMATOLOGY

Lasers and Lights Volume I

Goldberg

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Procedures in Cosmetic Dermatology

Series Editor: Jeffrey S. Dover MD FRCPC FRCP

Associate Editor: Murad Alam MD MSCI

Lasers and Lights Volume I

Vascular—Pigmentation—
Hair—Scars—Medical Applications

Second edition

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Vascular Lesions

Thomas E. Rohrer, Roy G. Geronemus,
Alexander L. Berlin

INTRODUCTION

Cutaneous vascular lesions are one of the most common indications for laser treatment in dermatology. Vascular lesions require proper diagnoses and a clear understanding of their biologic behavior.

This chapter discusses the evaluation and treatment of acquired and congenital vascular lesions of the face including telangiectasia, erythema, and vascular anomalies. Significant developments in laser and light based technology have had tremendous impact on the therapeutic options for these conditions, making it the preferred treatment for vascular lesions. Treatment of these common conditions is efficacious, well tolerated, and can be tailored for all skin types.

The theory of selective photothermolysis is the ability to target a specific chromophore in the skin with minimal damage to surrounding structures through the selection of the proper wavelength, pulse duration, and fluence. Treatment parameters can therefore be optimized, permitting precise treatment of the intended structure while minimizing collateral injury to other tissues. The target chromophore in the treatment of vascular lesions is oxyhemoglobin. The major peaks of light absorption by oxyhemoglobin include 418 nm, 542 nm, and 577 nm, as well as a smaller broad absorption band from approximately 800 to 1100 nm (Fig. 1.1). Although 418 nm represents the largest absorption peak, this wavelength does not penetrate into the skin sufficiently to reach clinically significant cutaneous vasculature. The other wavelengths, on the other hand, have found their way to current clinical use.

When oxyhemoglobin is selectively targeted, light energy is absorbed and transferred into heat. The heat produced in the oxyhemoglobin in the red blood cells transfers to the vessel wall and results in coagulation and, as a goal, vessel wall closure. To minimize thermal injury to surrounding structures, the laser pulse duration—also known as pulse width—is kept equal to or shorter than the thermal relaxation time of the intended target. Thermal relaxation time is the cooling time (50%) of the target and is proportional to the square of the target diameter. For example, a port wine stain, which contains blood vessels averaging 50–100 μm in diameter, has a

thermal relaxation time of approximately 1–10 ms. Pulse durations longer than the thermal relaxation time can lead to thermal diffusion and resultant damage to other structures. Therefore, small vessels are optimally targeted with shorter pulse duration than larger vessels.

• History of developments in the laser treatment of vascular lesions

Many lasers have been described for the treatment of vascular skin disorders with variable efficacy and safety. The first major advancement in laser treatment for vascular lesions was the 488 nm and 514 nm continuous argon laser in the 1970s. Early reports were very promising. The blue-green light emitted by the argon laser is well absorbed by oxyhemoglobin. Unfortunately, the continuous wave laser system (producing a continuous beam of light with little or no variation in power output over time) caused nonspecific coagulation necrosis of the superficial dermis that often led to subsequent scarring and depigmentation. Twenty one per cent of adult patients and 38% of children under 12 years old had permanent hypopigmentation and scarring.

The argon pumped tunable dye laser, with wavelengths adjusted to the yellow range (577 or 585 nm), was more selective for blood vessels. It is a continuous wave mode laser with wavelengths ranging from 488 to 638 nm, which could be operated in the 577–585 nm range. The laser could be modified to deliver pulse durations of 20 ms, but the majority of clinical applications require a minimum of 100 ms pulse duration. There was minimal post-procedural purpura and hyperpigmentation compared to traditional dye laser, but, unfortunately, the risk of atrophic or hypertrophic scarring was as high as 25% in some treatment groups.

Commercially available in 1981, copper vapor and copper bromide lasers are quasicontinuous wave mode lasers that deliver yellow light with a wavelength of 578 nm. Also available at 510 nm, they can be utilized for the treatment of cutaneous pigmented lesions. Light is emitted as 20 ns pulses at a repetition rate of 6000–15 000 pulses per second. Various types of vascular lesions, such as facial telangiectasias, cherry angiomas, and pyogenic granulomas, have been treated with good efficacy by these

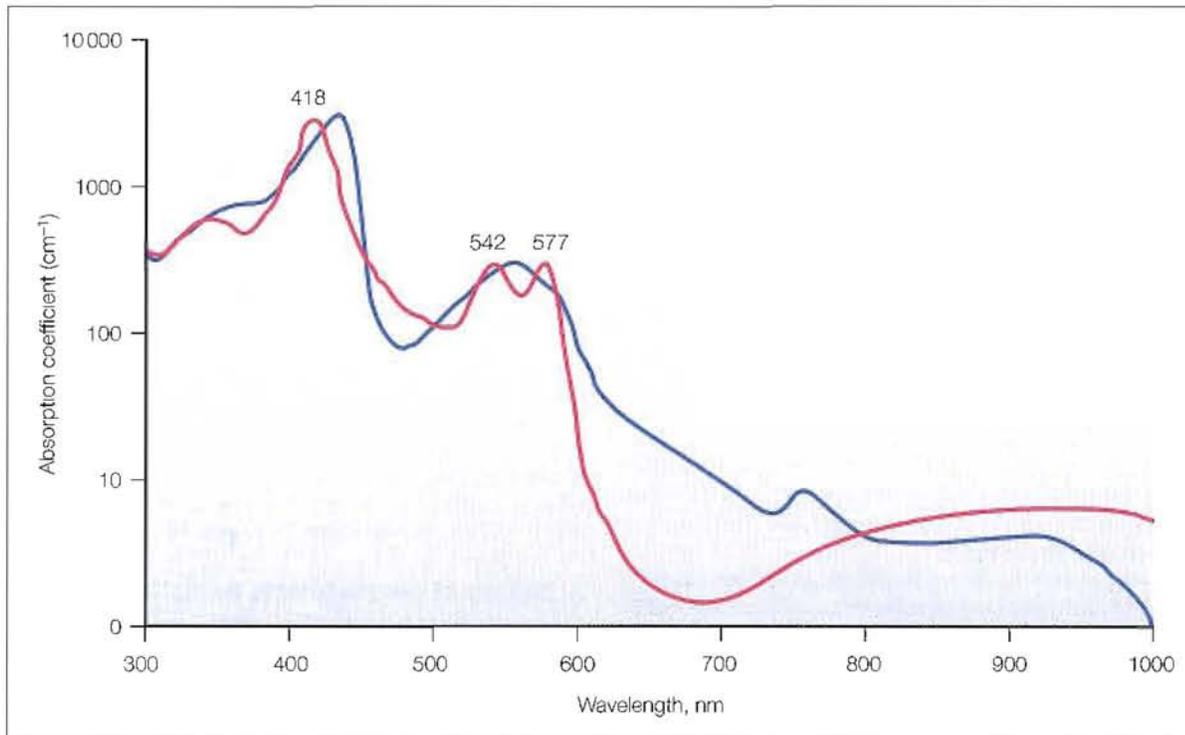


Fig. 1.1 Hemoglobin absorption curve: oxyhemoglobin (red line) and deoxyhemoglobin (blue line)

heavy metal vapor lasers. Large blood vessels with longer thermal relaxation times are also well suited for treatment by these lasers. However, energy is also absorbed by epidermal and dermal melanin and therefore should be restricted to patients of lighter skin types, namely, Fitzpatrick skin types I and II. Patients with darker skin types are at high risk of postinflammatory pigmentary changes and should not be treated with this laser system. Other adverse effects include crusting and blistering.

The introduction of the pulsed dye laser (PDL) in 1986 revolutionized the treatment of vascular lesions. It quickly became the treatment of choice for port wine stains, hemangiomas, and telangiectasias given its safety and efficacy. The first PDL emitted laser light at 577 nm, coinciding with the last peak of the oxyhemoglobin absorption spectrum. By lengthening the wavelength to 585 nm, the PDL gained deeper penetration into the dermis without compromising vascular selectivity. Currently available PDL systems emit a wavelength of 585 or 595 nm with longer pulse durations. Although there is deeper penetration of energy at 595 nm compared to 585 nm, the absorption of oxyhemoglobin is less than at 585 nm. In order to compensate for the decreased absorption, the longer-wavelength PDL (595–600 nm) requires an increase in fluence—energy per unit area, measured in joules/cm²—of 20–50% compared to the 585 nm PDL systems.

Clinical studies of port wine stains treated with the 595 nm PDL have demonstrated excellent clinical effi-

cacy, comparing favorably with the results of the 585 nm PDL, and improving the clearance of resistant port wine stains previously treated with the 585 nm PDL. This effect is further enhanced by cooling systems, which protect the epidermis by chilling the skin prior to treatment. Skin cooling also allows higher energy to be delivered to target vessels and provides anesthetic relief during treatment.

When the thermal relaxation time of blood vessels in port wine stains was determined to be between 1 and 10 ms, modified PDL systems with pulse durations of 1.5 ms were designed. These systems permitted the use of higher fluences with lower peak energies, thereby decreasing adverse effects while enhancing efficacy. Most modern PDL systems use a wavelength of 595 nm and have variable pulse durations between 0.45 and 40 ms. Thus, operators can choose shorter pulse durations for small-vessel lesions, such as port wine stains, or longer pulse durations for larger telangiectasias. As will be discussed below, utilizing pulse durations of 6–10 ms allows for effective treatment of facial telangiectasias without purpura.

A limiting factor of PDL is the depth of penetration. Histologic studies have shown poor coagulation of dermal vessels beyond 1.16 mm in depth after exposure to the 585 nm PDL beam. The 595 nm wavelength does penetrate slightly—albeit frequently not sufficiently—deeper.

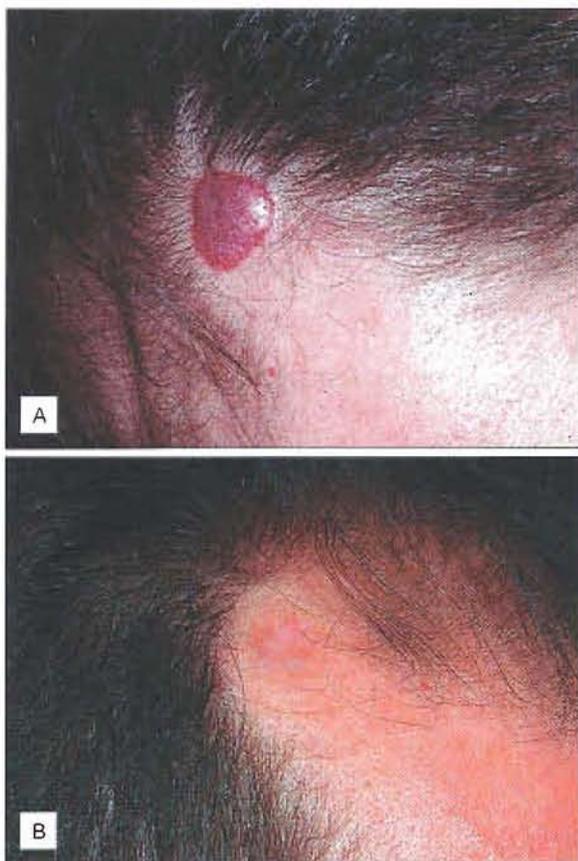


Fig. 1.2 Hemangioma. (A) Pretreatment. (B) Post-treatment with PDL

The Nd:YAG laser is available as continuous or pulsed beams and can penetrate to a depth of 4–6 mm to coagulate deeper, larger vessels. Continuous wave Nd:YAG lasers cause shrinkage of hemangiomas primarily by non-specific thermal damage and have an inherent risk of scarring. They have been used to treat mixed or deep hemangiomas. Deeper hemangiomas have been reported to reduce by 50% after one treatment. In one study utilizing a long-pulsed Nd:YAG laser system, 13 hemangiomas were treated once, resulting in 50–99% resolution in all lesions. Unfortunately, the precise details of the type and locations of these lesions were not specified.

Interstitial Nd:YAG laser therapy, in which a probe is inserted into the hemangioma, has been reported to be helpful, especially for deep subcutaneous hemangiomas. However, the high risk of scarring makes it a less favorable approach for most hemangiomas.

IPL systems are sources of noncoherent polychromatic light with wavelengths ranging between 420 and 1400 nm. Polychromatic light can target superficial vessels with the shorter wavelengths while penetrating to deeper vessels with the longer wavelengths. Long pulse durations—ranging from 1 to 100 ms—enable delivery of energy with

uniform heating of the vessels. Single, double, or triple pulses can be emitted with variable intervals between pulses to allow the epidermis and smaller vessels to cool down. This leads to selective thermal injury, as heat is concentrated in the deeper, larger vessels. The large spot sizes typically used with the IPL systems enhance the penetration of light with decreased scatter. As a result, hemangiomas that have been resistant to other treatments, including deep lesions, have been reported to respond with this system. Thus, between 75% and 100% clearance has been reported after one to four treatments. The disadvantages of these systems may include a greater number of treatment sessions necessary for clearance, a higher potential for adverse effects including scarring, and a higher degree of discomfort during the procedure. It should also be noted that due to differences in spot sizes, spectral output, beam geometry, and device calibration, IPL parameters vary significantly between systems. Practitioners are encouraged to consult the individual system's manual for the recommended settings.

Prior to treatment, patients and their families should be informed that laser and light based treatment options, especially PDL, may be associated with post-treatment purpura, which typically lasts 7–10 days (see Box 1.2). Multiple treatments are required, usually at 2–3-week intervals. Faster growing lesions may need more frequent sessions. The degree of improvement after each treatment can be variable. If, however, the hemangioma continues to proliferate rapidly after several treatment sessions, alternative therapeutic options should be explored.

• Port wine stains (capillary vascular malformations)

Vascular malformations may be localized or diffuse and occur as errors of embryonic development. They are subdivided into arterial, arteriovenous, venous, capillary, and lymphatic malformations. Capillary malformations (port wine stains) and lymphatic malformations are usually noticed at birth, whereas venous malformations can appear congenitally or become apparent during adulthood. Arterial and arteriovenous malformations often manifest during hormonal fluctuations such as pregnancy or puberty.

Port wine stain (nevus flammeus) is a type of capillary vascular malformation that presents at birth and does not resolve. Occurring in 0.3% of the population, port wine stains have an equal incidence in males and females. They are composed of ectatic vessels in the papillary dermis and can vary in size from a few millimeters in diameter to greater than 50% of the body surface area. Any part of the body may be affected, but the head and neck region is the most common site of involvement. Fifty per cent of port wine stains affecting the face are restricted to one of the three trigeminal sensory regions, most commonly in the V2 distribution. Extensive cutaneous involvement by a port wine stain increases the likelihood of underlying neurological, ophthalmologic, or other systemic abnormalities.

Table 1.4 Nd:YAG lasers commonly used in the treatment of vascular lesions

	Manufacturer	Wavelength (nm)	Pulse duration (ms)	Spot size (mm)	Fluence (J/cm ²)	Cooling
Aura	Iridex	532	1–50	1–5	1–240	None
DioLite	Iridex	532	10–50	0.2,0.5,0.7,1,1.4	0.1–950	None
Gemini	Iridex	532/1064	10–100	1–5,10	1–990	Contact
Lyra	Iridex	1064	20–100	1.5,3,5,10	5–200	Contact
CoolGlide	Cutera	1064	20–100	3,5,7,10	1–300	Contact
Varia	CoolTouch	1064	300–500	2,4,6,8	1–500	Cryogen (pre and post)
GentleYAG	Candela	1064	0.25–300	1.5–18	1–500	Cryogen
Cynergy	Cynosure	1064/595 (PDL)	15–40	3,5,7,10,12,15	20–80	Air

Table 1.5 IPL devices commonly used in the treatment of vascular lesions

	Manufacturer	Spectrum (nm)	Optical filters	Fluence (J/cm ²)	Pulse sequence	Pulse duration (ms)	Spot size (mm ²)
IPL Quantum	Lumenis	560–1200	560,590,640	15–45	2,3	6–26	272
Lumenis One	Lumenis	515–1200	515/560/590/615/640/695/755	10–40	1–3	3–100	120,525
StarLux LuxG	Palomar	500–670 and 870–1400	Preset with handpiece	22–60	1	10–200	150
Clareon VR	Novalis Medical	500–610 and 740–1200	Preset with handpiece	15–35	2	30,50,70	528
PhotoLight/Photosilk Plus	Cynosure	560–950	500,560,650 (as handpieces)	1.5–16	1	5–35	210,460, 828
BBL	Sciton	420–1400	420/515/560/590/640/695	5–30	1–3	5–150	225,675

Due in part to their large spot sizes, IPL systems are helpful in treating facial telangiectasias and poikiloderma of Civatte, especially when it extends over a large area (Table 1.5). In a large study of 518 patients, 88% achieved clearance of 75–100%, with most patients requiring 1–3 treatment sessions. In a separate study, patients with poikiloderma of Civatte on the neck experienced an improvement of 50–75% after an average of 2.8 treatment sessions with IPL source. New IPL systems incorporate sophisticated filtering systems that allow for much more selective targeting of vascular structures. These new IPL devices have been shown to be as effective as PDL in the treatment of facial telangiectasia.

Reticular veins remain one of the more challenging vascular lesions and multiple treatment sessions are generally necessary. As previously noted, the periarial region is another location resistant to treatment. Telangiectasias in

this area require multiple treatments and may recur in the future.

OTHER VASCULAR LESIONS

• Cherry angiomas

Cherry angiomas are well-circumscribed, small, red papules composed of vascular ectasias, which typically appear in early adulthood and tend to increase with age. They may occur anywhere on the body, especially on the abdomen and respond very well to most vascular lasers.

Treatment options for this benign proliferation include electrocautery, shave excision, and laser therapy. A variety of lasers can be used including the KTP, PDL, argon, continuous wave dye, and Nd:YAG lasers. With the PDL, purpuric doses are necessary and patients should be

Jeffrey T.S. Hsu, Ashish Bhatia, Robert Weiss

INTRODUCTION

Venulectasia on legs occurs in 29–41% of women and 6–15% of men in the United States. Lasers have been used to treat leg veins since the 1970s, although laser surgeons did not achieve acceptable results until the advent of the pulsed dye laser in the 1980s. In the 1990s, the development of lasers with longer wavelengths and longer pulse durations ensured a consistent outcome and branded a niche for lasers in the treatment of leg veins. As with other indications, laser treatment of leg veins relies on the principle of photothermolysis. The ideal laser must have the following characteristics: (i) a wavelength that is better absorbed by hemoglobin than the surrounding chromophores; (ii) penetration to the depth of the target blood vessel; (iii) sufficient energy to damage the blood vessel without injuring the epidermis; and (iv) a pulse duration to slowly coagulate the vessel without damaging the surrounding tissue.

• Patient evaluation

When larger truncal varicose veins are present, the associated telangiectases cannot be successfully treated without addressing the underlying hydrostatic pressure. In cases of great saphenous vein (GSV) and small saphenous vein (SSV) incompetence, surgical techniques or endovenous ablative techniques may be required. Ambulatory phlebectomy allows treatment of virtually all large varicose veins, while compression sclerotherapy can be used to treat large varicose veins and reticular varicose veins. Only then should the telangiectases be treated with sclerotherapy or with laser or light based devices. However, in patients with only isolated telangiectases without pressure problems, sclerotherapy or laser/light therapy may be used primarily.

Physicians must diagnose the origin of the reverse flow. Physical examination is necessary to determine whether the surface telangiectases originate from a deeper source of incompetence. One must have adequate knowledge of the basic superficial venous anatomy and proper diagnostic tools. Important superficial venous systems include the great saphenous vein (GSV), the small saphenous vein (SSV), and the lateral subdermic venous system (LSVS) (Figs 2.1–2.3). Younger patients usually present with tel-

angiectatic webs originating from reflux in the lateral venous system. When there is a positive family history of large varicose veins, the physician must consider reflux from the GSV or SSV.

• Patient expectations

Aside from proper counseling regarding the possible side effects, such as dyspigmentation, matting, or even ulceration and scarring, patients must also understand that perfection is not possible, that there will always be veins, albeit very tiny veins, that may not resolve. Once the patient understands the nature and risk of treatment, digital images are recorded. These images are indispensable tools to evaluate treatment progress, and more importantly, to document improvement for the patient. All too often, patients fail to recognize partial resolution. Comparison of the 'before' and 'after' images will enhance patient satisfaction. Patients should also understand that the treatment of leg veins is not a case of instant gratification. When using laser and light devices, 8–12 weeks may be the optimal interval between treatments. Often telangiectases will ultimately improve despite no signs of change within the initial 2 weeks.

• Diagnostic tools

While most physicians are familiar with tools to diagnose cardiac disease, few are familiar with the equivalent tools when it comes to venous disease (Table 2.1). The handheld Doppler is the most common and cost effective tool to detect reflux in the superficial venous system (Fig. 2.4). The optimal frequencies for examining superficial vessels (less than 2 cm below the skin) are 8–10 MHz, while deeper vessels require frequencies of 4–5 MHz. Manual compression of the calf generates an audible signal of flow. When compression is released, reverse flow ensues, but ceases within 0.5–1.0 s when competent valves close. However, when the valves are incompetent, flow continues.

Plethysmography measures pressure or volume changes (Fig. 2.5). Photoplethysmography is the most common variant, taking advantage of hemoglobin absorption of light to calculate change in blood volume. The patient is first asked to dorsiflex several times to allow the calf muscle

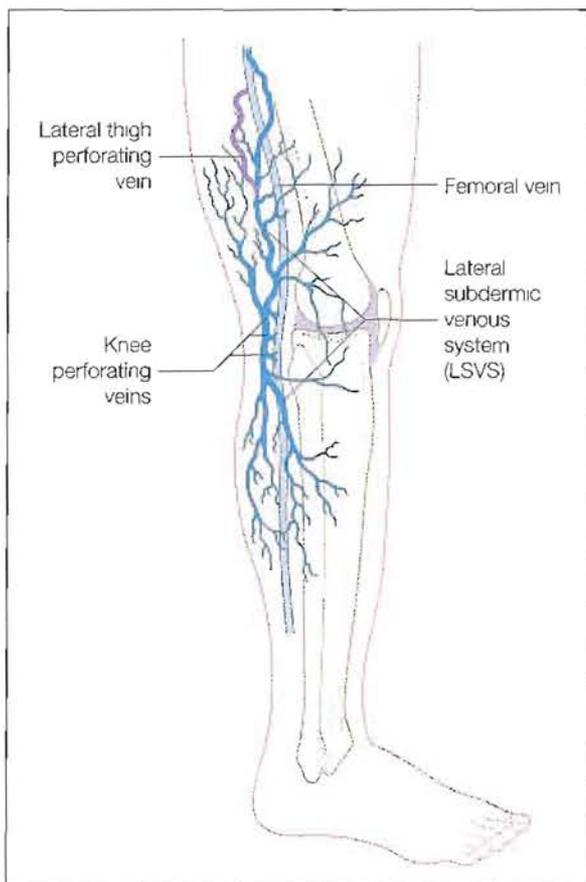


Fig. 2.3 Lateral subdermic venous system

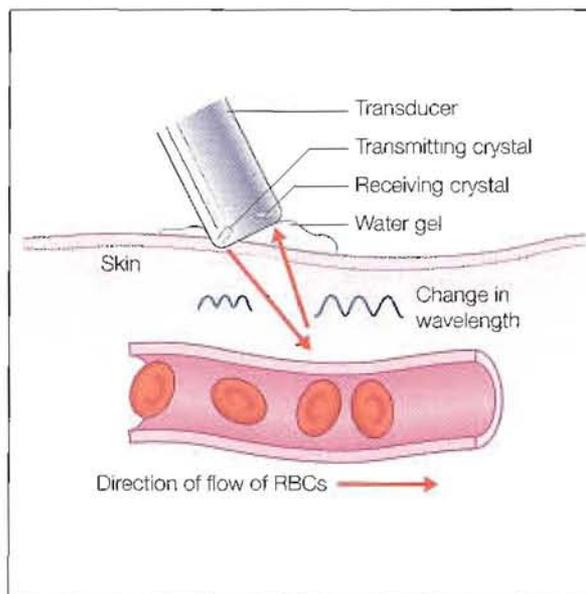


Fig. 2.4 Handheld Doppler

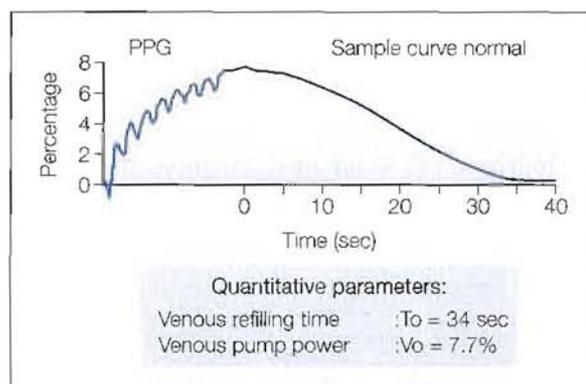


Fig. 2.5 Plethysmography

Table 2.1 Analogous tools in the evaluation of the heart and leg veins

Heart	Leg vein
Stethoscope	Handheld Doppler
Electrocardiogram	Photoplethysmography
Echocardiogram	Duplex ultrasound

cial vessels are connected to deeper reticular veins, which often require adjunctive treatment such as sclerotherapy. The choice of wavelength and pulse duration is related to the type and size of the vessels treated. One may compare the target vessel to a needle of known gauge to estimate the vessel size (Table 2.2). In general, longer wavelengths allow for deeper penetration, and longer pulse durations are needed to slowly heat vessels with larger diameters. Larger spot sizes penetrate deeper and optimize fluence delivery to the target. Another advantage of the longer wavelength laser is the dynamic nature of absorption peaks as a function of vessel size and depth.

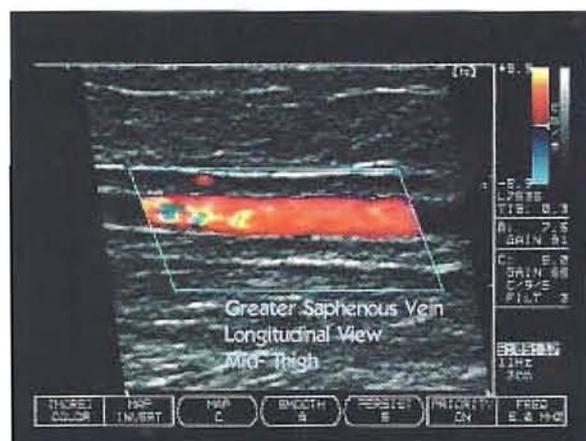


Fig. 2.6 Duplex ultrasound

Box 2.1 KTP lasers

- ❖ Pulsed KTP (532 nm), 1–200 ms)
- ❖ Viridis (Quantel)
- ❖ Diolite (Iridex)
- ❖ Ultrawave (Quanta)

spot sizes and pulse durations of 10 ms or less were disappointing. The outcomes were much more favorable with larger spot sizes of 3–5 mm, and longer pulse durations of 10–50 ms at fluences of 12–20 J/cm².

The disadvantages of the KTP laser are the inadequate penetration and also heavy absorption by melanin, both properties of the 532 nm wavelength. Patients with darker or tanned skin experience a high risk of dyspigmentation. Cooling is especially important in these cases to protect the epidermis. Given these limitations, the pulsed KTP is best suited for small, superficial telangiectases in skin types I–III. Treatment is technique dependent. Multiple passes with adequate time and cooling in between passes are often needed to achieve the clinical endpoints of vessel spasm or intravascular coagulation, which are associated with better results. However, pulse stacking (i.e. one pulse immediately followed by another at the same location) should be avoided, as this may lead to 'grooving' or scarring.

PULSED DYE LASER

The original pulsed dye laser (PDL) at 585 nm and 450 μs pulse duration was successful in treating port wine stains, which are composed of very superficial (average depth of 0.46 mm) and minute 100 μm vessels. However, they proved to be unsatisfactory in treating leg veins. The short pulse duration is effective only for superficial fine vessels of 0.1 mm or less. Based on the theory of selective photothermolysis, the ideal pulsed duration for destruction of leg veins 0.1 mm to several millimeters in diameter is in the 1–50 ms range. The high energy delivered in the short time frame leads to rupture of the vessels with purpura and hemosiderin deposit, seen clinically as long term hyperpigmentation. Polla et al used this laser to achieve 75% clearing in only 15% of telangiectases treated and found little if any improvement in 73% of the vessels. As expected, the vessels that responded were minute superficial telangiectases. Furthermore, 50% of the patients experienced dyspigmentation. However, when used appropriately, the results can be favorable. In another study, superficial red telangiectases of 0.2 mm or less and telangiectatic matting induced by sclerotherapy underwent treatment with the 450 μs PDL, using 5 mm spot and fluence of 6.5–8 J/cm², followed by compression for 72 hours. Seventy-six per cent of linear telangiectases cleared completely within 4 months of a single treatment. Transient hyperpigmentation developed in 10% of the subjects.

The advent of long pulsed dye laser enabled treatment beyond superficial tiny telangiectases. Several devices

Table 2.3 Pulsed dye lasers (some are no longer manufactured)

Pulsed dye (585, 590, 595, 600 nm)	Pulse duration (ms)
LV (Cynosure)	0.45
ScleroPlus (Candela)	1.5
PhotoGenica LVS (Cynosure)	1.5
Vbeam (Candela)	0.5–40
PhotoGenica V-Star (Cynosure)	0.5–40

using rhodamine dye are capable of pulse durations ranging from 1.5 to 40 ms (Table 2.3). The wavelengths range from 585 to 600 nm, which has better penetration to target deeper vessels. However, at these wavelengths, melanin absorption is still significant. The risk for dyspigmentation can be high without proper epidermal cooling.

Several studies with the 1.5 ms PDL revealed variable results. A single treatment with a 585 nm PDL on vessels up to 1 mm in size, using a 3 × 7 mm elliptical handpiece and up to 18 J/cm² in fluences, yielded 67% clearing. Another study using the 595 nm PDL showed slightly better results. Both studies reported side effects including crusting and dyspigmentation. Reichert showed more success when the areas treated were first cleared of refluxing reticular veins. In this study, telangiectases of 0.1–1 mm were treated with the 1.5 ms PDL at wavelengths of 585–600 nm. Total clearing was observed in vessels less than 0.5 mm in diameter after one or two treatments, while 80% clearing was achieved in vessels 0.5–1.0 mm after four treatments. Transient dyspigmentation was found in 50% of subjects. Bernstein examined the newest generation of ultra-long pulse 595 nm PDL (40 ms). In skin types I–II, three treatments at 6 week intervals using average fluence of 20.4 J/cm² and 3 × 10 mm spot size, 60% of the subjects yielded moderate or better results objectively. Vessels up to 1.5 mm were included in this study. However, dyspigmentation remains a significant side effect, especially at higher fluences (Fig. 2.10).

LONG PULSED ALEXANDRITE LASER

Several other pulsed lasers have successfully taken advantage of the small peak of hemoglobin absorption in the 700–900 nm range. They include long pulsed alexandrite, diode lasers, and long pulsed Nd:YAG lasers. The longer wavelengths afford deeper penetration to treat larger caliber veins and relative low absorption by melanin.

With wavelengths of 755 nm, alexandrite lasers are capable of penetrating 2–3 mm into the skin (Table 2.4). Coupled with a pulse duration up to 20 ms, these lasers have treated telangiectases with some success. McDaniel et al reported 63% overall clearing after three treatments.



Fig. 2.10 Treatment with PDL

Table 2.4 Alexandrite lasers (some are no longer manufactured)

Alexandrite laser (755 nm)	Pulse duration (ms)
EpiTouch (Lumenis)	2–40
Ultrawave 755 (Quanta)	up to 100
GentleLaser (Candela)	3
Apogee (Cynosure)	up to 300

Table 2.5 Diode lasers (some are no longer manufactured)

Diode laser (800, 810, 940 nm)	Pulse duration (ms)
VariLite (Iridex)	5–100
Soprano (Alma)	10–1350
Velure (Lasering)	10–1000
LightSheer (Lumenis)	5–400

Medium sized vessels (0.4–1 mm) responded best, followed by larger vessels (1–3 mm). Vessels smaller than 0.3 mm responded poorly, highlighting the need for shorter pulse durations to target these tiny vessels. The optimal parameter in the study was a pulse duration of 5 ms and a fluence of 20 J/cm². Another study showed up to 75% clearing of two thirds of all veins (0.3–2 mm) with a single treatment, using 8 mm spot, 3 ms pulse, at a fluence of 60–80 J/cm². Transient hyperpigmentation occurred in a third of the treatment sites.

DIODE LASERS

At 800–930 nm, the diode lasers are similar to alexandrite lasers in their ability to penetrate deeper and target larger reticular veins, and to match the tertiary hemoglobin absorption peak at approximately 900 nm with relatively less interference from melanin (Table 2.5). Using an 800 nm diode array laser, Dierickx saw more than 75% clearing in two thirds of veins after three treatments, with 5–30 ms pulses and 15–40 J/cm² in fluence. The 940 nm wavelength penetrates about 3 mm into the skin, which is capable of reaching most small veins up to 1 mm in diameter when coupled with fluences of 250–400 J/cm². Theoretically, red telangiectasias contain proportionally higher oxyhemoglobin and therefore should respond more favor-

ably. Kaudewitz et al report short term results of more than 50% clearance of vessels less than 1 mm in 76% of patients and 75–100% clearance in 46% of patients after one laser pass. Interestingly, 1 year follow-up demonstrated continued improvement, with 75% of the patients achieving 75–100% clearance. The mechanism of this process is yet undetermined. Based on this observation, the patients should be reassured that results may continue to improve over time, and that additional treatment may be unnecessary. Transient dyspigmentation and telangiectatic matting were observed in some patients, but cleared within 1 year. Most recently, the Spanish team of Trelles et al used a 800 nm diode device, yielding 70% clearance rate. Using aggressive parameters with fluence up to 336 J/cm², 50 ms pulse duration, 3 mm spot, and 5–8 stacked pulses, the investigators saw clearance even in veins up to 3–4 mm in size.

LONG PULSED Nd:YAG 1064 NM LASER

The development of long pulsed Nd:YAG lasers was an exciting milestone in the treatment of leg veins (Table 2.6). The long wavelength affords even more penetration into the skin to target deep, relatively large caliber vessels. The Nd:YAG laser has maximum penetration of 3 mm, making it ideal for the destruction of large vessels in the

3

Pigmented Lesions and Tattoos

Ronald G. Wheeland, Ellen S. Marmur

INTRODUCTION

This chapter will cover laser and intense pulsed light treatment options for removing or lightening tattoos and benign pigmented lesions. Frequently, the same laser may be used for treating both benign pigmented lesions and tattoos, however the management of each entity is different. Traditional laser systems for the removal of pigmentation and tattoos are classified as the Q-switched lasers. Newer systems such as the intense pulsed light (also covered in Chapter 9) and the fractional lasers can be used for the removal of benign pigmented lesions and, less frequently, for the enhanced removal of tattoos.

This chapter will discuss the mechanisms of the removal of pigment, optimal patient selection, realistic benefits, and treatment algorithms. The chapter will provide treatment pearls, important tips on the management of side effects, and advanced techniques.

• Tattoo removal

In tattoo removal, the target for the laser light consists of small particles of tattoo ink which are found either within macrophages or scattered extracellularly throughout the dermis. For treating benign pigmented lesions, the laser primarily targets melanin as its chromophore. However, unlike laser hair removal, in which the large melanin-laden unit of the hair follicle is the target, treatment of benign pigmented lesions relies upon targeting small particles of melanin found within melanocytes, keratinocytes or dermal macrophages. The mechanism of action is thought to be principally from photomechanical (photoacoustic) injury. The laser energy essentially explodes the target ink into smaller particles that are scavenged by dermal macrophages. The targets in both tattoos and benign pigmented lesions are quite small in size. As a result, using the concept of thermal relaxation time to minimize collateral thermal injury to the normal surrounding tissue, the pulses of light required for effective treatment must be very short. Thus, Q-switched lasers with pulse durations in the nanosecond range are the mainstay of therapy for both benign pigmented lesions and tattoos. Most of these lasers have pre-set, nonadjustable pulse durations that cannot be changed by the operator. The recent devel-

opment of lasers, like the titanium:sapphire laser, with even shorter pulse durations than the Q-switched lasers (in the picosecond range), offers the potential for further reducing unwanted injury and simultaneously improving the results.

Fractional photothermolysis is a new class of technology using arrays of thermal zones to stimulate remodeling of the skin. The prototype is a diode laser emitting a wavelength of 1500 nm targeting water as a nonspecific chromophore. Newer systems use the 1550 nm erbium fiber. Unlike all other laser systems, fractional systems emit energy in a microscopic pattern with untreated zones in between. It has been described as a pegboard pattern where columns of laser energy enter the skin. The untreated zones serve as both a source of rejuvenative cells and as a natural cooling system where heat dissipates. Cooling is also achieved using air cooling. Two variables can be adjusted to achieve different therapeutic effects: density of microthermal zones and energy. Immunohistochemical studies show that by changing these variables, different depths of treatment occur. Pigmentation is removed in two ways. One is similar to the mechanism described using the Q-switched lasers—by dermal melanophages. The second is novel. Pigment is shed from the epidermis within seven days of treatment through microscopic epidermal necrotic debris (MENDS).

The discussion of tattoo removal applies equally well to the treatment of decorative tattoos applied by professional and nonprofessional personnel, cosmetic tattoos for enhancing the lips, brows or areolae, traumatic tattoos resulting from explosions, motor vehicle accidents and other types of injuries as well as medical tattoos for radiation therapy of internal malignancies. [See the Advanced Topic section at the end of this chapter for a discussion of cosmetic and flesh-toned tattoos.] The discussion of treatment of benign pigmented lesions will be limited to solar lentigines, nevi of Ota and Ito, and café au lait macules (CALMs). This limitation on discussing laser treatment for other pigmented lesions, like melasma, nevocellular nevi and lentigo maligna, is warranted as the efficacy of laser therapy for these lesions has not yet been firmly established. Fractional laser systems have shown success with melasma. Despite the fact that some of these lesions have been successfully treated with lasers, the



Fig. 3.1 Black amateur tattoo on the chest seen: pre-operatively (A), immediately following treatment with the Q-switched Nd:YAG laser showing punctate bleeding (B)

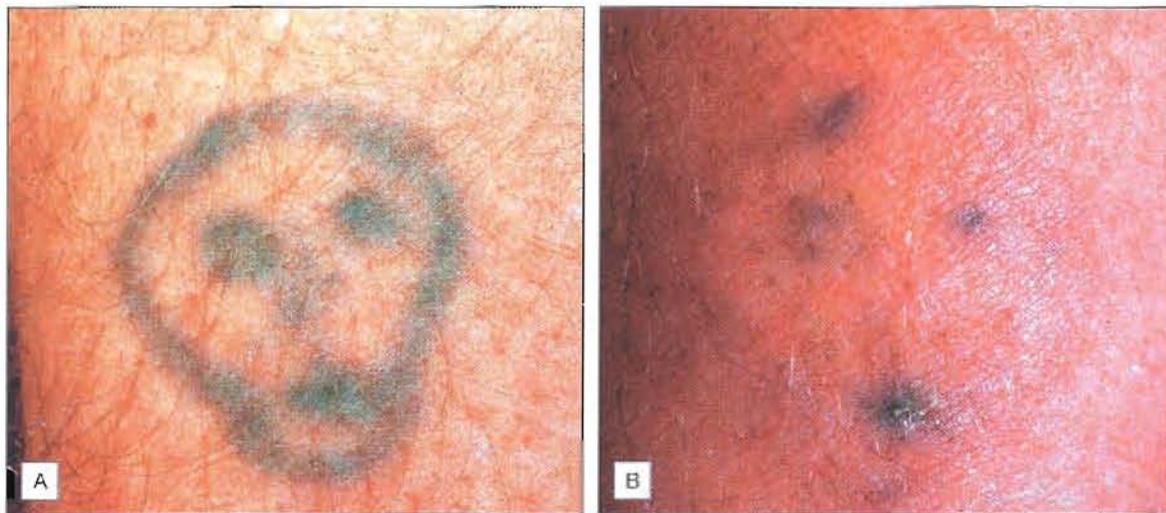


Fig. 3.2 Black amateur tattoo on the arm seen: pre-operatively (A) and 6 weeks later following a single treatment with the Q-switched ruby laser (B) with only small speckles of ink remaining

tremendous variability in the responses does not allow traditional laser therapy to be considered as the standard of care for such lesions. [See the Further Reading section for articles on laser therapy for nevi.] Melasma is still best treated by combination therapy. It is also extremely important to note that laser therapy has no role in the treatment of invasive melanoma.

Several studies have looked at the potential carcinogenic effect of laser stimulation of melanocytes. All studies have shown no significant increase in DNA markers seen with carcinogenesis. At this time it is considered safe to use lasers on pigmented lesions with no increased risk of skin cancer.

• Patient selection for tattoo removal

The growing trend of decorative tattooing among teens and young adults has led to an increase in the number of

patients requesting tattoo removal. Most tattoos today are professional tattoos which are more difficult to remove than the amateur variety (Figs 3.1–3.4) since they often consist of multiple colors of ink placed at different depths within the dermis. In addition, there is no regulation of tattoo inks and many different compounds that all may respond differently to laser treatment have been used to create the same clinical color. For that reason, variable responses can be anticipated, making the establishment of realistic expectations for each patient of paramount importance in order to achieve a result with which the patient will be satisfied. Multiple treatments, performed at 4–6 week intervals, are normally required and may vary anywhere from five to as many as 20 in number. Furthermore, even after numerous treatments, some tattoo pigment may still remain (Fig. 3.5).

Treatment of patients with darker skin (Fitzpatrick skin types IV–VI) or with tans must be done with caution

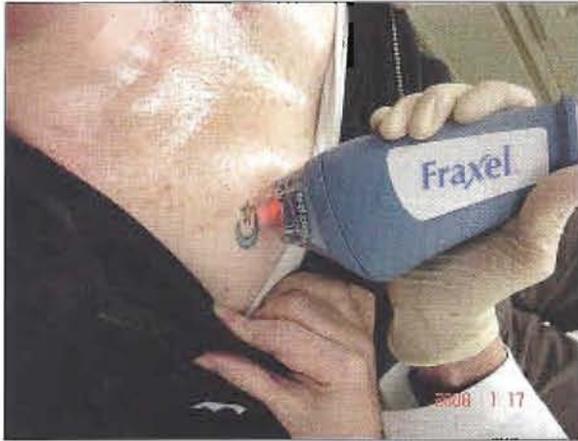


Fig. 3.8 Fractional photothermolysis

into smaller fragments, facilitating more rapid removal by macrophages, and in some cases may allow complete removal of the tattoo. Conversely, recently applied, multicolored tattoos in darker-skinned patients can be very difficult to remove completely with traditional laser systems and treatment should be performed only after the patient fully understands the potential for pigmentary alterations or scarring.

Fractional photothermolysis may allow for tattoo removal in darker skin types without the interference of epidermal pigment seen with Q-switched lasers. Microthermal zones may break up the pigment in the dermis nonselectively while bypassing the epidermis. Future studies will be necessary to establish these guidelines. Generally, treatments are done every 4–6 weeks for at least three sessions (Fig. 3.8).

• Patient selection for benign pigmented lesion removal

A primary consideration in the treatment of benign pigmented lesions is establishing the correct diagnosis prior to initiating treatment. A biopsy must be performed if melanoma or any other malignancy is in the differential diagnosis. For example, a thin shave biopsy of the edge of large macular pigmented patches on the cheeks should be done to rule out lentigo maligna, pigmented squamous cell carcinoma, or pigmented superficial basal cell carcinoma.

As with tattoo removal, there is a significant risk of pigmentary alteration and scarring in darker-skinned patients (Fitzpatrick skin types IV–VI) undergoing benign pigmented lesion removal. Care must be taken to avoid such risk of complications in these patients.

• Expected benefits of pigmented lesion treatment

Lentigines can usually be removed completely in one to three treatments (Figs 3.9–3.11). However, CALMs



Fig. 3.9 Multiple small brown lentigines on the back of the hand seen: pre-operatively (A), with nearly complete resolution 6 weeks after a single treatment with the Q-switched Nd:YAG laser (B)

(Fig. 3.12), postinflammatory hyperpigmentation (Fig. 3.13), and nevi of Ota (Fig. 3.14) and Ito may require multiple treatments, perhaps as many as five to 10 in number, and some cannot be completely removed with any number of treatments. Nevus of Ota patients should be made aware that the scleral component of the lesion is not treatable with current technology.

The results of laser treatment of benign pigmented lesions are generally permanent. However, due to the relationship between chronic ultraviolet light (UVL) exposure and the later development of lentigines, patients should be told that in spite of an excellent response new lesions may develop over a period of years after the treatment has been successful. This is especially true if the patient is not careful about protecting their skin by using sunscreens or clothing when outside. [See Tables 3.1 and 3.2 for information on clearance and improvement rates for pigmented lesions treated with laser and IPL therapy.] The treatment of the lentigines found on the mucosal surfaces in Peutz–Jeghers syndrome may produce equally good results (Fig. 3.15) as those found on the skin.

Costs: Before initiating laser treatment of benign pigmented lesions, it is very important to discuss with the patient the cost of treatment, as the removal of lentigines is generally not covered by health insurance while some insurance plans may cover laser treatment of CALMs, nevi

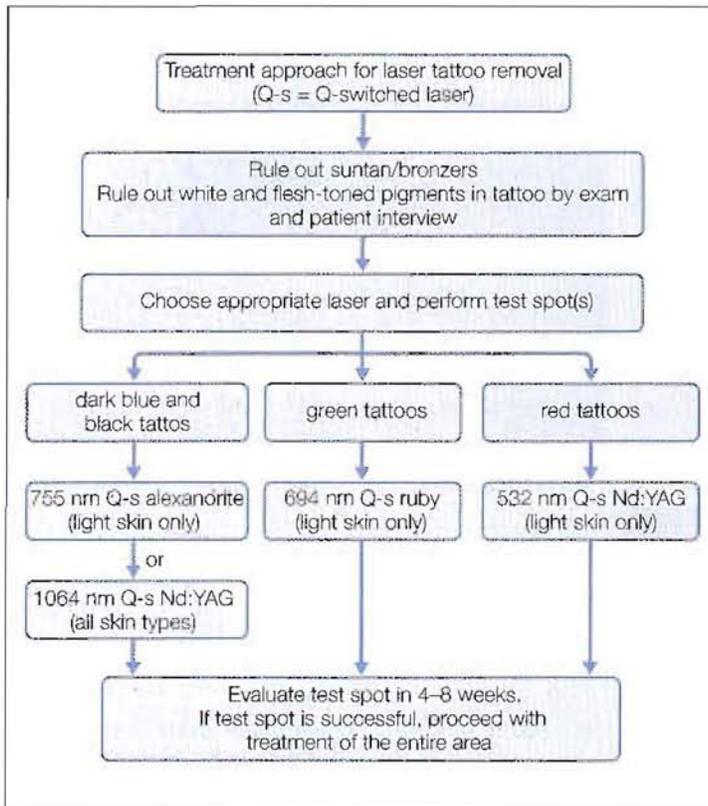


Fig. 3.22 Treatment approach for laser tattoo removal

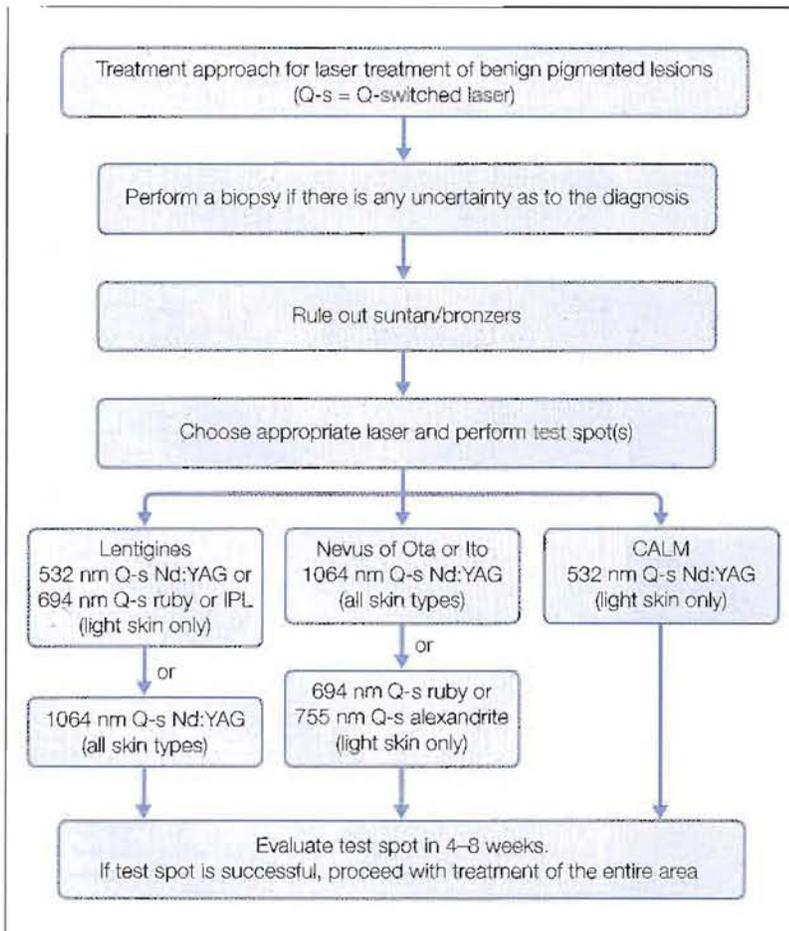


Fig. 3.23 Treatment approach for laser treatment of benign pigmented lesions

Box 3.2 Pigmented lesion patient history**PIGMENTED LESION PATIENT HISTORY**

How long has the lesion(s) been present?
 Has a biopsy of the lesion been performed?
 Has it grown, bled without injury, developed symptoms like itching or changed color?
 Does the patient or any blood relative have a history of melanoma?
 Has the patient attempted to remove or alter the lesion previously? If so, how was this attempted?
 Has patient used oral retinoids within the past year?
 Is there a personal history of herpes infection or cold sores?
 Has the patient previously developed keloids or abnormal scars after prior surgery or injury?
 Does the patient currently actively pursue a tan or use a tanning bed or bronzer?
 What is the patient's Fitzpatrick skin type?



Fig. 3.26 Red cosmetic tattooing of the vermilion borders is present and should represent danger since hyperpigmentation or even blackening of this tattoo can occur following treatment with any of the Q-switched lasers [Note: This patient was not treated after having been consulted on the risks and complications.]

lasers. Thus, the Q-switched Nd:YAG laser operated at a wavelength of 1064 nm is the treatment of choice for dark blue and black tattoos in darker-skinned patients.

- **Patients and equipment for red tattoo treatment**

The optimal laser wavelength for removing red tattoo ink is 532 nm. Thus, the Q-switched, frequency-doubled Nd:YAG laser operated at a wavelength of 532 nm is the best laser for red tattoo ink removal. This wavelength can cause both hyperpigmentation (Fig. 3.26) and hypopigmentation in darker-skinned patients so treatment should be limited to light-skinned (type I–III) patients. [See Advanced Topics section for treatment options for darker-skinned patients.]

- **Patients and equipment for green tattoo treatment**

The optimal laser wavelength for removing green tattoo ink is 694 nm. Thus, the Q-switched ruby laser operated at a wavelength of 694 nm is the best laser for green tattoo ink removal. Like the 532 nm Nd:YAG, this wavelength can cause pigmentary alterations which may make green tattoos difficult to treat (Figs 3.16, 3.17) in dark-skinned patients. [See Advanced Topics section.]

- **Patients and equipment for lentigo treatment**

For light-skinned patients, the Q-switched, frequency-doubled Nd:YAG laser operated at a wavelength of 532 nm is usually the safest and most effective choice available. However, the ruby laser operated at a wavelength of 694 nm can also be very effective for treating lentigines. Intense pulsed light (IPL) systems can also be effective but somewhat less predictable than the Q-switched lasers due to the wider range of wavelengths

being used. Most often the removal of lentigines by the IPL is an added benefit that occurs during full face photorejuvenation to correct rhytides and poor skin turgor from chronic sunlight exposure. Because the light from the IPL must traverse the epidermis in order to stimulate the dermal fibroblasts in photorejuvenation, the focal melanin deposits that account clinically for the appearance of lentigines are treated as well. These lesions generally immediately turn a slightly darker chocolate brown color and then peel off in 7–10 days. Because the rejuvenation aspects of IPL treatments generally take 6–8 weeks to be seen, much of the early patient enthusiasm seen with these treatments is the eradication of the lentigines and not the reduction in rhytides. In darker-skinned patients, the Q-switched Nd:YAG laser operated at 1064 nm laser is usually the safest choice and also very effective.

- **Patients and equipment for nevus of Ota and Ito treatment**

In darker-skinned (type IV–VI) patients, the Q-switched Nd:YAG laser at 1064 nm is usually the safest laser to lighten a nevus of Ota or a nevus of Ito. In lighter-skinned patients, Q-switched ruby laser at 694 nm and Q-switched alexandrite laser at 755 nm can also be used. It is important to inform patients that there is currently no effective treatment for the scleral pigmentation of nevus of Ota and that a corneal protective eye shield must be placed on the surface of the cornea using topical anesthesia to protect the globe if the periorbital area or eyelids are being treated.

- **Patients and equipment for café au lait macule (CALM) treatment**

Green light from the frequency-doubled, Q-switched Nd:YAG laser at 532 nm is often the best choice for

Keyvan Nouri, Sean W. Lanigan, Maria Patricia Rivas,
Voraphol Vejjabhinanta

INTRODUCTION

• The problem being treated

Scars are ubiquitous and may be caused by surgical procedures, burns, trauma, or inflammation. Epithelial disruption unleashes a cascade of wound healing mechanisms that ultimately result in wound closure and scarring. A flat, flexible scar is the product of a normal wound healing process.

The wound healing process may be divided into three stages: inflammation, proliferation, and remodeling. The inflammation phase starts once the injury has occurred along with activation of the clotting and complement cascade. The release of chemotactic factors (i.e. prostaglandins, complement factors, IL-1, etc.) stimulates the migration of inflammatory cells such as neutrophils and macrophages. These cells initiate the debridement of the wound, and macrophages release cytokines and growth factors such as transforming growth factors (TGF- β), and platelet derived growth factors (PDGF), among others, leading to the formation of the provisional wound matrix. The proliferation stage is characterized by the migration of fibroblasts, endothelial cells, and keratinocytes to the wound site. Fibroblasts play a major role in the formation of the extracellular matrix composed of collagens III and I, fibronectin, elastin, and proteoglycans. The keratinocytes start the re-epithelialization of the wound with reconstitution of the basement membrane. The presence of endothelial cells in the wound bed, stimulated by hypoxia and angiogenic factors such as fibroblast growth factors (FGF), results in the formation of new blood vessels. During the maturation phase the collagen network and proteoglycans are remodeled. During this process hyaluronic acid is gradually replaced by glycosaminoglycans, such as chondroitin sulfate and dermatan sulfate. Both collagens type I and III increase during the wound healing process; however, as the scar continues to mature and remodeling takes place, the proportion of collagen type III decreases.

The precise mechanism that leads to the development of hypertrophic scars and keloids has not been established, thus multiple disturbances in the wound healing process have been implicated. The development of excessive scar tissue may result from excessive matrix deposition,

reduced degradation, or both. Fibroblasts from keloids show an abnormal response to stimulation, producing high levels of collagen, especially type I. Fibroblasts in hypertrophic scars, on the other hand, usually exhibit a normal response when exposed to growth factors, with a moderate increase in collagen synthesis. TGF- β linkage to increased collagen and fibronectin deposition has also been involved in the pathogenesis of excessive scarring. Furthermore, collagen fibers in these types of scars are found to be arranged as whorled, hyalinized bundles. Angiogenesis usually regresses during the maturation phase of the normal scarring process; however, keloids and hypertrophic scars are characterized by persistent hyperemia due to the constant presence of new vessels in the area. Other factors implicated in the development of hypertrophic scars and keloids are hyaluronic acid, proteoglycans, and mast cells, among others.

The estimated incidence has been reported to be between 4.5 and 16%, with African-Americans and Hispanics showing the highest rates. Patients in their second decade of life are more commonly affected, with the same prevalence in both sexes.

Hypertrophic scars usually arise within one month of injury and are consistently confined to the original injury site. They appear as red, raised, and firm scars. Hypertrophic scars may arise anywhere in the body; however, those areas under constant pressure and movement stretching are more commonly affected (Fig. 4.1).

Keloids, on the other hand, are purple/red nodules that extend beyond the original injury sites and are frequently disfiguring. These lesions may appear within weeks or years from original cutaneous insult. The most common locations for keloids are the earlobes, jawline, anterior chest, shoulders, and upper back. In addition to the usual cutaneous injuries that result in scarring, keloids may also result from ear piercing, abrasions, tattooing, and vaccinations, among others (Fig. 4.2).

Keloids usually persist indefinitely, whereas hypertrophic scars may involute with time. However, whether a hypertrophic scar will ultimately regress or not cannot be predicted. Furthermore, besides obvious aesthetic concerns, symptoms such as pruritus and dysesthesias may be associated with these abnormal scars, driving the patient to seek treatment alternatives.



Fig. 4.1 White male with a hypertrophic scar. Red, raised, firm scar limited to incision site on the right side of his forehead



Fig. 4.2 African-American female with a keloid located on her lower, anterior neck

Over the years several treatment options have been proposed, including excision, cryotherapy, electrosurgery, dermabrasion, radiation, intralesional corticosteroids, 5-fluorouracil (5-FU), bleomycin, mitomycin, doxorubicin, imiquimod, verapamil, tamoxifen, tacrolimus, botulinum toxin, retinoic acid, silicone gel/sheet, plant extracts, and compression therapy. The carbon dioxide (CO₂) and erbium:YAG lasers (ablative lasers) were also included as therapeutic alternatives; however, the high incidence of recurrence and side effects led to them being discontinued for the treatment of hypertrophic scars. Overall, treatment of new hypertrophic scars is consistently much more successful than treatment of old hypertrophic scars and keloids.

Currently, the pulsed dye laser (PDL) is widely used and accepted as the laser of choice for the improvement and management of hypertrophic scars and keloids. Its benefits, indications, and technique will be discussed in this chapter. Treatment of acne scars will be covered in Chapter 6.

• Mechanism of action

Under the principle of selective photothermolysis, PDL targets blood vessels, with the 585–595 nm wavelength selectively absorbed by hemoglobin. The precise mechanism by which the PDL improves scarring has not yet been established. Theories such as microvascular destruction with consequent ischemia, leading to deprivation of nutrients to the scar and interference in collagen deposition, have been proposed. Other hypotheses include increment of mast cells, suppression of TGF- β_1 , disulfide bond disruption, and collagenolysis, among others.

• Patient selection

Patients with hypertrophic scars usually seek treatment because of cosmetic issues or associated symptoms. There-

fore, a hypertrophic scar is usually treated when it is functionally impairing, the patient considers the lesion to be cosmetically unfavorable, or when associated symptoms such as pruritus and dysesthesias are present.

Patient-specific (skin type) and lesion-specific (age of scar and color) factors need to be considered when assessing therapeutic alternatives, such as lasers, for the treatment of hypertrophic scars.

The majority of the research studies on laser treatment of hypertrophic scars involve patients with skin types I–III. Skin tone is the main patient-specific characteristic to be taken into account when evaluating potential candidates for scar revision with lasers. Skin tone has a great influence in the outcome of the treatment, with fair-skinned individuals having an overall better response, with fewer side effects such as pigmentation changes. Assessment of the patient's skin type is also used to establish the most appropriate laser parameters. In patients with Fitzpatrick skin types IV–VI, there is a high risk of laser light absorption by epidermal melanin, therefore less effective targeting of the skin and increased risk of postoperative pigment alteration along with reduced treatment outcome. Patients should be specifically warned about the high risk of pigmentation alterations that may result from laser treatment. Some authors suggest that laser fluences should be adjusted and lowered in dark-skinned individuals. Due to the adjustment of the laser parameters, more sessions are usually required when treating these individuals. In general we do not recommend laser treatment of dark-skinned individuals; however, when treating these patients we suggest doing a 'test spot' in an effort to foresee any side effects and help determine the most appropriate parameters to be used.

In summary, the ideal patients for scar revision with lasers are light-skinned individuals, with relatively new (less than 6 months to 1 year), red, raised scars.

sizes the energy must be increased. Initial treatment visits should be started with low fluences, which can be adjusted according to the response in subsequent sessions. Energy densities are also adjusted according to the patient's and scar's characteristics (i.e. reduce fluence in dark-skinned individuals).

7. Inform the patient that you are about to start the procedure. Remind him or her that he or she will experience a 'rubber band snapping' discomfort during the treatment.
8. Place the handpiece over one end of the scar and start applying laser pulses over the entire scar surface in a continuous pattern until the opposite end is reached. Overlapping of 10% is generally accepted.
9. Post-operative care instructions should include strict sun avoidance to avoid pigmentation alterations. The treated area may be cleansed normally with soap and water. Trauma to the site should be avoided.

The next treatment can be done within 4–6 weeks.

• Side effects, complications, and alternative approaches

Immediately after the laser treatment the patient will experience a pruritic or burning sensation, which may persist from a few hours up to 2 days. The most commonly expected side effect after the procedure is purpura localized over the treated area. This side effect usually persists for up to 10 days. Hyperpigmentation of the treated area may also occur. If this happens, consider treating the area with a bleaching cream, or defer the following treatment session to avoid light absorption by epidermal melanin and assure effective laser targeting of the scar.

Crusting, oozing, vesiculation, and ulceration are rare complications that sometimes occur. In such cases, the area should be kept moist with ointment and may be covered with nonstick occlusive dressing to avoid touching of the area. The following treatment session must be postponed until complete healing of the treated site has been achieved. Furthermore, laser energy should be lowered during the following treatment sessions.

• Advanced topics

As previously stated, the use of intralesional steroids or 5-FU in addition to laser treatment is considered an alternative approach for hypertrophic scars and keloids.

When treating relatively new, red, hypertrophic scars, some dermatologists like to use intralesional steroids or 5-FU after the laser procedure has been done. When old, not red, scars are to be treated, the PDL is usually not as effective and occlusion plus intralesional steroids and/or 5-FU is one common approach (Fig. 4.4). Flattening of the scar, as well as improved pliability and associated symptoms can be achieved with this approach.

We recommend that injection of intralesional drugs is done after the laser procedure, otherwise blanching of the

area may occur with subsequent loss of the laser target, specifically the vessel. Triamcinolone (TAC) is one of the most commonly used steroids for intralesional injection of keloids and hypertrophic scars (10–40 mg/mL). Intralesional TAC can be administered every 4–6 weeks until the desired effect is achieved. 5-FU at concentrations of 45–50 mg/mL in combination with corticosteroids may be injected at different intervals ranging from 3 times per week to once per month depending on the degree of induration and inflammation.

The effects of corticosteroids on the scarring process include inhibition of the migration of inflammatory cells, vasoconstriction, and inhibition of fibroblast and keratinocyte proliferation. The main mechanism implicated in 5-FU's effectiveness in the treatment of hypertrophic scars is inhibition of fibroblast proliferation. Both intralesional 5-FU and steroids cause pain at the injection site. Other side effects such as purpura at the injection site, necrosis, telangiectasia, atrophy, and pigmentation changes should be mentioned.

Additional treatments such as the application of a silicone gel/sheet or pressure dressing can be recommended to the patient to improve the quality of scars.

A recent development in laser technology has been the ability to deliver high intensity light fractionated through focused lenses to produce arrays of microscopic columns of thermal injury surrounded by uninjured tissue. The original clinical device in this field, first introduced in 2003, was a 1550 nm fiber laser from Reliant Technologies (Palo Alto, CA). The laser delivers microscopic columns of laser light that are closely and uniformly aligned. The tiny columns of injury are termed microscopic treatment zones (MTZ). The operator can adjust the energy of the laser and the density of the MTZ.

Intelligent Optical Tracking™ technology is used for a consistent MTZ pattern. The laser requires a tracking device (a proprietary blue dye applied to the skin before treatment) and topical anesthesia. The Food and Drug Administration (FDA) has approved this device in the treatment of periorbital rhytides, skin resurfacing, soft tissue coagulation, and melasma. In 2007, the FDA approved the second generation fractional resurfacing device from Reliant. This device has an ergonomic roller tip and computer software which allows the user to provide predictable pattern delivery as well as greater depth of heating without the requirement for blue dye contrast agent.

Alternative fractional technologies are now available and are primarily ablative using erbium:YAG or CO₂ lasers with fractionated delivery or nonablative using mid infrared wavelengths such as 1540 nm or 1440 nm. There has been increasing interest in the use of fractionated devices to treat acne scarring and several authors have reported good results in the treatment of this disorder. Alster et al treated 53 patients (skin phototypes I–V) with mild to moderate atrophic facial acne scars with a 1550 nm erbium-doped fiber laser. Clinical response was determined at each treatment visit and 6 months after the final

8

Photodynamic Therapy—Cosmetic

Michael H. Gold

INTRODUCTION

The past several years have seen a significant rise in the use of photodynamic therapy (PDT) for the treatment of a number of dermatologic disorders, including actinic keratoses (AKs) with or without photorejuvenation, squamous cell carcinoma in situ (Bowen's disease), non-melanoma skin cancers (especially superficial basal and squamous cell carcinomas), moderate to severe inflammatory acne vulgaris, as well as several other entities which will be described in this chapter. PDT has gained widespread use as a therapeutic agent over these past several years and has found a home in dermatologic surgery which will only be expanded in the years ahead.

PDT has a long history in medicine, dating back to the early 1900s. It was not, however, until recently that clinicians and researchers found suitable ways to utilize the available photosensitizers which are required to make a PDT response. Now, with two Food and Drug Administration (FDA) photosensitizers approved for use, we are once again at the beginning of a very exciting time for PDT research and its potentials in modern medicine. It is hoped that through this chapter the reader will gain a firm understanding of where we have been with PDT, the struggles that made it appear and disappear, and its triumphant return in the 1990s through today.

PDT, in its simplest form, is a reaction process which requires a photosensitizer, oxygen, and a light source to selectively destroy a targeted cell. In today's use of PDT, 20% 5-aminolevulinic acid (ALA) is the most common drug used as the photosensitizer. A methyl ester form of the drug is also available and will be described as well. A variety of lasers and light sources have been utilized for PDT and it is this multitudinous number of potential light sources that probably has sparked the growing interest in the use of PDT in dermatology.

• History of PDT

The use of PDT can be traced to the early 1900s. Raab reported that paramecia cells (*Paramecium caudatum*) were not affected when exposed to either acridine orange or light separately, but that they died within 2 hours after exposure to both acridine orange and light when given at

the same time. In 1904, Von Tappeiner and Jodblauer were the first to use the term 'photodynamic effect' in medicine when they showed an oxygen-consuming reaction process in protozoa after the application of aniline dyes with fluorescence. The next year, 1905, Von Tappeiner and Jesionek described experiences with topical 5% eosin as a photosensitizer with an artificial light source to treat dermatologic entities in humans. The dermatologic disorders successfully treated included nonmelanoma skin cancers, lupus vulgaris and condylomata lata. They postulated that the eosin incorporated into the cells and produced a cytotoxic reaction when exposed to an appropriate light source and oxygen.

The use of porphyrins as photosensitizers emerged shortly thereafter. In 1911, Hausman reported experiences with hematoporphyrin as a photosensitizer. Hausman was able to demonstrate that light-activated hematoporphyrin could photosensitize both guinea pigs and mice. In 1913, Meyer-Betz, attempting to demonstrate a PDT effect in humans with hematoporphyrin, injected himself with the hematoporphyrin. He found that areas of his skin exposed to light became intensely swollen and painful. This phototoxic reaction lasted upwards of 2 months, which created a major difficulty for its regular use as a photosensitizer in humans and in dermatologic disease states. The medical literature was quiet for almost the next 30 years as interest in PDT seemed to quietly fade away.

In 1942, Auler et al showed for the first time, in a significant contribution to PDT research, that hematoporphyrin would concentrate more in certain dermatologic tumors than in their surrounding tissues, and that when these tumors were fluoresced with a light source, they would become necrotic. Figge et al later reported that hematoporphyrin was also selectively absorbed into other cells, including embryonic, traumatized skin, and neoplastic cells.

The principles of PDT in human cancer cells had finally been firmly established and presented in the medical literature. A proper photosensitizer could be concentrated into tumor cells, activated by a proper light source and in the presence of oxygen cause a cytotoxic reaction to occur selectively in the tumor cells. In 1978, Dougherty et al reported on a new photosensitizer, hematoporphyrin

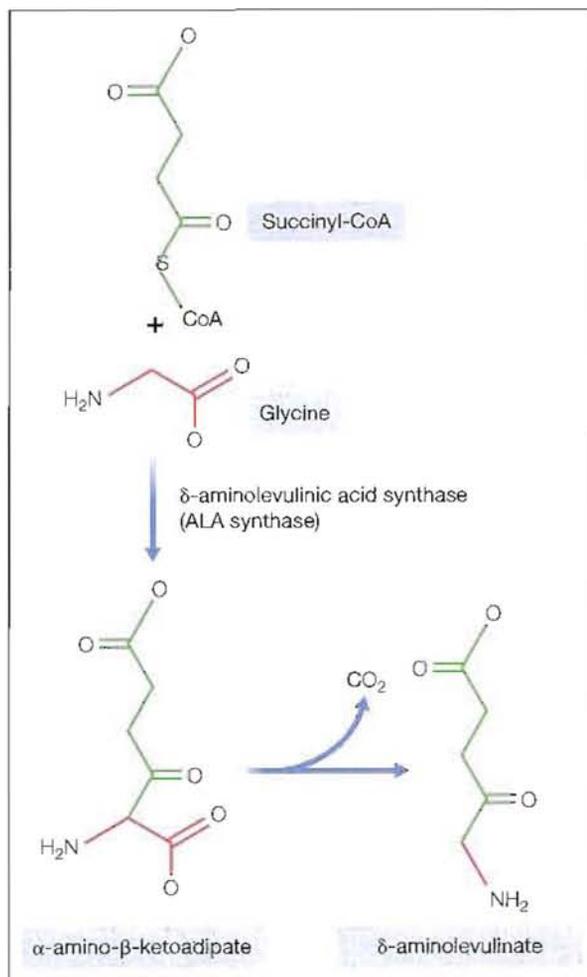


Fig. 8.1 Heme biosynthetic pathway

Norway; Metvixia®, Galderma, Ft Worth, TX). Its primary use has been in treating nonmelanoma skin cancers and AKs. Interest in photorejuvenation and inflammatory acne vulgaris is just beginning with methyl-ALA. Metvix is shown in Figure 8.3 and the red light source currently available (Aktelite®, PhotoCure ASA, Norway; Metvixia, Galderma, Ft Worth, TX) is shown in Figure 8.4. Further discussions on Metvix/Metvixia will follow later in the chapter.

Levulan, at the time of this writing, is available for use in the USA and has marketing rights assigned for Asia (Daewoong Pharmaceutical Co. Ltd, Seoul, South Korea and South/Latin America Stiefel Laboratories, Coral Gables, FL). The use of Levulan in Europe is currently being negotiated. Levulan has US FDA clearance for the treatment of nonhyperkeratotic AKs of the face and scalp utilizing a 14–18-hour drug incubation period of the ALA and using a blue light source for 16 minutes and 40 seconds (1000 seconds). All other indications being studied, as indicated, with Levulan are considered off-label use of the product.

PIVOTAL US TRIALS FOR ALA-PDT FOR ACTINIC KERATOSES

The pivotal US FDA Levulan clinical trials will be reviewed. In the Phase II US pivotal clinical trial, 39 patients with extensive nonhyperkeratotic AKs of the face and scalp received 16 minutes and 40 seconds of blue light after a 14–18-hour drug incubation. Pain was common during and after the treatment, and post-treatment erythema and edema, leading to crust formation for up to 1 week, was common. Eight weeks following treatment, 66% of the individually treated AKs resolved. A second treatment increased clearance to 85%. The positive results

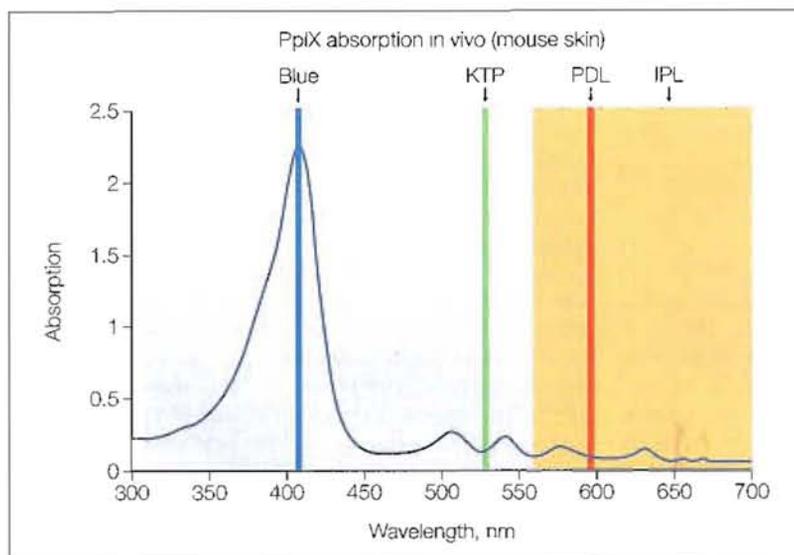


Fig. 8.2 Protoporphyrin IX absorption spectrum



Fig. 8.7 ALA-PDT with rejuvenation effect. Before treatment and three months after 4 ALA-PDT treatments.

62.5% of patients in their study who had had previous cryotherapy for their AKs preferred PDT over cryotherapy as a treatment modality. Avram et al looked at an IPL device in 17 patients with a 1-hour full-face drug incubation. In their study, 69% of the AKs responded with one IPL treatment as well as an improvement of 55% in telangectasias, 48% in pigmentary changes, and 25% in skin texture. Alexiades-Armenakas et al studied 19 individuals with actinic cheilitis and a PDL and showed a 68% clearance at 12 months in these individuals. All of these studies supported the use of ALA-PDT in treating AKs, actinic cheilitis, and the signs of photoaging all with fewer treatments than with other modalities.

SPLIT-FACE CLINICAL TRIALS IN THE USA—AKS/PHOTOREJUVENATION

Five split-face US clinical trials have been published in the peer-reviewed medical literature. The first, by Alster et al, compared ALA with an IPL on one side of the face compared to IPL alone on the other side of the face in 10 individuals. The group found that the side receiving ALA-IPL improved in the parameters of photorejuvenation compared to the IPL treated side. Key examined subjects utilizing a PDL with ALA on one half of the face; the ALA-PDL side showed improved parameters of photorejuvenation over the PDL side alone. Marmur et al examined a split-face ALA-IPL versus IPL alone study and through skin biopsies examined ultrastructural changes as a result of both the IPL treatment and the ALA-IPL treatment, specifically looking at the production of type I collagen. They found that there was a greater increase in

type I collagen production in those patients receiving ALA-IPL over IPL alone.

Dover et al examined an ALA-IPL split-face protocol where patients received three split-face ALA-IPL treatments at 3-week intervals followed by two additional IPL full-face treatments and were evaluated at 4 weeks following the last IPL treatment. Twenty-nine individuals participated in this clinical trial. They found an improvement in the global score for photoaging (80% vs. 50%); mottled hyperpigmentation (95% vs. 65%); and improvement in fine lines (55% vs. 20%). They found no statistical change in tactile skin roughness or sallowness over baseline.

Gold et al reported a split-face clinical trial utilizing ALA-IPL on one half of the face with an IPL on the other half. Three split-face treatments at 4-week intervals, with follow-up at 1 and 3 months following the last treatment were performed. Thirteen patients were included in this study. They found changes in the ALA-IPL side versus the IPL side of: improvement in AKs (78% versus 53.6%); crow's feet (55% vs. 28.5%); tactile skin roughness (55% vs. 29.5%); mottled hyperpigmentation (60.3% vs. 37.2%); and erythema (84.6% vs. 53.8%). No adverse effects were noted and no 'PDT effect' was seen.

These open-label and split-face clinical trials confirmed the use of a short-contact, full-face ALA-PDT in the treatment of AKs and photorejuvenation. Many clinicians are utilizing this therapy on a regular basis in their clinical practices and patients have responded positively to the therapy. Most clinicians utilize a 1-hour drug incubation time for ALA to be on the skin before exposure to a proper laser or light source. Clinical examples of AKs/photorejuvenation responses to ALA-PDT are shown in Figures 8.7 and 8.8.

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INTRODUCTION

Laser hair removal is an accepted modality for long-term hair reduction since first being described about 10 years ago. It rivals electrolysis in the successful treatment of small hair-bearing areas. It surpasses any modality in the treatment of larger hair-bearing anatomic areas. This chapter provides guidelines for laser- or light-assisted hair removal in a typical patient, discusses the scientific background of laser hair removal, and examines the specifics of different laser systems.

Unwanted hair falls into four main categories. Each one of them can be a reason for seeking a method for hair removal.

1. Hypertrichosis is defined as an increase in hair growth that is not androgen dependent. It may result from intake of certain medications such as phenytoin, cyclosporine, cortisone, or penicillamine. It has also been seen in a variety of diseases such as porphyria cutanea tarda, thyroid disorders, metastatic carcinoma, and malnutrition/anorexia nervosa.
2. Hirsutism is characterized by the growth of terminal hair in women on androgen-dependent areas of the body such as the upper lip, chin, or chest. Often the result of androgen excess, hirsutism may be accompanied by acne, androgenetic alopecia, and acanthosis nigricans. The most common hormonal cause of hirsutism is polycystic ovary disease, estimated to occur in 1–4% of the female population of reproductive age. Rapid onset of hirsutism or other signs of androgen excess should prompt a hormonal evaluation, including levels of free testosterone and dehydroepiandrosterone sulfate (DHEA-S), to rule out the presence of an androgen-secreting neoplasm.
3. Hair-bearing flaps, used for reconstruction of any kind, may contain unwanted hair that interferes with proper function. Epilation of hair-bearing flaps before surgery is therefore indicated. For example, myocutaneous flaps used in urethral reconstruction may cause urinary obstruction, calcification or infection.

4. Most individuals seek consultation for unwanted hair, primarily because of cosmetic concerns. Facial or body hair in excess of the cultural norm can be very distressing to some patients. The most common areas treated include the axillae, bikini line, legs, and face in women, and the chest, back, shoulder, neck, and ears in men.

• Patient selection

Any individual wishing to have hair removed permanently may be considered a candidate for laser hair removal. Hair can be removed from children and adults alike from most areas of the body. The individual's skin type and hair color and coarseness will determine which device is the most appropriate as well as predict response to treatment. The ideal candidate for laser hair removal is a patient who presents with dark, coarse hair. Current techniques are not generally successful in permanently removing white hairs or fine vellus hairs. Additionally, due to increased risk for eye injury, patients should not be treated within the orbital rim. Perianal and perivaginal areas may be at increased risk for infection and should be treated with caution. As stated above, certain medications and hormonal imbalances may inhibit permanent hair removal due to hair stimulation. The ideal patient has realistic expectations, normal endocrine status, thick dark hair and light skin tones.

Laser treatment is much more effective when the pigmented hair shaft is present within the follicle. Therefore patients are advised to refrain from plucking or waxing for a period of time prior to treatment. Shaving, bleaching, and use of chemical depilatories are acceptable alternatives for patients awaiting laser treatment. While treatment can be safely performed with a shorter wavelength device (e.g. ruby laser) in fair-skinned patients, it is preferable to use longer wavelength devices in darker skinned patients. Further epidermal protection is also afforded by utilizing longer pulse durations and active cooling. Sun-tanned patients are advised to avoid treatment until skin tan has faded. Recent reports indicate the rare induction of hair growth after laser hair removal. This usually occurs in young female patients with skin types III–VI, who present with fine dark hairs on the lateral face.

Laser-induced hypertrichosis is observed in the treated areas as well as in the adjacent nontreated zones. Although the exact mechanism for this observation is not known, patients should be advised of this possibility prior to treatment.

• Expected benefits

Generally, the average number of hair removal treatments to achieve a significant reduction of excess hair is between five and seven treatments performed at 1–3-month intervals. Clinical improvement includes absolute hair number reduction, finer, lighter regrowing hair, and slower regrowth.

The concept of hair removal has been defined in the following way. 'Temporary hair loss' is defined as a delay in hair growth, which usually lasts for 1–3 months, consistent with the induction of telogen. 'Permanent hair reduction' refers to a significant reduction in the number of terminal hairs after a given treatment, which is stable for a period of time longer than the complete growth cycle of hair follicles at the given body site. Recently, it has been suggested to add another 6 months to this post-treatment observation time, i.e. the time it takes for damaged follicles to recover from the laser injury and reenter a normal growth cycle.

A distinction needs also to be made between permanent and complete hair loss. Complete hair loss refers to a lack of regrowing hairs (i.e. a significant reduction in the number of regrowing hairs to zero). Complete hair loss may be either temporary or permanent. Laser treatment usually produces complete but temporary hair loss for 1–3 months, followed by partial but permanent hair loss.

The range of outcome can be summarized as:

- ❖ Fewer hairs
- ❖ Thinner hairs
- ❖ Slower regrowing hairs
- ❖ Lighter hairs.

Patients have different expectations of treatment (e.g. temporary vs. permanent, partial vs. complete hair removal). All responses are clinically significant and may be separately desirable for different patients. Growth delay that provides a few months of hairless skin is far more reliably achieved than permanent hair loss. All laser systems have been shown to temporarily reduce hair growth for all hair colors (except white) and at all fluences. Blonde, red, or gray haired patients are unlikely to experience a permanent reduction, but hair loss in these patients can be maintained by treatment at approximately 1–3-month intervals.

Laser hair removal was cleared by the FDA in 1996 and has an excellent safety and efficacy profile. Complications are rare if treatments are done carefully and with the patient's skin type in mind. The most common side effects are temporary pigmentation changes.



Fig. 9.1 Chest before (A) and 8 months after (B) fourth IPL hair removal treatment

Effectiveness for permanent hair reduction is strongly correlated with hair color and fluence. Long-term, controlled hair counts indicate an average of 20–30% hair loss with each treatment, indicating the need for multiple treatments to obtain near complete hair removal. Research also shows that in the ideal patient with fair skin and dark hair, the probability for long-term hair removal is about 80–89%, depending on the device used (Fig. 9.1). Long-term comparison of different lasers (ruby, alexandrite, diode, neodymium:yttrium-aluminum-garnet (Nd:YAG)) and light sources (intense pulsed light) indicates that effective long-term hair removal can be achieved with all systems.

The maximum fluence tolerated is determined by the epidermal pigmentation. Fair-skinned, dark-haired patients are most easily treated. Dark-skinned patients pose a greater challenge. Any of the hair removal devices are safe and effective in light-skinned patients, while longer wavelengths (near-infrared) and longer pulse durations have been shown to treat darker skin types more safely when combined with cooling devices. A Q-switched Nd:YAG laser, with or without an external chromophore, has been shown to be very useful for treatment of dark skin types but appears to be ineffective for permanent hair removal.

For patients presenting with recent sun exposure, pre-treatment with a bleaching agent, sunscreen, and/or sun avoidance is recommended prior to laser treatment.

The number of treatments needed to obtain the best results for different anatomic sites is unknown. A rare patient can obtain long-term complete hair removal after a single treatment, while others may respond poorly, for yet unknown reasons. However, most patients (80–89%) respond favorably.

Often, regrowing hairs are thinner and lighter in color, as indicated by measurements of diameter and color of regrowing hairs. This also contributes to the overall cosmetic outcome since the clinical impression of hairiness is not only defined by the absolute number of hairs, but also by the color, the length, and the diameter of the hairs.

OVERVIEW OF TREATMENT STRATEGY

Historically it was assumed that the hair shaft was produced by rapidly dividing matrix stem cells located in the deepest portion of the hair follicle, 2–7 mm below the skin surface. However, recent evidence suggests that follicular stem cells are located in the outer root sheath, in an area called the bulge, near the attachment of the arrector pili muscle, approximately 1.5 mm below the epidermis. Thus both bulge and bulb are important targets for permanent hair follicle destruction.

Animal studies have shown that the hair growth cycle affects the hair follicle destruction by ruby laser pulses: actively growing and pigmented anagen stage hair follicles were sensitive to hair removal by normal mode ruby laser exposure, whereas catagen and telogen stage hair follicles were resistant to laser irradiation. However, in humans, the efficacy of laser hair removal does not appear to always be influenced by the hair growth cycle. Unlike the animal model, there is enough melanin present in each growth cycle of the human hair follicle to obtain selective damage to the hair.

A recent study showed no acute changes in the immunohistochemical staining properties of hair follicles treated with an 800 nm diode laser or a 1064 nm Nd:YAG laser. These findings challenge the widely accepted belief that the mechanisms of laser hair removal are mediated by frank destruction of follicular stem cells. Instead, functional alterations of these cells may lead to the desired clinical outcomes. Future studies may elucidate the exact mechanism of laser hair removal.

There are three ways light can potentially destroy hair follicles: thermal (due to local heating), mechanical (due to shockwaves or violent cavitation), and photochemical (due to generation of toxic mediators like singlet oxygen or free radicals). All of these methods have been studied for hair removal (Box 9.1).

• Photothermal destruction

Photothermal destruction is based on the principle of selective photothermolysis. This principle predicts that

Box 9.1 Methods for hair removal

I PHOTOTHERMAL DESTRUCTION

- ❖ Normal mode ruby lasers (694 nm)
- ❖ Normal mode alexandrite lasers (755 nm)
- ❖ Pulsed diode laser (800 nm)
- ❖ Long pulsed Nd:YAG lasers (1064 nm)
- ❖ Intense pulsed light source (590–1200 nm)

II PHOTOMECHANICAL DESTRUCTION

- ❖ Carbon suspension—Q-switched Nd:YAG laser
- ❖ Q-switched Nd:YAG lasers

III PHOTOCHEMICAL DESTRUCTION

- ❖ Photodynamic therapy

selective thermal damage of a pigmented target structure will result when sufficient fluence at a wavelength preferentially absorbed by the target is delivered during a time equal to or less than the thermal relaxation time of the target.

The normal mode 694 nm ruby, normal mode 755 nm alexandrite, 800 nm pulsed diode lasers, long pulsed 1064 nm Nd:YAG lasers, and filtered flashlamp technology, alone or in combination with electrical energy from radiofrequency, all employ this mechanism.

In the visible to near-infrared region, melanin is the natural chromophore for targeting hair follicles. Lasers or light sources that operate in the red or near-infrared wavelength region lie in an optical window of the spectrum where selective absorption by melanin is combined with deep penetration into the dermis. Deep, selective heating of the hair shaft, hair follicle epithelium, and the heavily pigmented matrix is therefore possible in the 600–1100 nm region. However, melanin in the epidermis presents a competing site for absorption. Selective cooling of the epidermis has been shown to minimize epidermal injury. Cooling can be achieved by various means, including a cooled gel layer, a cooled glass chamber or cooled sapphire window, and a pulsed cryogen spray.

Laser pulse width also appears to play an important role, as suggested by thermal transfer theory. Thermal conduction during the laser pulse heats a region around each microscopic site of optical energy absorption. To obtain spatial confinement of thermal damage, the pulse duration should be shorter than or equal to the thermal relaxation time of the hair follicle. Thermal relaxation of human terminal hair follicles has never been measured, but is estimated to be about 10–50 ms, depending on size. Devices for hair removal therefore have pulse durations in the millisecond domain region.

Sometimes the actual target is not pigmented and is at some distance from a pigmented structure. An example is the follicular stem cells which line the outer root sheath. These cells are not pigmented and reside at some distance from the pigmented hair shaft and appear to be an important target for permanent hair destruction. The concept

of thermal damage time (TDT) has therefore been proposed in the case of the hair follicle. Pulses longer than the thermal relaxation time of the hair shaft allow propagation of the thermal damage front through the entire volume and better damage of the follicular stem cells. Super-long pulse heating (>100 ms) appears to allow for long-term hair removal.

• Photomechanical destruction

Photomechanical destruction due to small local 'explosions' results from Q-switched laser pulses. The spatial scale of thermal confinement and resulting thermal or thermomechanical damage is strongly related to laser pulse width. Q-switched (nanosecond domain) laser pulses effectively damage individual pigmented cells within hair follicles by confinement of heat at the spatial level of melanosomes, leading in animals to leukotrichia but not to hair loss after Q-switched ruby laser pulses. Consistent with this behavior, temporary hair loss with an absence of permanent hair loss has been reported in humans after Q-switched laser treatments, despite a decade of using Q-switched ruby and Nd:YAG lasers widely for tattoo removal.

Photomechanical destruction of hair has been attempted by the so-called 'Softlight' technique. The method uses a proprietary suspension of carbon particles applied to the skin, with relatively low energies (2–3 J/cm²) of Q-switched Nd:YAG laser light (1064 nm, 10 Hz, 10 ns pulse duration, 7 mm spot size). Higher powered, 1064 nm Q-switched Nd:YAG lasers have also been studied for laser hair removal. However, when these very short pulses are used to target hair follicles, there is an extremely rapid heating of the chromophore (melanin). This generates photoacoustic shock waves that cause focal photomechanical disruption of the melanocytes in the bulb but no complete follicular disruption.

• Photochemical destruction of hair follicles

Photodynamic therapy is the use of light and a photosensitizer to produce a targeted photochemical reaction and therapeutic effect. ALA is a precursor in the porphyrin synthesis pathway and is rapidly and selectively converted to protoporphyrin IX (PpIX) by cells derived from the epidermis and follicular epithelium. Upon absorption of a photon, PpIX efficiently crosses into an excited triplet state, which in turn generates singlet oxygen by collision with ground state oxygen. Singlet oxygen is a potent oxidizer that damages cell membranes and protein. This is a so-called 'photodynamic reaction'. A host of other porphyrins, chlorins, phthalocyanines, purpurins, and phenothiazine dyes can act as photodynamic agents and are under development as drugs for photodynamic therapy. It is likely that ALA or one of these other drugs will prove useful for hair removal. This approach will potentially provide an effective means of treating nonpigmented hair.

• Treatment approach

The first laser-assisted hair removal device was marketed in 1996. Today such hair removal devices include ruby, alexandrite, diode, and neodymium:yttrium-aluminum-garnet (Nd:YAG) lasers, and intense pulsed light sources. The numerous lasers and nonlaser light sources available today provide clinicians with multiple options. Several variables need to be considered when determining whether or not laser- or light-assisted hair removal is appropriate for a particular patient and which technique to use. These include a patient's hair color, hair type, hair density, skin color, hormonal factors, and anatomic location. In order to determine the various critical factors for this procedure, the following general approach is used:

- ❖ A history is taken for appropriate patient selection
- ❖ A physical examination is performed to evaluate skin color and skin condition, hair color, hair diameter, and hair density
- ❖ Instructions are given to the patient concerning pre-treatment hair management and skin care
- ❖ Treatment guidelines are determined by skin and hair properties
- ❖ Appropriate post-treatment care is provided.

• Major determinants

When seeing a patient for the first time, the individual's skin type, hair color, and coarseness are noted, because this will determine which device is most ideal as well as predict response to treatment (Table 9.1). Location and density of excess hair should also be taken into consideration.

• Patient interviews

When obtaining a patient history, information that will enable the best result should be obtained. It is vital to discuss patient expectations, medications, history of scarring, local infections, previous hair removal strategies, endocrine status, recent sun exposure, and the patient's habits (i.e. sports, hot tub use, etc.). Patients with active cutaneous infections are not treated. Patients with a history of recurrent staphylococcal and herpes simplex infections are started on appropriate prophylaxis to diminish the likelihood of an outbreak. Although a history of keloids or hypertrophic scarring is not an absolute contraindication to treatment, individuals with these conditions are treated less aggressively. Although it has been reported that laser treatment of individuals who are taking isotretinoin is safe, the issue remains controversial. Patients on minoxidil, or with spouses who use this medication, should be advised that hair removal attempts may be hindered by the stimulating effects of this drug. Patients on hormonal therapy or with underlying endocrine abnormalities are alerted to the potential limitations of hair removal treatment. There is a report of a patient whose arthritis was treated with elemental gold, and who was

anesthetics to avoid potential complications of anesthetic toxicity. Local infiltration of lidocaine or regional nerve blocks may be utilized, but these techniques are rarely necessary. An alternative to topical anesthetics is piroxicam gel, which has been shown to provide adequate pain relief and to decrease the inflammatory side effects of laser hair removal when compared to placebo.

EQUIPMENT LASER AND LIGHT SOURCE TECHNOLOGY (Table 9.2)

A summary of laser and light source hair removal devices is presented in Table 9.2. This table is not meant to be all-inclusive; rather, it should be used as a broad survey of various hair removal devices that may or may not be commercially available at the time of publication. We advise contacting the device companies directly to obtain the most updated product information possible.

• Endogenous chromophore

694 NM RUBY LASERS

Because of high melanin absorption at 694 nm, the ruby lasers are best indicated in light-skinned (Fitzpatrick skin type I-III) individuals with dark hairs. Because of this limitation, their high power consumption, and relatively slow repetition rate, ruby lasers have become less popular for laser hair removal over the years.

Of the original normal mode 694 nm ruby lasers, only two are still commercially available for hair removal: the RubyStar and the Sinon. The RubyStar (Asclepion, Jena, Germany) and the Sinon ruby laser (Wavelight, Erlangen, Germany) are dual mode ruby lasers. They can operate in the conventional Q-switched mode for the treatment of tattoos and pigmented lesions and in the normal mode for hair removal. An integrated cooling device consisting of a cooled contact handpiece for the RubyStar or cold air cooling for the Sinon precools the skin prior to laser pulse delivery.

755 NM ALEXANDRITE LASERS

Long pulsed alexandrite lasers (755 nm) are effective devices for hair removal. At this longer wavelength, the ratio of energy deposited in the dermis to the epidermis is greater because of greater depth of penetration. The risk for epidermal damage in darker skin types is therefore reduced. Various alexandrite lasers are available. These include Elite (Cynosure, Chelmsford, MA), GentleLASE (Candela, Wayland, MA), Ultrawave II-III (Adept Medical, Rancho Santa Margarita, CA) and Epicare (Light-Age, Somerset, NJ).

The Elite laser combines 755 nm and 1064 nm wavelengths. A cooling handpiece (SmartCool) allows a continuous flow of chilled air to the treatment area. GentleLASE employs a dynamic cooling device (DCD) to protect the epidermis. This DCD cooling method uses short (5–100 ms) cryogen spurts, delivered on the skin

surface through an electronically controlled solenoid valve; the quantity of cryogen delivered is proportional to the spurt duration. The liquid cryogen droplets strike the hot skin surface and undergo evaporation. Skin temperature is reduced as a result of supplying heat for vaporization. This cooling method allows for fast and selective cooling of the epidermis. The Epicare laser has a cold air cooling option and a Smartscreen software package that assists in record keeping, protocols, and even practice management. The UltraWave II and III offers the convenient combination of 755 and 1064 nm wavelength in a single device and is well suited for removing unwanted hair in all skin types.

800 NM DIODE LASERS

An extremely high powered (2900 W) diode laser (Light-Sheer, Lumenis, Santa Clara, CA) is a popular laser hair removal device. Long-term results suggest that the pulsed, 800 nm diode laser is very effective for removal of dark, terminal hair: permanent hair reduction can be obtained in a significant percentage of patients. This laser operates at 800 nm, has pulse widths between 5 and 400 ms, a 12 × 12 mm spot, a 2 Hz repetition rate, fluences between 10 and 100 J/cm², and a patented contact cooling device (ChillTip). Because of the longer wavelength, the active cooling, and the longer pulse widths, darker skin types can be treated more safely than with ruby and alexandrite lasers.

Various other diode lasers are available (Table 9.2).

Q-SWITCHED 1064 NM Nd:YAG LASER

A high powered, 1064 nm Q-switched Nd:YAG laser (MedLite 6, Hoya/ConBio, Fremont, CA) is now available for hair removal. This laser has a very short pulse duration in the nanosecond range, a 3–8 mm spot, a repetition rate of 10 Hz, and fluences up to 12 J/cm². The high repetition rate (10 Hz) delivers the laser pulses very rapidly, therefore larger areas can easily be covered and operative time is significantly shortened. The longer wavelength (1064 nm) makes it useful for darker skin types. Although capable of inducing a growth delay, it appears to be ineffective for long-term hair removal.

LONG PULSED 1064 NM Nd:YAG LASERS

Several long pulsed Nd:YAG lasers (1064 nm wavelength) that deliver pulses in the millisecond domain are now available for hair removal laser treatment on all skin types (Table 9.1). These lasers include Lyra i/ Gemini (Iridex Corporation, Mountain View, CA), CoolGlide (Cutera, Brisbane, CA), Ultrawave II-III (Adept Medical, Rancho Santa Margarita, CA), Profile (Sciton, Palo Alto, CA), Cynergy and SmartEpil II (Cynosure, Chelmsford, MA), Dualis (Fotona, Ljubljana, Slovenia), Varia (CoolTouch, Roseville, CA), Mydon (Wavelight, Erlangen, Germany), and GentleYAG (Candela, Wayland, MA).

The long pulsed Nd:YAG lasers emit deeply penetrating 1064 nm wavelengths. The reduced melanin absorption at this wavelength necessitates the need for high fluences in order to adequately damage hair. However, the poor melanin absorption at this wavelength coupled with an epidermal cooling device makes the long pulsed Nd:YAG laser a safer laser treatment for darker skin types up to phenotype VI. The Nd:YAG laser is also often used for treatment of pseudofolliculitis barbae, a skin condition commonly seen in darker skin types.

PULSED, NON-COHERENT BROAD BAND LIGHT SOURCES

Many different intense pulsed, nonlaser light sources, emitting noncoherent, multiwavelength light, have also been used for hair reduction (e.g. Lumenis One, Lumenis, Santa Clara, CA; Ellipse, Danish Dermatologic Development, Hørsholm, Denmark; StarLux, Palomar, Burlington, MA). By placing appropriate filters on the light source, wavelengths ranging from 590 to 1200 nm can be generated. Cut-off filters are used to eliminate short wavelengths so that only the longer, more deeply penetrating wavelengths are emitted. Pulse durations vary in the millisecond domain. A single or multiple pulse mode (2–5), with various pulse delay intervals, can be chosen. The wide choice of wavelengths, pulse durations, and delay intervals makes this device potentially effective for a wide range of skin types. The devices come with software which guides the operator in determining treatment parameters depending on the patient's skin type, hair color, and coarseness.

The newest emerging hair removal technologies are the lower priced, small, pulsed light hair removal systems. These include the SpaTouch photoepilation system (Radiance, Orangeburg, NY), Cynergy PL (Cynosure, Chelmsford, MA), Quadra Q4 (DermaMed USA, Lenni, PA), and Estelux (Palomar, Burlington, MA). These systems have been optimized for hair removal with wavelengths preferentially absorbed by melanin, long pulse widths, and large spot sizes.

Recently, IPL systems have been developed that are combined with 1064 nm laser light (Lumenis One, Lumenis, Santa Clara, CA; Starlux, Palomar, Burlington, MA; Harmony, Alma, Fort Lauderdale, FL). These devices should allow for treatment of a wide spectrum of hair and skin colors.

ELECTRO-OPTICAL SYNERGY (ELOS) TECHNOLOGY

ELOS technology utilizes a synergy between electrical (conducted radiofrequency (RF)) and optical (laser or light) energies. The electrical energy creates heat that is focused on the hair follicle and the bulge area, while the optical energy heats mainly the hair shaft. When combined, a uniform temperature distribution across the hair shaft and the follicle should be obtained to achieve effective hair removal.

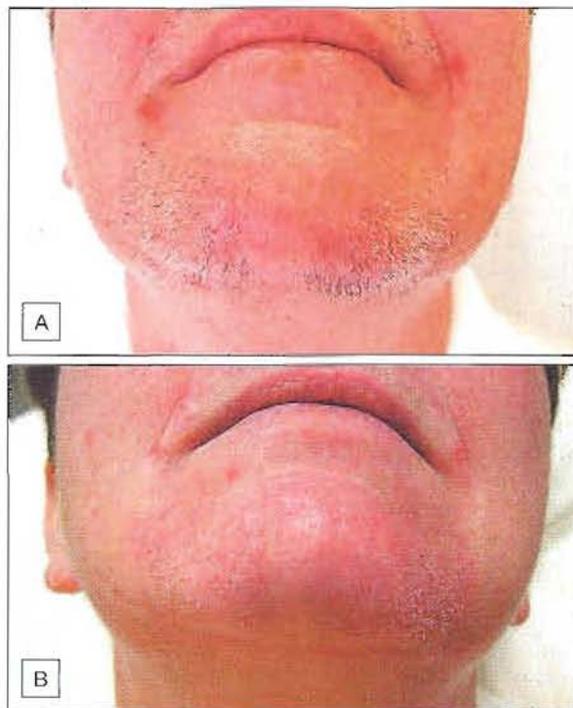


Fig. 9.2 Effective laser hair removal can be obtained for dark, pigmented hairs, but not for white hairs (A) Before. (B) After

Based on this ELOS technology, Syneron (Yokneam Illit, Israel) has developed the eMax, eLaser, and eLight systems. All devices are equipped with cooling. The use of the RF energy should also allow for treatment of all skin types, since this form of energy is not absorbed by epidermal melanin.

• Exogenous chromophore

In persons with blonde, gray or white hair, an effective permanent laser hair removal treatment is still lacking (Fig. 9.2). Potentially, the exogenous chromophore approach could solve this problem. Rather than targeting endogenous melanin, an exogenous chromophore (like dyes, photosensitizers, or carbon particles) can be introduced into the hair follicle and then irradiated with light of a wavelength that matches its absorption peak. The main problem is reliable penetration of the chromophore into all depths of the hair follicle. Therefore, the technique in its present form is apparently inadequate for inducing permanent hair loss.

CARBON SUSPENSION–Q-SWITCHED

Nd:YAG LASER

In this method, an exogenous chromophore (carbon suspension) with a peak absorption in the near-infrared portion of the spectrum is used in combination with a Q-switched Nd:YAG laser. The Softlight system (Telsar,

2

Nonablative Skin Resurfacing

Ellen S. Marmur, David J. Goldberg

Introduction

At the forefront of laser and nonlaser light source technology, dermatologists have led the way to remarkable innovations in the field of nonablative laser resurfacing. A rapidly expanding group of technically diverse systems including the KTP (532 nm), pulsed dye (585 nm, 595 nm), Nd:YAG (1064 nm Q-switched, 1064 nm long pulse, 1320 nm), diode (1450 nm), erbium:glass (1540 nm) lasers, and intense pulsed light (500–1200 nm) devices have been shown to be effective for nonablative treatment of photoaging skin (Fig. 2.1). Radiofrequency technology also used for nonablative treatments is described in Chapter 3. Historically, ablative lasers were the optimal treatment for photodamaged skin. However, ablative skin resurfacing has become increasingly unpopular with both patients and physicians due to the significant risks of prolonged recovery time, possible permanent hypopigmen-

tation, and/or scarring. Nonablative skin resurfacing has become the treatment of choice for photorejuvenation. It offers an elegant, effective, noninvasive treatment for problems related to photodamage and aging. This chapter will focus on the use of nonablative skin resurfacing to treat patients with mild to moderate photodamage.

Ultraviolet-induced photodamage accelerates and magnifies the physiologic changes of the normal aging process. Ultraviolet exposure produces a myriad of changes in the skin, including free radical formation, apoptosis, angiogenesis, melanogenesis, DNA mutations, oncogenesis, immunosuppression, matrix metalloproteinase induction, and degradation of connective tissue. The histologic manifestations of photodamaged skin include loss of collagen and abnormal clumping of elastic fibers in the superficial dermis. In addition, ultrastructural analysis shows a thin epidermis, flattened rete, increased

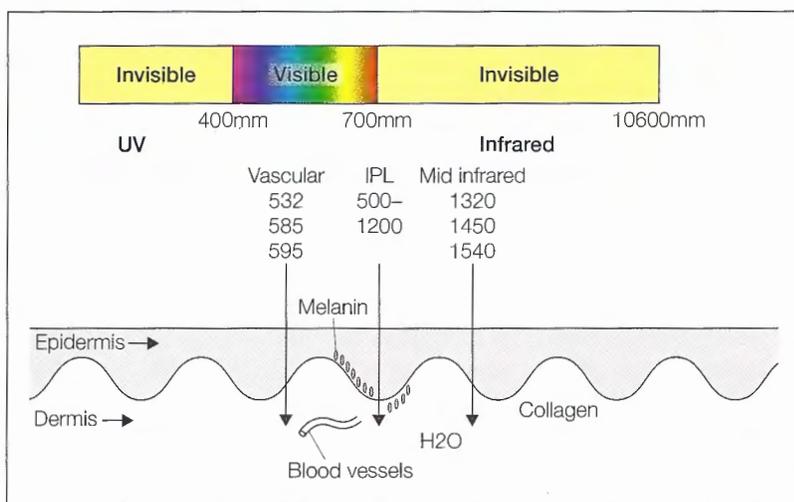


Fig. 2.1 Electromagnetic spectrum and target chromophores

Photodamage classification

Type I

Lentigenes, telangiectasias, increased coarseness, symptoms of rosacea

Type II

Rhytides, laxity, dermatochalasis

Type III

Actinic keratoses, nonmelanoma skin cancers

Box 2.1 Photodamage classification

vasculature, chronic inflammation, elastotic changes including the accumulation of large amounts of elastic material, wide spaces between the collagen bundles, and random deposition of collagen fibers. These histologic and ultrastructural changes are clinically correlated with rhytides, laxity, yellow discoloration, and telangiectasias. Nonablative skin resurfacing triggers a wound healing response to restore the normal architecture of collagen in the dermis. Associated vascular damage recruits inflammatory mediators that lead to fibroplasia and homogenization of the collagen.

Clinical photodamage is classified into three types (Box 2.1). Type I photodamage includes telangiectasias, solar lentigenes, increased skin coarseness, and symptoms of rosacea. Type II photodamage includes rhytides, dermatochalasis, comedones, and skin laxity. Type III photodamage includes actinic keratoses, nonmelanoma skin cancers, and melanoma. Standard nonablative skin resurfacing is successful in patients with types I and II photodamage. Generally, photorejuvenation treatments are undertaken on the sun-exposed areas of the face, neck, upper chest, and hands.

Nonablative skin resurfacing technology can be categorized into four different general modalities; vascular lasers, mid-infrared lasers, intense pulsed light systems, and radiofrequency devices. Recently developed, light emitting diode (LED), devices may also play a role in improving photodamaged skin (Box 2.2) The term 'nonablative skin resurfacing' includes the terms *subsurfacing*, *noninvasive resurfacing*, *skin toning*, and *wrinkle reduction* due to dermal neocollagenesis, and *photorejuvenation* due to both epidermal improvement and dermal collagen remodeling. Each group of nonablative devices will be discussed along with clinical pearls to ensure optimal treatment outcomes, realistic

Device classification

Vascular lasers
Mid-infrared lasers
Intense pulsed light systems
Radiofrequency systems
LED

Box 2.2 Device classification

expectations for the patient, management of potential complications, and potential future nonablative techniques.

Nonablative skin resurfacing is for the patient with mild to moderate photodamage and signs of skin aging. This approach is not meant for the patient who wants the degree of improvement and is willing to accept the added risks associated with more aggressive surgical options. Nonablative technologies stimulate collagen fiber synthesis to reduce wrinkles and lax skin. The final effect is clearly more subtle than that seen with invasive cosmetic treatments. However, nonablative skin resurfacing requires essentially no recovery time. With nonablative treatments, one avoids the risk of general anesthesia, with most treatments accomplished with little or no topical anesthesia. Such treatments also avoid the risk of infection, a leading cause of morbidity and complication seen after invasive cosmetic surgery. Nonablative skin resurfacing treatments are easily and expeditiously achieved in an outpatient setting. They have become known as 'lunch-time' laser procedures. The results from these procedures are not as dramatic as those seen after standard surgical procedures. In fact, patients who ultimately plan to have more extensive cosmetic surgery often choose to begin with nonablative skin resurfacing treatments. Invasive dermasurgery laser procedures such as laser blephoroplasty and ablative laser resurfacing will be covered elsewhere in this text.

Patient Selection

Patient selection for nonablative skin resurfacing is based on an evaluation of the individual's degree of photodamage and aging. The ideal patient is 35–55 years old with moderate signs of photodamage and aging. (Fig. 2.2) Younger patients with mild photodamage may also show improved skin texture after nonablative skin resurfacing; however the results



Fig. 2.2 Ideal patient for photorejuvenation

will be subtle. Conversely, patients with deep rhytides and severe laxity may show minimal to no response. Such patients may be better candidates for ablative resurfacing or other more invasive cosmetic techniques.

Darker skin types may preclude the use of certain types of nonablative skin resurfacing. In such patients light sources and lasers that target pigment must be used with caution and at settings to minimize thermal damage. Side effects such as blisters, scars, focal atrophy, textural change, and hyper- or hypopigmentation are all more likely to be seen in darker complected individuals. Mid-infrared lasers with emitted wavelengths varying between 1320 and 1540 nm target water in the dermis and theoretically can be used safely in darker skin types. However, when irradiated at high fluences non-specific laser energy absorption by melanin can lead to thermal damage and side effects even in darker skin types. The most common albeit rare side effect experienced by patients with darker skin color after nonablative skin resurfacing is transient hyperpigmentation. This is usually seen with those nonablative devices that utilize cryogen epidermal cooling. The hyperpigmentation may be due to cryoinjury and can be avoided by reducing the amount of cryogen delivered with each pulse. A detailed discussion of laser and nonlaser light sources in the treatment of darker skin phototypes may be found elsewhere in this text (see Chapter 6).

There are some individuals who are not appropriate candidates for nonablative resurfacing. These include those patients who have taken oral retinoids (for 6 months) prior to nonablative treatment, who have had recent ablative resurfacing with either

Exclusion criteria

Oral retinoids—6 months
 Ablative resurfacing—6 months
 Chemical peels—medium or deep, 6 months
 Active skin disease within the treatment area—herpes, impetigo, autoimmune disease

Box 2.3 Exclusion criteria

Commonly used vascular lasers

Trade name	Wavelength (nm)	Spot size (mm)	Pulse duration (ms)
V Star	585, 595	7, 10, 12	0.5–40
V Beam	595	7, 10	0.45–40
N Lite	585	5, 7	350
Aura	532	1, 2, 4	1–50
Versapulse	532	2–6	1–50
Diolite	532	5, 7, 10, 14	1–100

Table 2.1 Commonly used vascular lasers

lasers or deeper chemical peels, and/or have active skin disease within the treatment area (Box 2.3). Finally, in the rare patient reactivation of herpetic eruptions may occur. Pre-medication in these patients is indicated.

Vascular Lasers (532–1064 nm)

The flashlamp-pumped pulsed dye laser (FLPDL) was the first vascular laser (Table 2.1) that was developed based on the principle of selective photothermolysis. It was specifically designed to treat port wine stains. Although initially used with a 577 nm wavelength (a hemoglobin absorption peak) and a 450 μ s pulse duration (shorter than the thermal relaxation time of targeted cutaneous vascular lesions), currently available pulsed dye lasers emit wavelengths between 585 and 595 nm with pulse durations between 350 μ s and 40 ms. Variable wavelengths and pulse durations lead to the targeting of a variety of different vessel sizes.

The FLPDL uses a high-power flashlamp to excite electrons in an organic dye (rhodamine). Originally, this led to emission of yellow light at 577 nm. The dye has been modified to emit photons at different wavelengths corresponding with the absorption peaks

in the 1450 nm diode laser handpiece but generally treatment fluences range between 9 and 14 J/cm². Theoretically, there should be no epidermal absorption by melanin when this laser is used in darker skin types. However, there is still a risk of post-treatment hypopigmentation when this laser is used with skin types IV, V, or VI. This may be secondary to cryoinjury and/or nonspecific energy absorption.

The 1540 nm erbium:glass laser is widely used in Europe for the treatment of mild to moderate rhytides. As with all mid-infrared lasers, selective vaporization of water-containing tissue dermis leads to subsequent collagen remodeling and reduction of rhytides. This laser penetrates up to a depth of 2 mm. Theoretically, this depth correlates with the depth of maximum solar elastosis. This system differs from the 1320 nm and 1450 nm lasers in several ways. Instead of a three-phase cryogen cooling system, the 1540 nm erbium:glass handpiece delivers continuous contact cooling with a sapphire lens cooled to 5°C. The efficacy of the 1540 nm laser has been demonstrated by photography, profilometry, and ultrasound imaging showing a 40% reduction in wrinkles and a 17% increase in epidermal thickness at 6 weeks after the fourth treatment (Fournier et al 2002). In another study, histologic evidence of significant dermal remodeling, clinical satisfaction, and few side effects were noted after treatment with the 1540 nm laser (Lupton et al 2002).

Side effects common to the use of all mid-infrared lasers include transient pain, edema, and erythema of the treatment areas that resolve within 48 hours. Uncommon side effects include reactivation of herpes simplex infections, pigmentary alteration, blister formation, or scarring (Fig. 2.7, 2.8). Despite

fairly consistent ultrastructural evidence of dermal collagen remodeling with new type I collagen, clinical improvement does not always correlate with the degree of histologic fibroplasia. Advances in technology and establishment of optimal treatment parameters will undoubtedly lead to more consistent improvement in clinical outcomes with a continuing low side effect profile.

Intense Pulsed Light (400–1200 nm)

Polychromatic light devices were first developed to thermocoagulate vascular malformations in the 1970s. In the mid 1990s, the first high-intensity intense pulsed light sources (IPL) were marketed to physicians. Since then, multiple IPL and combinations of IPL with laser and/or radiofrequency sources have become available for nonablative resurfacing.

IPL systems are high intensity polychromatic light sources that emit pulsed light in a broad band of wavelengths between 400 and 1200 nm. Cut-off filters are available to narrow the bandwidth of emitted wavelengths in order to selectively target variable structures at different depths in the skin. For example, filters may be changed to correspond to vessels of different depths and caliber, the hair follicle, or pigmented cells. High cut-off filters can be used to reduce melanin absorption and protect the epidermis in patients with darker skin types. In addition, higher cut-off filters emit longer wavelengths for nonspecific absorption of dermal water. This results in widespread dermal heating that causes collagen damage and subsequent remodeling.

Similar to lasers, IPL systems produce their effect based on the principle of selective photothermolysis.



Fig. 2.7 Mid-infrared complication: hyperpigmentation



Fig. 2.8 Mid-infrared complication: blister formation