David J. Goldberg

Laser Dermatology

Pearls and Problems

Blackwell Publishing

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The writing of any book requires hours of work, rework, and more work. This book could not have been written without the tireless efforts of my 2006 Procedural Dermatology fellow, Dr. Alexander L. Berlin. I cannot thank him enough.

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Pearls and Problems

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Foreword

Enthusiasm and knowledge only go so far. But industrious capitalization of these features can result in infectious and significant achievements with long lasting benefits. And so David Goldberg's excellent review of energy based systems entitled *Laser Dermatology: Pearls and Problems* is arriving at a most propitious time.

Not so long ago, there were only a few therapeutic lasers available and the choices were easy. It was all about how to use the continuous wave CO_2 laser in one of its three modes—cutting, vaporization, or coagulation—which all related to spot size and power. Or how to improve the appearance of port wine stains with the argon or copper vapor lasers without scarring the heck out of the patient. In retrospect, we used to do a pretty good job considering the lack of selectivity and low tissue tolerance for these devices. There were few "Problems" and even fewer in the way of "Pearls."

But now it's a different ball game. The varying different energy based devices (not just lasers) are numerous, more selective, safer, and in many cases less effective than we would like them to be. Problems can exist if they are not used appropriately. Pearls come through the experience of using such devices effectively. This book moves beyond laser and light based wavelengths, fluences and pulse durations and focuses on the wealth of experience of one of today's leaders in laser dermatology.

Dr. Goldberg should be congratulated for bringing together a very practical compilation of the pearls and problems in the current practice of laser dermatology. His well presented, organized series of concepts will be extremely useful for the experienced laser surgeon as well as the novice. Very evident in this book is the accuracy and honesty of the author. Laser dermatology is exciting. *Laser Dermatology: Pearls and Problems* is an essential read for all physicians interested in the nuances of this field.

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Preface

Laser Dermatology: Pearls and Problems is not meant to be just another book written about lasers in dermatology. There are plenty of such books already written on that topic – some by me. All other books dealing with this vast arena either focus on (a) the skin entities that can be treated with lasers; (b) the latest in dermatological lasers; or (c) complications that may induced by those lasers. Where this book is different is the manner in which it looks at lasers in dermatology. This book is divided into five chapters. Each chapter starts off by highlighting essential concepts. This is then followed by a focus on pearls and problems of five major areas of laser dermatology. In addition, the photographs contained within each of the chapters are meant to serve a different purpose than is seen with most textbooks. The focus of pictures in this book is not to present before and after photographs. Such a focus is contained in many outstanding textbooks. Although there are occasional before and after pictures contained within the text, the focus, in this book, is to use pictures to illustrate some of the many pearls and problems that can be seen in the realm of laser dermatology. Twenty years of laser dermatology have given me a chance to see the beauty of the "Pearls" and the difficulties of the "Problems" in Laser Dermatology. Enjoy!

David J. Goldberg, MD, JD
March 2007

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Vascular Lasers

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Vascular Lasers

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KEY POINTS

- The pulsed dye laser, originally only used in a purpuric mode, is now highly successful without the induction of purpura for the treatment of most vascular lesions
- Pulsed dye lasers used for the treatment of port-wine stains lead to the best results when the clinical endpoint is purpura
- Facial erythema can be treated equally well with both pulsed dye laser and intense pulsed light treatment
- Twenty years after pulsed dye laser treatment of port-wine stains was initiated, the exact number of treatments remains an enigma
- Some leg spider veins can be treated with laser treatment; sclerotherapy remains the gold standard

Introduction

Cutaneous vascular lesions, especially those occurring on visible sites, such as the face, may cause significant psychological distress. This is true not only of port-wine stains (PWS), whose detrimental effect on patient is well recognized [1,2], but also of other vascular malformations, proliferations, and ectasias. Frequently, however, the latter conditions tend to be underdiagnosed and undertreated. The introduction of compact and more affordable lasers, being used in an outpatient setting, allowed for easier patient access with more reliable and cosmetically pleasing results.

The treatment of vascular lesions is one of the most commonly requested cutaneous laser procedures. Since the introduction of the argon laser, a variety of lasers and light sources have been used in the treatment of vascular lesions. These include visible and infrared lasers, as well as broadband light sources. Despite some limitations, lasers and light source devices remain the modality of choice for a variety of vascular lesions.

Essential Concepts

Vascular Laser Biology, Chromophores, and Tissue Targets

A large variety of vascular-specific lasers and light-based devices have been developed over the years. All of the systems currently in use are based on the principles of selective photothermolysis introduced by Anderson and Parrish [3]. Photons of light produced by lasers are absorbed by tissue chromophores within a specific target of interest, producing heat. The heat is dissipated through conduction; therefore, if sufficient energy is delivered faster than the rate of cooling, heat accumulates within the target and selectively destroys it.

Tissue absorption and scattering determine penetration of laser light into the skin. Collagen is the major cause of scattering, which decreases as the wavelength of light increases. Therefore, longer wavelengths can penetrate deeper into the skin and, subsequently, the choice of a specific laser will depend on the depth of the desired tissue target. As the wavelength is increased into the far-infrared region, light begins to be heavily absorbed by water, which limits its penetration.

Oxyhemoglobin and, to a lesser extent, deoxyhemoglobin are the main chromophores for vascular lasers. The major absorption peaks of oxyhemoglobin are 418 nm (blue), 542 nm (green), and 577 nm (yellow) [4]. The largest peak is at 418 nm; however, this wavelength does not allow adequate penetration into the skin. The other two peaks, as well as a broad absorption band between 800 and 1100 nm form the basis for vascular lasers in use today.

The patient's Fitzpatrick skin type is important when considering a vascular laser, as melanin may compete with oxyhemoglobin for light absorption, potentially resulting in dyschromia. Melanin absorbs mainly in the ultraviolet and the visible light spectrum, with decreasing absorption in the near-infrared region of the spectrum. Therefore, longer wavelengths are better used in patients with Fitzpatrick types IV toV to minimize the risk of dyspigmentation.

Laser Settings: Pulse Duration, Spot Size, Fluence, and Cooling Methods

Heat is transferred from erythrocytes containing the hemoglobin to the surrounding endothelial cells, causing damage to the blood vessel wall. If light is pulsed with exposure time less than or equal to the thermal relaxation time (TRT), heat is

maximally confined to the target – in this case, the blood vessel wall.

TRT is directly proportional to the square of the size of the object and inversely proportional to thermal diffusivity, an intrinsic property of a material to diffuse heat [3]. Thus, as the blood vessel diameter is doubled, the cooling time increases fourfold. A useful quick approximation of TRT, in seconds, is the square of the target size in millimeters [5]. Additional considerations in determination of TRT for larger targets, such as large-caliber vessels of the legs, will be discussed in a later section.

Once the TRT is determined, an appropriate pulse duration, also known as the pulse width, is selected to match the target blood vessel diameter. As an example, the TRT of capillaries is in the order of tens of microseconds, that of venules is in the hundreds of microseconds, whereas in adult PWS, the TRT is between 1 and 10 ms [6]. As the delivered pulse duration surpasses the TRT of smaller blood vessels, sufficient heat diffusion is afforded, allowing for the preferential treatment of larger-caliber vessels [3]. It is thus crucial to know the specific structure and composition of the vascular lesion to be treated [7].

The theory of selective photothermolysis requires sufficient fluence, also known as energy density, to reach a damaging temperature within the target – approximately 70ºC for blood vessels [3]. Precise choice of fluence is important, as excessive fluences may result in increased incidence of adverse effects, such as scarring and dyspigmentation.

Laser beam diameter, or spot size, also influences the choice of fluence. Compared to a smaller spot size, a larger spot size results in a smaller percentage of light being scattered outside the actual delivery of light, with subsequent delivery of greater amount of energy and greater damage to the deeper dermal target. Consequently, with all other factors being equal, lower fluences can be used with larger spot sizes [8]. In addition to the depth of the target, the choice of spot sizes is also influenced by the overall size of treated lesion. The largest spot size accommodated by the treatment area is typically selected, with small spot sizes usually reserved for isolated small superficial blood vessels.

Absorption of light energy, by competing epidermal melanin, and retrograde conducted heat from the actual treated dermal target may result in undesired epidermal damage. This may eventuate in blistering, dyspigmentation, and scarring. Epidermal cooling is employed to minimize the risk of such undesired damage. Cooling allows for higher fluences to be used, thus enhancing treatment efficacy [9]. Localized cooling

also has an additional benefit of providing local anesthesia and reducing swelling, making the treatment more tolerable to the patient. Epidermal cooling can be achieved through contact, including ice packs, cold gel, and sapphire window; cold air convection; or automated liquid cryogen spraying immediately prior to laser pulse, a process known as dynamic cooling [9].

Classification of Vascular Lesions

The composition and structure of the vascular lesion, as well as its natural history, need to be ascertained prior to treatment. Such assessment will allow the proper selection of the appropriate vascular laser and laser settings. In some instances, varying composition within the same lesion will require changes in laser parameters or a decision to use multiple separate lasers. In other instances, such as some hemangiomas of infancy, laser therapy may not always be appropriate and may be reserved for very early or for complicated cases.

With continuing expansion of clinical indications for vascular lasers, a proper classification system is important. The most useful classification system is based on endothelial characteristics. Thus, congenital vascular lesions can be subdivided into (1) hemangiomas, with endothelial cell hyperplasia, and (2) vascular malformations, with normal endothelial cell turnover and variable degree of vessel ectasia [10]. Most acquired vascular lesions, such as telangiectasias, spider and cherry angiomas, venous lakes, pyogenic granulomas, and leg vein abnormalities, are characterized by vessel ectasia.

PWS are the most common type of congenital vascular malformation. They represent low-flow capillary malformations, are present at birth, and most commonly occur on the face and neck. They may also be part of several rare conditions, such as Sturge–Weber and Klippel–Trenaunay syndromes. PWS increase in size, proportionally to the growth of the child, and never involute. As the degree of vascular ectasia increases over time, the lesion becomes darker and frequently develops hypertrophy and nodularity in adulthood. Histologically, an abnormal papillary dermal plexus of ectatic vessels varying in size between 10 and 300 μm underlies a normal epidermis at the depth of 0.1 to 1 mm [11]. Such variability, within the same lesion, may make laser treatment that much more difficult.

Hemangiomas of infancy most often appear after the first few weeks of life, although a white or pink macule may sometimes be discerned prior to the onset of actual hemangiomas growth. Following the initial presentation, hemangiomas grow at a much faster rates when compared to the rest of the body

[10]. Depending on the location of the lesion, such rapid growth may at times impinge on the larynx, trachea, or eyes, endangering breathing or vision. Ulceration may also occur and may result in bleeding, pain, infection, and scarring. Hemangiomas may be subdivided based on the depth in tissue into three categories: superficial, appearing as bright red plaques; deep, appearing as bluish subcutaneous nodules; and combined or mixed [12]. Multiple or extensive hemangiomas also occur and may be segmental or diffuse, sometimes with visceral involvement. Most hemangiomas begin to involute after 12 to 15 months of growth, a process that may take up to 10 years. Following involution, residual epidermal atrophy with telangiectasias and fibro-fatty tissue may persist [13]. It is also important to recognize a recently described rare hemangioma variants, such as the non-involuting congenital hemangioma (NICH) and the rapidly involuting congenital hemangioma (RICH). The prognosis for these lesions is different from the conventional hemangioma of infancy [14].

Pearls and Problems

PWS: Pulsed Dye Laser

The pulsed dye laser (PDL) is generally considered to be the gold standard in the treatment of PWS (Figure 1.1). This laser has undergone several modifications since its original inception in an attempt to allow the laser to penetrate deeper into the dermis, to target deeper and larger vessels, and to better protect the epidermis, especially in darker skin.

Several factors, including the patient's age and Fitzpatrick skin type, anatomical location, size, composition, and color,

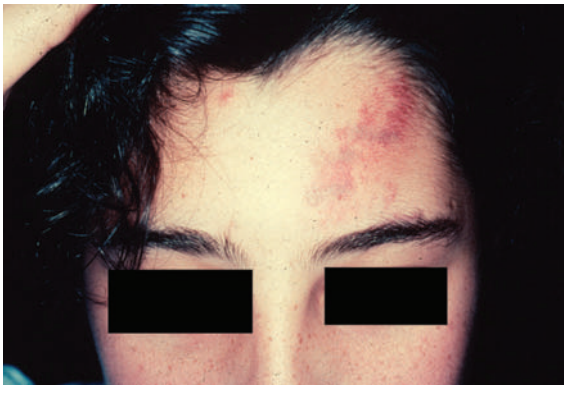


Figure 1.1 PWS ideally treated with the PDL.

influence the response of the PWS to the PDL. Of the head and neck lesions, those that are centrofacial, or dermatomal in the V2 distribution, are slower to respond to laser treatment [15]. PWS located on the extremities, and especially on distal extremities, respond more slowly than those on the trunk [16]. Smaller lesions respond better, with a 67% decrease in post-laser treatment size for those under 20 cm^2 compared to a 23% decrease in those over 40 cm^2 [17]. Ectasia, within ring-like vessels in the superficial horizontal plexus, as demonstrated by videomicroscopy, respond better to laser treatment, than those within capillary loops [18]. While application of this finding is difficult in clinical practice, it may explain some of the cases of differential response to treatment using identical laser parameters. Red color indicates more superficially located vessels and portends a better treatment prognosis. Purple color is attained by deeper-located larger-caliber vessels, whose response to treatment is intermediate, while that of pink lesions, with deep smaller-caliber vessels, is poor [19,20]. Early treatment of PWS has been shown to have better outcome [21,22], although this point remains somewhat controversial [23]. In general, fewer treatments are required, and better clearance can be achieved, in children less than 10 years old. Those PWS patients in whom therapy is started before 2 years of age potentially getting the best results [24,25].

After the above factors are analyzed through physical examination, realistic expectations have to be discussed with the patient or the parents. Such a discussion includes the number of required treatments, potential adverse effects, and the possibility of lightening rather than complete clearance of the PWS. Digital photographs prior to, and following treatments, are important to document gradual improvement.

Anesthetic requirements should also be considered prior to treatment. Cooling techniques, especially cryogen spraying, have made laser treatments tolerable for most adults. Topical anesthetics may be used, but may also cause vasoconstriction and render treatments less effective. Children may require conscious sedation or general anesthesia, especially when large lesions are being treated. Such techniques should be performed by a trained anesthesiologist and care must be taken to avoid any oxygen escape following intubation, as laser ignition of the oxygen may occur.

Generally, when using a 585-nm PDL, treatment of a PWS in a child, treatment is initiated at 6 to 8 J/cm^2, which may then be increased by 0.5 to 1 J/cm^2 at subsequent visits, if tolerated without adverse effects. Alternatively, several test spots using incremental fluences can be performed in the least obvious

portion of the PWS lesion 4 weeks prior to the actual treatment to determine the minimal purpuric dose. Lower fluences may be used for the eyelids, upper lip, neck, and over bony prominences. Fluences should also be lowered if moderate to extensive tanning is present, due to increased absorption of laser energy by the epidermal melanin with subsequent higher risk of scarring.

Laser emitted pulse duration is adjusted to the size of the vessels to be treated, and usually varies between 0.45 and 3 ms on the 585-nm PDL. As discussed previously, the largest spot size, usually 7 or 10 mm, is used to decrease scattering at the periphery of the laser beam and to deliver more of the original energy to the target. As a result, a 10-mm spot size requires only about half to two-thirds of the fluence of the 5-mm spot size [5]. If cryogen spray cooling is utilized, spray duration of 30 to 50 ms is used with a delay of 30 to 50 ms before the laser pulse. Spray duration may be lowered on darker skin tones to prevent cryogen-induced blistering and dyspigmentation.

Increasing the wavelength of the PDL to 595 or 600 nm allows for deeper penetration of the laser beam. This currently popular 595-nm wavelength is farther away from the oxyhemoglobin absorption peak at 577 nm; thus, higher fluences – 1.5 to 2 times those used with the 585 nm laser – may be used. This wavelength modification, with fluences of up to 16 J/cm^2, has been shown to be safe and efficacious when a longer pulse duration, 1.5 ms, and appropriate cooling are used [26–28]. In addition, PWS previously resistant to the 585-nm, 0.45-ms PDL may significantly lighten with increased wavelengths, pulse durations, and fluence [29].

Because significant and prolonged purpura may be a complication of treatment with the PDL, attempts have been made to use subpurpuric doses in combination with multiple passes to achieve clearance of PWS (Figure 1.2). This may be achieved by lowering the fluence or by increasing the pulse duration, usually to 10 ms. Results have been mixed, with most studies documenting some improvement, but not equivalent to that achieved with a purpuric dose [30,31]. Thus, patients should be warned that considerably more treatments would be required if such a technique were to be undertaken.

During treatment, pulses are overlapped by approximately 10% to avoid skip areas. Direct overlapping, or pulse stacking, at vessel-rupturing doses should be avoided to prevent non-specific collateral damage from extravasated hemoglobin from the first pulse. Although controversial, multiple passes may at times be done if fluences are carefully chosen to only produce intravascular purpura, rather than vessel rupture [32].

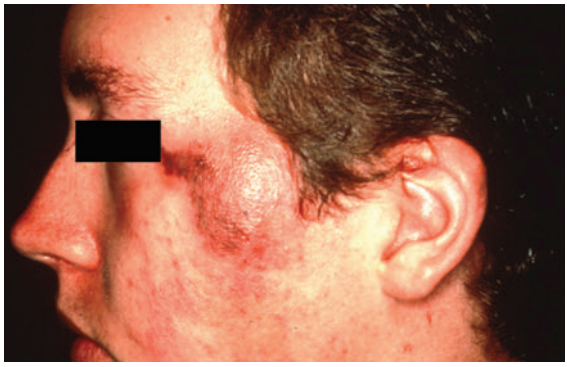


Figure 1.2 Typical purpura ideally seen after PDL of PWS.

As larger-caliber vessels generally respond better to PDL treatment, several in-treatment maneuvers may be undertaken to increase vessel clearance. Dependent position of the treated area, increased ambient temperature, and increased central venous pressure, through positive end-expiratory pressure during intubation, may all achieve dilation of the blood vessel with possible better laser-induced results [33,34].

The immediate clinical endpoint of treatment is transient intravascular purpura, also known as coagulum. Whitening of the treatment area should be avoided, as it indicates impending blistering, which may potentially result in scarring. Following treatment, local edema and pain may be experienced and may be alleviated with the use of ice packs or mild analgesics. If blistering or crusting occurs, topical antibiotics should be applied. Sun protection following laser treatment is important to decrease the risk of hyperpigmentation. Treatments are usually repeated at 4- to 8-week intervals.

On the average, a lightening of around 12% may be expected after each treatment and 4 to 15 or more treatments are needed for sufficient, though not necessarily complete, clearance [35]. Continued improvement may be observed with additional treatments.

The incidence of long-term adverse effects associated with PDL is low. As described above, purpura is the most common side effect of treatment, but usually only lasts 5 to 14 days. Even with the use of test spots, post-treatment crusting may be observed in 25% of patients [36]. Transient spongiotic dermatitis has been reported in 3.7% of patients with a personal or family history of atopic dermatitis. Among possible long-term laser-induced complications, the most common is hypopigmentation of at least 6 months with an incidence of 3.7%. Atrophic scarring

has been noted in 1.3% of patients, but may be more commonly related to the use of older laser systems. Hypertrophic scarring, and the development of pyogenic granuloma following treatment, is rare [37,38]. Patients on oral isotretinoin therapy may have to wait for at least 6 months following discontinuation of medication before PDL treatments can be undertaken due. This issue is controversial and relates to a possible increased incidence of post-treatment keloid formation and hypertrophic scarring. It must be kept in mind that the incidence of these and, potentially, other adverse effects is likely to change with the introduction of the newer, even safer, systems.

PWS: Other Lasers and Light-Based Devices

The development and recent advances in the PDL technology have improved, but not perfected, the treatment of capillary malformations. Deeper-seated and nodular PWS in adults still remain problematic for PDL treatment. In response to this problem, various additional lasers and light-based devices with vascular specificity have been tried with some success. Although generally not as well studied as PDL, such devices offer promise for improved future treatment options in the future.

Potassium-titanyl-phosphate (KTP) lasers produce a green light with a wavelength of 532 nm, near the 542-nm absorption peak of oxyhemoglobin. Although this laser's penetration into the skin is more superficial when compared to the PDL, it has been used on PDL-resistant PWS with resultant further lightening. Fluences between 18 and 24 J/cm^2, with pulse widths between 9 and 14 ms, produce the best results [39]. The KTP laser is more operator dependent than is the PDL. The handpiece has to be moved continuously during treatment, with care being taken not to stack pulses. The clinical endpoint of treatment with the KTP laser is transient vessel clearance without epidermal blanching. Because of this laser's more superficial penetration into the dermis, higher fluences must be used with this laser as compared to the PDL. In addition, a higher proportion of KTP laser energy is absorbed by the epidermis. This may lead to increased rates of adverse effects, which include blistering, erosions, and crusting (eventuating in scarring) and hyperpigmentation in 10% and 7% of treated patients, respectively [39,40]. Recently, however, significant improvement in KTP laser treated PWS was noted with lower fluences, 9.5 to 20 J/cm^2, and longer pulse widths, 15 to 50 ms. Such treatment parameters may also be associated with a much lower risk of adverse effects [41]. Thus, optimal treatment parameters, while using the KTP laser for PWS, may still have to be determined.

At 1064 nm, the long-pulsed neodymium:yttrium–aluminum–garnet (Nd:YAG) laser allows for much deeper penetration into the dermis with vascular specificity due to the broad absorption peak of oxyhemoglobin above 800 nm. Coagulation of blood vessels, as deep as 2 to 3 mm from the dermo-epidermal junction, can be achieved [42]. This allows targeting of some of the deeper vasculature that the PDL may not be able to reach. These deeper, larger-caliber blood vessels typically require pulse durations between 3 and 15 ms. Since the absolute absorption of hemoglobin at 1064 nm is lower than that at 585 nm, substantially higher fluences need to be used with this longer wavelength. Because of this, proper cooling is paramount with this laser. Such cooling can be achieved through pre- and post-pulse contact cooling using a cooling handpiece, frozen gel, or ice packs. The choice of proper delivered treatment fluence can be somewhat complicated with the Nd:YAG laser, as even minimally slightly higher than required fluences may result in epidermal damage and potential scarring. It is recommended that a minimum purpura dose – defined as the minimum fluence causing subtle darkening or purpura lasting longer than 15 minutes – be determined and used in subsequent treatments. Generally, the purple color within a PWS requires Nd:YAG laser fluences between 40 and 60 J/cm^2, red requires between 50 and 130 J/cm^2, and pink requires 90 and 250 J/cm^2 [42,43]. During treatment, non-overlapping pulses are delivered following contact cooling. The immediate clinical endpoint is subtle dusky purpura without signs of epidermal damage, such as grayish discoloration. Such purpura typically resolves in 3 days. Following treatment, patients may also develop moderate urticaria-like edema, which may be improved with the use of mid-potency topical steroids [43]. Additional short-term effects may include erythema, transient post-inflammatory hyperpigmentation, and, rarely, erosions. Focal thrombosis, presenting as darkening and hardening of portions of the PWS may sometimes occur days to months following treatment [43]. Treatments are usually performed every 4 to 6 weeks.

Although not a laser, the intense pulsed light (IPL) device is a non-coherent light source that delivers multiple wavelengths of visible and near-infrared light simultaneously. The IPL may also be used in the treatment of vascular lesions, including PWS. The high-intensity flashlamps used in IPL typically emit wavelengths between 500 and 1200 nm. Various filters may be used to (1) adjust emitted wavelengths to the depth and size of treated target structure, as well as (2) to decrease melanin absorption to allow for treatment of darker skin types. Emitted

pulse durations can be highly variable and can be set to values between 0.5 and 88.5 ms, depending on the TRT of the target. Fluence must be carefully chosen, as the large spot size (120 to 600 mm^2) and multiple IPL delivered simultaneous wavelengths may result in epidermal heating and potential adverse effects. If higher fluences need to be delivered, this can be accomplished with multiple pulses, or pulse splitting. Delay between pulses may be set between 1 and 300 ms – usually 20 to 30 ms – to allow for sufficient cooling of the epidermis and smaller blood vessels. The heating achieved with such a technique is not additive, but follows a complex curve. Red and pink PWS can be treated with pulse durations of 2.5 to 5 ms, whereas purple PWS may require longer pulse duration and possibly multiple pulses. Chilled gel is used to cool the epidermis and/or contact cooling, plus topical anesthetics are used to reduce pain associated treatment. Treatments are usually repeated every 3 to 6 weeks. Clearance, even in patients with skin type IV, may be achieved in previously untreated lesions with fluences ranging from 24 to 75 J/cm^2, with the best improvement achieved in pink and red PWS [44,45]. Adverse effects following IPL treatment are mostly transient and may include immediate erythema and purpura in up to 75% of patients, lasting for up to 7 days, blistering in up to 8%, and swelling for several hours to a week in up to 27% of patients [44,45]. A rare complication of terminal hair development within a treated PWS has also been reported [46]. Scarring, although rare, may always occur [44,45]. Most authors do report a steep IPL treatment learning curve. Extensive experience with this device may be necessary prior to the successful treatment of PWS.

Hemangiomas

PDL laser treatment of uncomplicated hemangiomas represents one of the major controversies in laser surgery today (Figure 1.3) [47]. The scarcity of published prospective, randomized controlled studies and the use of multiple laser wavelengths and widely varying treatment parameters further complicates the matter of laser hemangioma treatments. In addition, there is a lack of a standard goal in the laser treatment of uncomplicated hemangiomas. Some studies report on such characteristics as lightening or clearance, whereas others assess clinical involution.

While the involution of hemangiomas likely involves induction of cellular immunity, the precise mechanism underlying this process is very poorly studied. It has been argued that low-fluence, shorter pulse durations may induce limited

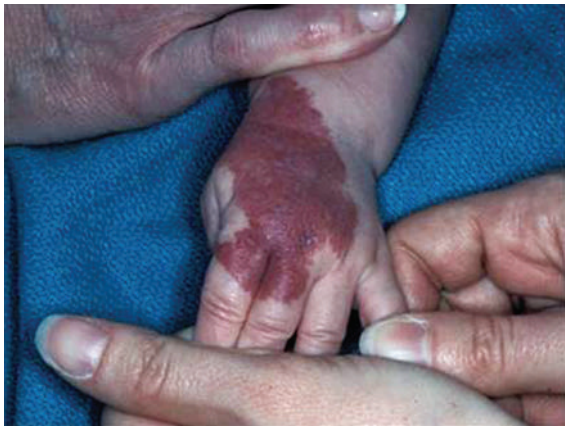


Figure 1.3 Ideal flat red hemangioma for treatment response to PDL.

vascular endothelial damage with thrombus formation, complement activation, and Vasculitis [47]. However, since the precise pathophysiology of the hemangioma involutionary process has yet to be worked out, the development of targeted laser treatments based on this mechanism cannot realistically proceed at this time.

The current goal of laser therapy for hemangiomas is complete or partial clearance of the lesion. Laser parameters are selected based on the depth and size of blood vessels comprising the lesion. The choice of parameters may, at times, be elusive, as the lesion represents an active rapidly growing tumor.

Since the PDL has very limited penetration into the dermis, only the treatment of flat matured or early, pre-proliferative red hemangiomas less than 2 mm in thickness is realistic with this laser. There is no laser-induced effect on deep hemangiomas, while only the superficial component of mixed hemangiomas may improve with this treatment. Compression of mixed hemangioma with a glass slide to reduce the thickness has not been found to increase the effectiveness of treatments. Multiple studies have documented reduction in the thickness of hemangiomas treated at an early stage [48–50], although some have also noted increased incidence of adverse effects, especially with older laser equipment that may have been used without effective cooling [51]. Complete clearance in early flat hemangiomas is achievable with the PDL at a much higher rate than would be expected with natural resolution. It has also been noted that good clearance can be achieved with the use of subpurpuric doses, while scarring is more common when confluent purpura is reached. Thus, lower fluences, between 6 and 7 J/cm^2 using a

585-nm PDL and between 9 and 12 J/cm^2, or using a 595-nm PDL, and longer pulse durations of 1.5 to 20 ms in combination with cryogen cooling, may result in clinical efficacy with lower risks of complications [52]. Treatments can usually be tolerated without anesthesia. During treatment, spot overlap should not exceed 10% to 20%. Confluent purpura should be avoided, as vessel rupture may lead to non-specific heating of the dermis from extravasated erythrocytes. Laser therapy may be performed every 3 to 4 weeks, with very superficial early hemangiomas requiring 2 to 4 treatments on the average. In addition to purpura lasting up to 2 weeks, adverse effects associated with treatment of superficial hemangiomas may include short-term swelling, blister formation, and crusting, transient dyschromia in 4% to 7% of patients, and atrophic scars in approximately 2% to 4% of treated patients. Rarely, ulceration may be induced by PDL within 1 to 2 days of treatment [53].

During the proliferative or early involuting phases, PDL is typically reserved for treatment of ulcerations. Lower fluences, 5 to 7 J/cm^2, are used with cryogen cooling to induce superficial vessel closure without further ulceration of the lesion. Treatments can be undertaken at 2-week intervals, with most hemangiomas requiring 1 to 2 treatments for complete re-epithelialization. In addition, pain is reported to be decreased within the first 3 days following PDL treatment [54,55].

As previously mentioned, residual changes are common following complete involution of hemangiomas and may include telangiectasias, atrophic or redundant skin, and underlying fibro-fatty tissue. These changes present several different targets for laser surgery. Telangiectasias associated with resolution of hemangiomas are effectively treated using the PDL with protocols similar to those described below for other types of telangiectasias [56]. Atrophic or redundant skin may be treated with surgical excision. Alternatively, either ablative or non-ablative laser remodeling may be attempted to induce dermal collagen deposition.

The KTP laser has also been evaluated for treatment of small superficial hemangiomas. Using a 5-mm spot size, fluence of 20 J/cm^2, and pulse duration of 50 ms, improvement, in terms of cessation of growth, regression, and complete resolution were found to be slightly less likely than those results achieved with a short-pulsed (0.3 to 0.45 ms) 585-nm PDL. However, purpura, crusting, blistering, and transient hyperpigmentation are also less prevalent compared to the PDL laser. Swelling is more pronounced and longer lasting with the KTP laser. The incidence of atrophic scarring following KTP laser treatment is similar to that seen with the PDL [57].

Owing to its deeper penetration into the dermis, the long-pulsed 1064-nm Nd:YAG laser can be used percutaneously or intralesionally to induce involution in deeper or rapidly proliferating hemangiomas. The intralesional technique involves the use of a flexible fiberoptic wand introduced through a cutaneous puncture. Percutaneous Nd:YAG laser irradiation using fluences of 80 to 90 J/cm^2 can be effective in reducing lesion size or inducing complete resolution in deep or mixed-type hemangiomas. Pre-cooling with ice water, ice cubes, or cryogen spraying is used to prevent epidermal damage and is especially important in darker skin tones [58]. Local anesthesia may be required to reduce patient discomfort. The immediate clinical endpoint of treatment is blanching of the lesion. Pulses should not overlap and may be delivered 2 mm apart to decrease the risk of scarring. Following treatment, transient erythema and swelling occur in most patients and may last several days, while crusting may be present for as long as 2 weeks. The incidence of atrophic scarring may be slightly higher as compared to what is seen with the PDL. Treatments are usually repeated every 6 to 8 weeks.

Treating hemangiomas with IPL represents a new application of this device. In the few studies to date, promising results have been obtained in centrofacial hemangiomas using an IPL with a 590-nm filter, fluences of 36 to 45 J/cm^2, and triple pulses with pulse durations of 2.5 to 6 ms and pulse delay of 20 to 30 ms [59]. The large IPL spot size allows for greater penetration into the dermis and for shorter overall treatment time. During treatment, pre-cooling is achieved with a chilled gel, followed by ice packs immediately after therapy. Burning and erythema lasting up to 2 days are common. Also of note, the number of sessions required to clear a hemangioma is usually larger than that with the PDL. Additional studies are needed before the efficacy of this treatment modality can be properly assessed.

Venous Malformations

Venous malformations are low-flow vascular lesions characterized by ectasia of venous blood vessels lined by normal endothelium. They are most commonly present at birth and continue to grow proportionally with the rest of the body. Occasional acquired cases can be seen, frequently occurring on the lips (Figure 1.4). Clinically, venous malformations present as faint blue macules, doughy, easily compressible bluish masses, or, less commonly, complex deep-infiltrating structures. Additional studies, such as magnetic resonance imaging or Doppler ultrasonography, can be obtained to confirm the

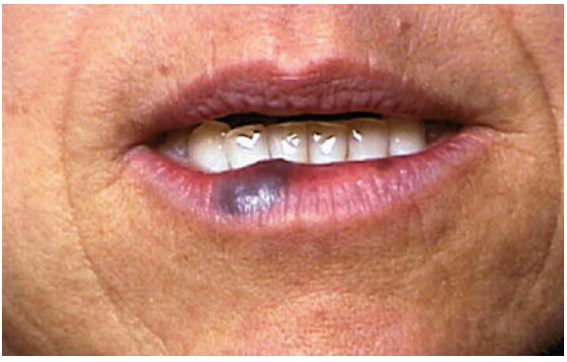


Figure 1.4 Venous lake uniquely responsive to millisecond-domain Nd:YAG laser.

diagnosis. Histologically, phleboliths and organizing thrombi can be seen within dilated vascular channels. Complications, including pain, bleeding, or intravascular coagulopathy, may occur. Treatment options for venous malformations include surgical excision, sclerotherapy, and lasers.

The choice of lasers is limited by the relative depth of vessels within the lesion. Due to their very superficial penetration into the dermis, KTP and dye lasers are typically not effective in the treatment of these lesions.

In contrast, the long-pulsed 1064-nm Nd:YAG laser has been used successfully for venous malformations. Topical or general anesthesia, depending on the location and size of lesion, is usually required to decrease patient discomfort. Fluence of 250 J/cm^2 and pulse duration of 10 ms would be appropriate for the deep, highly ectatic variety of this malformation [60]. The concomitant use of a cooling device reduces the risk of scarring.

Adverse effects associated with the use of the Nd:YAG laser for treatment of venous malformations include reports of pyogenic granuloma formation, scarring [60], superficial burns, and herpes labialis [61]. Of note, venous malformations are very prone to recanalization and subsequent recurrence as late as 6 months following treatment, so patients should be properly advised and followed [61].

Recently, IPL devices have also been used in the treatment of venous malformations. Small lesions under 100 cm^2 respond best, sometimes after 2 to 3 treatments, with clearance of 70% to 100%. Typical parameters include an IPL with a 590-nm filter, long-pulse mode, triple pulses, and fluences around 80 J/cm^2. Adverse effects may include prolonged erythema for up to 5 days, swelling, blistering, and crusting for up to 2 weeks, prolonged pain, and, rarely, bleeding, dyschromia, and scarring

in less than 1% of treated patients [62]. However, since IPL treatment of this lesion is not well described in the literature, optimal treatment parameters and clearance rates need to be confirmed through larger studies.

Arterial and Arteriovenous Malformations

These high-flow malformations are present at birth and most frequently occur on the extremities or trunk as macular erythema. Nodular proliferation typically starts at puberty or following trauma and results in an erythematous to violaceous subcutaneous pulsatile mass, in which a palpable thrill may frequently be discerned [33]. Angiography, Doppler ultrasonography, or magnetic resonance imaging may be used to confirm the diagnosis. Because of their high-flow rates, selective photothermolysis is not feasible and laser therapy for these conditions is disappointing.

Facial Telangiectasias

Facial telangiectasias are a common acquired condition, affecting around 15% of adults with Fitzpatrick skin types I to III. Diffuse telangiectasias may be associated with a variety of conditions, including rosacea, chronic steroid use, actinic damage, and connective tissue diseases, such as CREST syndrome. The lesions are characterized by ectatic post-capillary venules, ranging from 0.1 to 1 mm in diameter, located in the superficial dermis at the average depth of 0.2 to 0.25 mm [33]. Because of their relatively superficial location within the dermis, facial telangiectasias are very amenable to laser and light-based therapy, with PDL, KTP, Nd:YAG lasers, and IPL devices used most frequently (Figure 1.5).

Both the 585-nm, 0.45-ms and the 595-nm, 1.5-ms dye lasers have been used extensively for facial ectasias. Traditionally, fluences of 4 to 10 J/cm^2 were used, depending on the spot size, with 1 to 3 treatments needed for good cosmetic clearance. During treatment, pulses should not overlap by more than 30%. Because of the circular spot size, a reticulated or meshwork-like pattern may be created following a single treatment. The immediate endpoint is similar to that in treatment of PWS, namely vessel coagulation with blanching, followed by purpura. Although makeup may be worn in the absence of blistering or crusting, long-lasting purpura of up to 2 weeks is cosmetically unacceptable to many patients. Additionally, post-treatment edema may be extensive, occasionally obscuring vision when the PDL is used near the eyelids [63]. As a result,

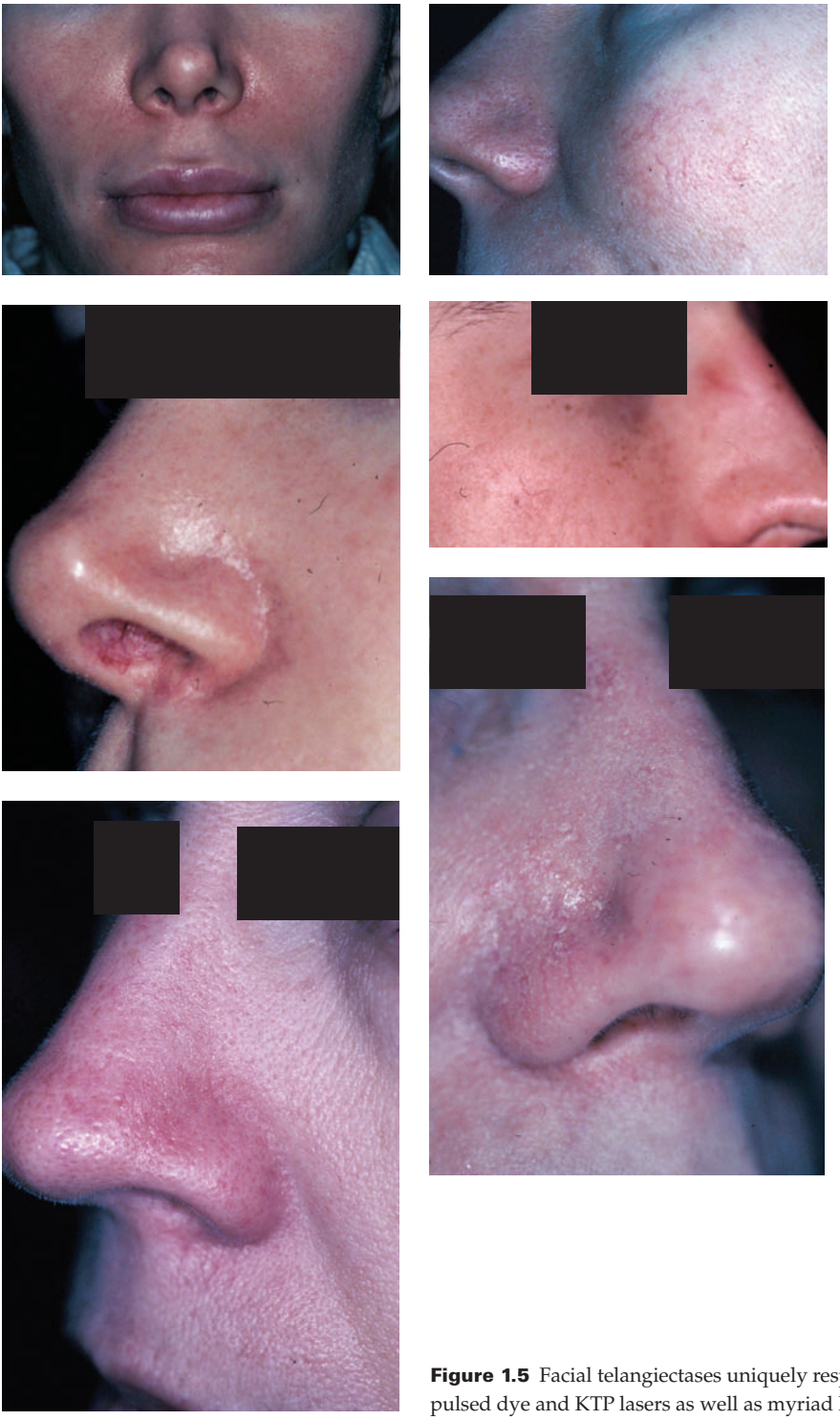


Figure 1.5 Facial telangiectases uniquely responsive to pulsed dye and KTP lasers as well as myriad IPL sources.

subpurpuric doses – achieved by using longer pulse durations of 6 to 10 ms and lowering fluences to just below the purpuric threshold – have been utilized in this region, frequently in combination with pulse stacking or multiple passes. Although somewhat less efficacious, especially in the treatment of larger-caliber, blue telangiectasias, subpurpuric doses are considerably more cosmetically elegant [63–65]. Adverse effects associated with the long PDL may include erythema, swelling, crusting, and transient hyperpigmentation [66]. Patients should also be instructed to avoid sun exposure following treatment to lesson the incidence of post-inflammatory hyperpigmentation.

The 532-nm KTP lasers are ideally suited for tracing small isolated linear telangiectasias less than 1 mm in diameter, as their small spot sizes – between 0.25 and 4 mm – may be difficult to use on larger areas. When used with pulse duration in the millisecond range and fluences between 9 and 25 J/cm^2, depending on spot size, good cosmetic clearance may be achieved after a single treatment [67]. During treatment, the handpiece is moved in a continuous manner to prevent pulse overlap that may result in scarring. The immediate clinical endpoint is blood vessel graying and clearance. The addition of a cooling device and chilled gel reduces the incidence of pain and other potential adverse effects, which may include erythema, edema, blistering, and crusting [68]. Despite slightly lower clearance rates with the KTP laser, the lack of purpura leads to higher patient satisfaction and tolerability compared to the traditional PDL therapy. High-flow vessels, such as those seen on the sides of the nose, will invariably require multiple KTP laser treatments.

The variable-pulse 1064-nm Nd:YAG laser can also be used for facial telangiectasias (Figure 1.6). With deeper penetration and decreased absorption by melanin compared to the PDL, laser light emitted by this device is a good treatment option for larger, bluish telangiectasias, such as the ones found around the nasal alae, as well as for lesions in darker-pigmented individuals. A small spot size – between 1.5 and 3 mm – in combination with long pulse durations of 20 to 40 ms and pre- and post-treatment cooling is recommended in order to avoid overheating of the surrounding dermis with subsequent risk of scarring. Fluences may range between 120 and 170 J/cm^2 for a 3-mm spot size and 220 to 420 J/cm^2 for a 1.5-mm spot size [69,70]. Shorter pulse durations with higher fluences are typically required for the treatment of smaller, red vessels. Longer pulse durations with lower fluences should be used in darker skin types to decrease the risk of dyschromia. The actual selection of treatment parameters depends on observation of the clinical endpoint of vessel blanching. By using small spot sizes

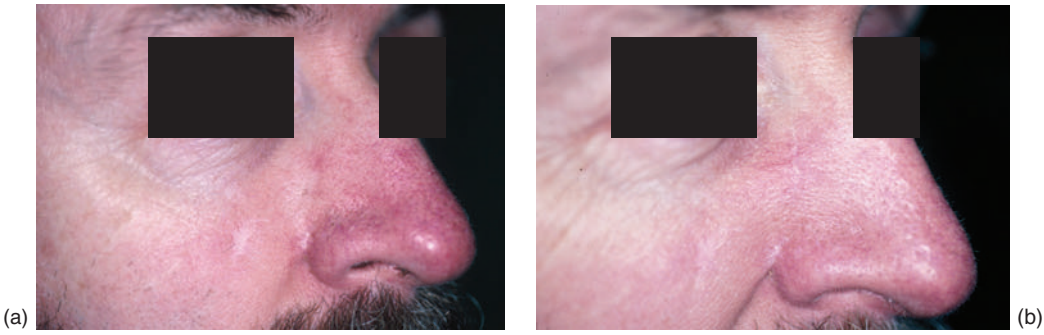


Figure 1.6 **(a)** Facial telangiectasia before treatment with a millisecond Nd:YAG laser and **(b)** improvement in facial telangiectasia after treatment with a millisecond Nd:YAG laser.

and avoiding high fluences, the rates of complications are relatively low, with adverse effects including mild pain during the procedure, mild blistering, and crusting [69,70]. While very effective for treating individual vessels of various diameters, the small spot sizes used for treatment of telangiectasias preclude the use on more extensive surface areas.

As previously mentioned, IPL devices have a large spot size, making it one of the most convenient treatment options for diffuse facial erythema, such as that associated with rosacea (Figure 1.7). Both small and large vessels can be safely and effectively cleared after an average of 2 to 4 treatments in patients with skin types I to IV. Most frequently, larger telangiectasias require a 590-nm cutoff filter with long pulse durations of around 10 ms delivered as triple pulses, with average fluence of 50 J/cm^2. Fine telangiectasias may be treated with a 560- or 570-nm filter in double-pulse mode with pulse duration of 6 to 7 ms and average fluence of 40 J/cm^2. The clinical endpoint is vessel blanching with perilesional erythema. Adverse effects may include erythema, edema that may last over 1 week, purpura for over 3 days, blisters, and transient hypo- or hyperpigmentation [71,72]. However, the effective treatment of telangiectasias and rosacea using an IPL device with low incidence of adverse effects requires experience and prolonged learning time of up to 18 months [71].

Telangiectatic Leg Veins

Ambulatory phlebectomy and sclerotherapy remain the gold standards for treatment of telangiectatic leg veins. However, sclerotherapy may not be feasible in patients with needle phobia,

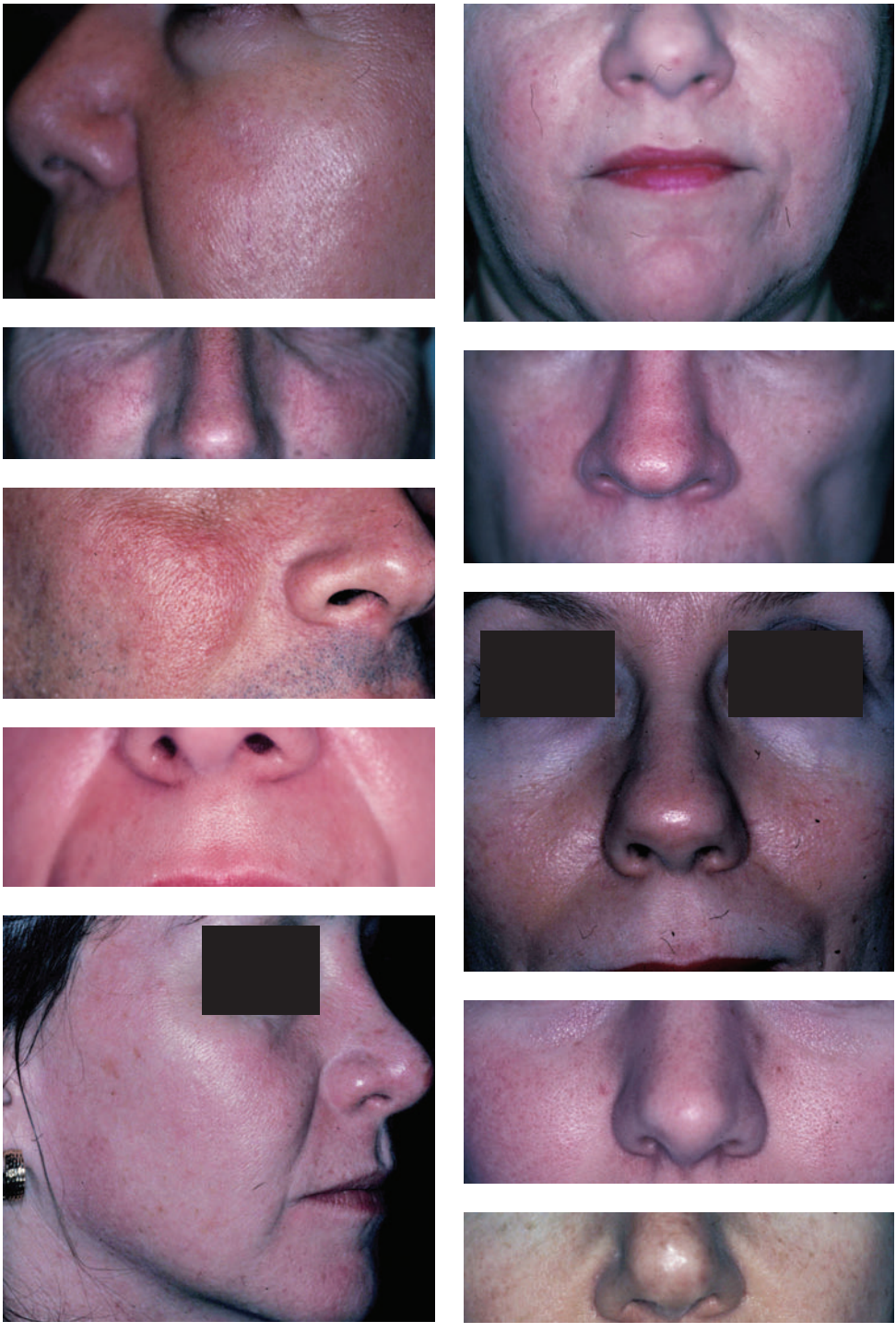
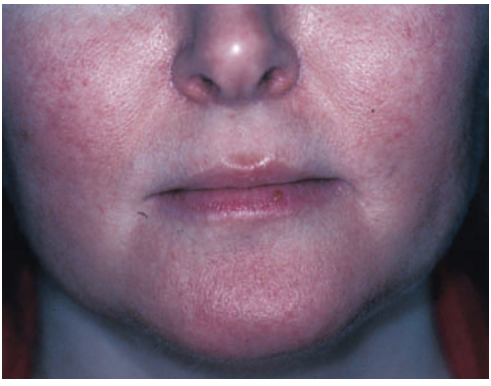


Figure 1.7 Facial erythema can be successfully treated with either the PDL or IPL source.



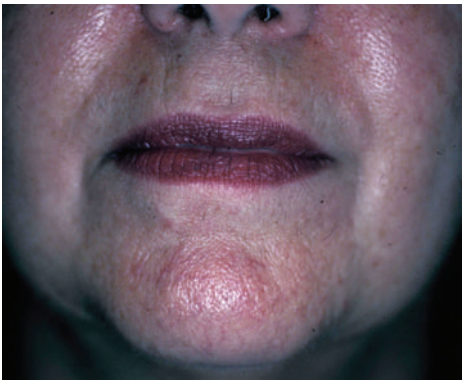


Figure 1.7 (Continued)

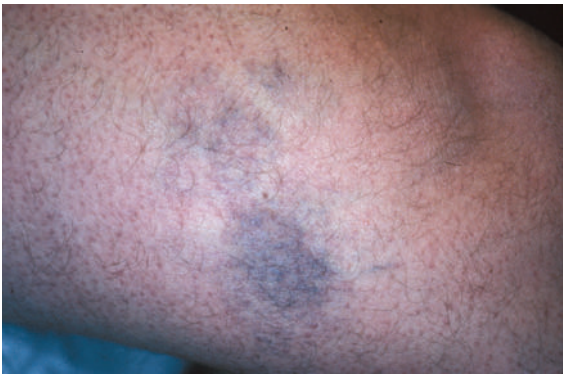


Figure 1.8 Leg spider veins that may be amenable to Nd:YAG laser treatment.

allergies to components of sclerosants, popliteal fossa or ankle telangiectasias, and telangiectatic matting. Recent advances in laser technology, as well as better understanding of leg vein pathology and laser physics, hold a promise for improved treatment options with fewer complications (Figure 1.8).

The unique pathophysiology of leg vein ectasias lies in their relatively large diameter, increased depth in the skin, increased deoxyhemoglobin content, greater hydrostatic pressure, and vessel wall thickening as part of stasis changes. The underlying pathology is clearly complex. Part of the problem appears to be incompetent valves in the communications between the superficial and deep venous channels. Since valves are absent in the superficial venous system, increase in hydrostatic pressure as a result of unobstructed communication with the deep system results in back pressure, vascular dilation, and thickening of

the blood vessel wall. This communication further complicates treatment, as recurrences are common unless the underlying vascular pathology is corrected. Small ectatic leg veins may be subdivided into telangiectasias, venulectasias, and reticular veins, measuring 0.03 to 0.3 mm, 0.4 to 2.0 mm, and 2.0 to 4.0 mm, respectively. These vessels course through the dermis at various depths between 0.15 and 1 mm, with those smaller than 1 mm in diameter typically lying more superficially [73]. The red vessels have a higher concentration of oxygen and oxyhemoglobin compared to the blue ones, which have higher deoxyhemoglobin levels [74].

Several additional laser concepts become important when treating large-caliber vessels. An extended theory of selective photothermolysis relates to the selective destruction of non-uniformly absorbing targets, such as blood vessels. Since the highly absorbing target – in this case, hemoglobin – has to transfer energy through diffusion to the blood vessel to cause sufficient heating of the vessel wall, the pulse duration needs to be considerably longer than the calculated TRT. This duration is known as the thermal damage time [75]. In addition, the TRT of a cylindrical object, such as leg vessels, is higher than that of a sphere. Thus, much longer pulse durations, up to 50 or 70 ms, may at times be used for leg vein laser treatments.

For effective vessel damage to occur, the entire wall has to be heated sufficiently. With vessel diameters of over 1 mm, it is important to select wavelengths and fluences that will not only penetrate the dermis to the depth of the vessel, but will also deliver sufficient energy to the distal wall.

Finally, methemoglobin, an oxidized form of hemoglobin, is formed when blood is heated [76]. Methemoglobin has an absorbance that is 4.75 times higher than that of oxyhemoglobin in the near-infrared range [77]. For larger-caliber vessels, higher energies are used to heat larger volumes; thus, changes in the optical properties of blood with heating become more important and may influence the response of the vessel wall to multiple laser pulses. Higher energies may also result in epidermal damage unless adequate cooling is employed.

Shorter wavelengths, such as those emitted by the pulsed dye and KTP lasers, are generally reserved for treatment of small superficial telangiectasias, especially matted telangiectasias – a frequent complication of sclerotherapy or laser treatment of leg veins. While effective for this indication, as discussed previously, the PDL causes prolonged purpura. In addition, transient or even permanent dyschromia is frequently noted following treatment on the legs with both lasers [78,79]. Although the

clearance rates are improved with the long-pulsed longer-wavelength PDL, the rates of hyperpigmentation are still very high, around 40% [79].

Several near-infrared lasers have been evaluated for treatment of leg telangiectasias. These include the long-pulsed alexandrite laser, diode lasers, and the long-pulsed Nd:YAG laser. These lasers take advantage of the broad oxyhemoglobin absorption peak from 800 to 1200 nm.

Light emitted by the alexandrite laser at 755 nm penetrates tissue for up to 3 mm. An additional advantage of this laser is a relatively high absorption of laser light by deoxyhemoglobin at this wavelength. However, melanin absorption is also significant and the laser can only be used in skin types I to III without a suntan. When a 3 ms pulse duration is used, higher fluences, up to 90 J/cm^2, are required to clear leg telangiectasias. Even with cooling, the incidence of purpura, dyschromia, and matting is high, limiting the usefulness of this laser [80]. Vessels smaller than 0.4 mm, or larger than 1.0 mm, in diameter respond poorly to alexandrite laser therapy [81].

Diode lasers have wavelengths of 800, 810, 910, or 940 nm. Although lower wavelengths, such as 810 nm, give relatively low rates of clearance [80], the newer 940 nm diode lasers equipped with a cooling device hold promise for successful treatment of vessels between 0.8 and 1.4 mm in diameter. The immediate clinical endpoint of treatment is vessel clearance. This longer-wavelength laser also allows for safe treatment of patient with skin types I to IV, with adverse effects limited to pain, mild short-lasting erythema, transient crusting, telangiectatic matting, and transient hypopigmentation [73].

Millisecond-domain Nd:YAG lasers currently offer the best results of all lasers for ectatic leg veins of up to 3 mm in diameter. Small spot sizes of 1.5 mm are used for smaller red telangiectasias with pulse durations of 30 to 50 ms and fluences of up to 600 J/cm^2, whereas larger blue veins require larger spot sizes, such as 3 mm, longer pulse durations of 50 to 60 ms and lower fluences of up to 370 J/cm^2 [82]. With proper parameters and cooling, this laser can be safely used in patients with skin types I to V. If contact or cryogen spray cooling is used, the adverse effects may include bruising, transient hyperpigmentation, and pain. However, treatment of larger-caliber veins may be associated with considerable discomfort, and patients may prefer sclerotherapy for such vessels [83]. An additional consideration in the treatment of leg veins using an Nd:YAG laser is the use of non-uniform pulse sequences. This concept is based on the increased laser energy absorption by methemoglobin

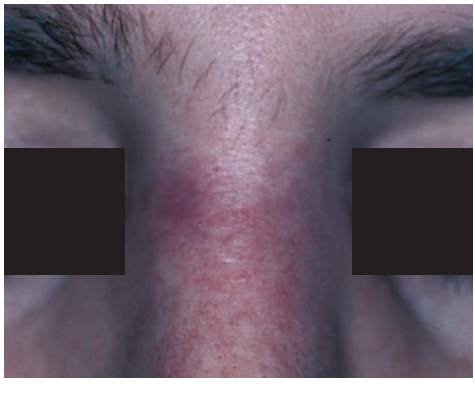
produced during heating of blood, as described above. If long exposure is achieved through a sequence of shorter pulses, the later pulses require considerably less energy than the first. Taking advantage of this concept, similar clinical improvement in leg veins can be achieved using less overall fluence. The result is decreased pain, lower incidence of adverse effects, and successful use in patients with skin type VI [84].

Miscellaneous Vascular Lesions

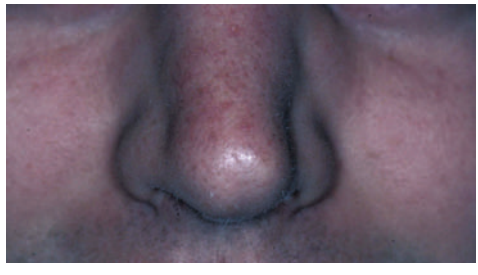
Spider Angiomas

Also known as spider nevi, spider angiomas consist of a central feeder arteriole 0.1 to 0.5 mm in diameter connected to superficial ectatic capillaries at the depth of 0.3 mm [33]. Multiple spider angiomas may be present in hyperestrogenic states, such as liver cirrhosis, and hereditary hemorrhagic telangiectasia, or Osler–Weber–Rendu, syndrome. Because of the superficial nature of these lesions, KTP and PDL are very effective at clearing spider angiomas (Figure 1.9).

The feeding arteriole is usually treated first. A helpful technique used to isolate and to decrease blood flow within the central arteriole is diascopy. Laser pulses are then delivered directly to the vessel, followed by release of diascopy and treatment of surrounding telangiectasias [33]. Good results can be achieved using a KTP laser with pulse duration of 10 to 14 ms and fluences between 10 and 12 J/cm^2 [85]. If using a PDL, a spot size of 5 or 7 mm and fluences between 8 and 10 J/cm^2 are usually effective [86]. One to two treatments administered 4 to 6 weeks apart may be needed for complete clearance. Aside from purpura seen with the PDL



(a)



(b)

Figure 1.9 (a) Spider angioma before laser treatment and **(b)** resolved angioma after laser treatment.

therapy, the incidence of adverse effects is low when treating these lesions.

Cherry Angiomas

Cherry angiomas are common acquired vascular tumors, most commonly found on the trunk. They present as bright red well-circumscribed papules and tend to increase in number with age. Histologically, large interconnected vascular dilations, ranging from 10 to 50 μm in diameter, are closely packed within the papillary dermis [87].

A variety of lasers and light sources can be used in the treatment of this benign vascular lesion, including argon, KTP, PDL, and Nd:YAG lasers and IPL devices [88,89]. All modalities of treatment work well.

Pyogenic Granulomas

Pyogenic granulomas, also known as lobular capillary hemangiomas, are eruptive vascular lesions frequently arising at sites of trauma. They are most commonly seen in children and are prone to bleeding. Multiple lesions may appear in association with isotretinoin or anti-retroviral therapy. Histologically, lobules of dilated capillaries are separated by myxoid stroma. A central feeding arteriole is always present and resembles that of a spider angioma [33].

Thin pyogenic granulomas are very amenable to laser treatment. PDL is most commonly used for these lesions (Figure 1.10). Standard purpuric doses with cooling are typically used with good clearance after 1 to 2 treatment sessions [90,91]. Alternatively, tissue vaporization using CO_2 laser may be performed, but may be associated with scarring [92].

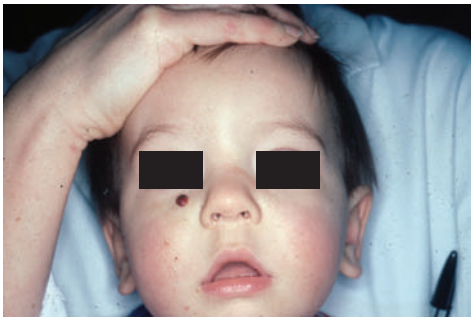
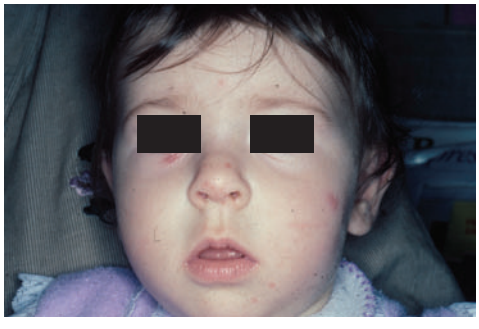
(a)   (b)

Figure 1.10 (a) Pyogenic granuloma before laser treatment and **(b)** improvement in pyogenic granuloma after PDL treatment.

Conclusions

Vascular lasers were among the first to be developed in accordance with the principles of selective photothermolysis. Over the years, multiple modifications have taken place to better adjust to the specific characteristics of treating vascular lesions. Treatment options have further expanded with the introduction of IPL devices. As new therapies emerge, treatment of vascular lesions will likely continue to improve with higher clearance rates, faster resolution, and fewer adverse effects.

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Laser Hair Removal

2

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Laser Hair Removal

2

KEY POINTS

- Laser and light-based hair removal leads to permanent hair reduction, but not necessarily lifetime permanent hair removal
- Attempts to correlate efficacious light-based hair removal with treatment of anagen cycles have failed
- Longer-wavelength systems are safer for darker skin types
- Longer-wavelength systems in general create more discomfort than shorter-wavelength systems

Introduction

Excess or unwanted hair is a common problem affecting both genders. Over time, this problem has been dealt with in various ways, including plucking, threading, shaving, waxing, and electrolysis. Although effective for short-term control of hair growth, most of these methods are associated with significant pain and prolonged treatment times, making them fairly impractical for larger areas.

First introduced in the mid-1990s, laser hair removal has become an accepted treatment modality for patients seeking to reduce unwanted hair and has been found to improve quality of life for many patients [1,2]. Lasers currently in use for hair removal include the normal-mode ruby, normal-mode alexandrite, diode, and neodymium:yttrium–aluminum–garnet (Nd:YAG) lasers, as well as intense pulsed light (IPL) devices. Newer combinations with radiofrequency (RF) devices have created additional possibilities in hair removal and will also be examined in this chapter.

Essential Concepts

Classification of Disorders Characterized by Excess Hair

Excess hair can be classified as either hypertrichosis or hirsutism. Hypertrichosis occurs in all genders and may be present

at any body site. It can be further subdivided into acquired and congenital, as well as localized and generalized forms. Hypertrichosis may be associated with a variety of underlying tumors and malformations, such as melanocytic and Becker's nevi, metabolic disorders, such as porphyrias, internal malignancies, as in acquired hypertrichosis lanuginosa, and medications, such as minoxidil, cyclosporine, and phenytoin.

Hirsutism is the presence of excess terminal hairs in women in androgen-dependent locations, most commonly on the face. Excess endogenous androgen may be released either by the ovaries or the adrenal glands, most commonly in the setting of polycystic ovarian syndrome, congenital adrenal hyperplasia, or adrenal tumors. Exogenous androgens may also cause this condition, whereas most other medications cause hypertrichosis rather than hirsutism. Genetic predisposition may also play a role, as some ethnic groups have relatively more facial hair than others.

However, the majority of laser procedures aimed at hair removal in both genders are not performed for medically excessive hair growth, but rather for unwanted hair. Patient preferences may be influenced by social or personal perceptions of normal hair distribution and density. Thus, clear understanding of the patient's specific expectations and of the actual capabilities of laser hair removal is a must for anyone undertaking such procedures.

Hair Anatomy and Physiology

Generally, three types of hair are recognized: lanugo, vellus, and terminal. Lanugo is fetal-type soft, fine hair. Vellus hairs are non-pigmented, superficially located, and are typically under 30 μm in cross-sectional diameter [3]. Terminal hairs are usually thicker than 40 μm, but may vary widely in their thickness, depending on the size of the hair bulb.

Anatomically, a terminal hair follicle can be subdivided into the inferior segment, the isthmus, and the infundibulum. The inferior segment extends from the deepest portion of the hair follicle to the bulge and contains the hair bulb with germinative matrix cells and melanocytes. It also envelops dermal papilla, a highly vascularized connective tissue. The isthmus includes the portion of the hair follicle from the bulge, where the arrector pili muscle attaches, to the opening of the sebaceous duct. The infundibulum then extends from the sebaceous duct opening to the surface of the epidermis. Of note, hair follicles are angled, so that the bulge lies on the deeper aspect of the follicle.

From the outside in, a hair follicle is composed of the outer root sheath, the inner root sheath, and the hair shaft, with further subdivisions within each structure. The inner root sheath provides a rigid support for the growing hair shaft and disintegrates above the level of the bulge in the isthmus. The slippage plane between thus encased hair shaft and the remainder of the hair follicle is at the companion layer of the outer root sheath [4]. In its turn, the outer root sheath becomes continuous with the epidermis at the level of the infundibulum. In addition to epithelial cells, the outer root sheath contains melanocytes, Langerhans cells, mast cells, Merkel cells, and neuronal stem cells, all of which function within the hair follicle itself and may serve as a reservoir for repopulation of epidermis following injury [5–9].

Hair undergoes asynchronous cycling between periods of active synthesis (anagen), regression (catagen), rest (telogen), and shedding (exogen) [10]. Hair shaft growth and pigmentation takes place only during anagen, which starts with the secondary hair germ at the level of the bulge, about 1.5 mm below the surface of the skin [11]. As the anagen phase continues, the hair bulb moves deeper into the dermis and reaches its deepest position within the subcutaneous fat, about 2 to 7 mm below the surface of the skin, depending on the location. Transition from anagen to catagen, an important process in hair removal, appears to be regulated by changes in the expression of multiple growth factors, such as transforming growth factor-beta 2 and fibroblast growth factor 5 [12,13]. During catagen, controlled involution results from massive apoptosis of follicular epithelial cells in the inferior segment [14]. By the end of this phase, the dermal papilla condenses and moves up to the level of the bulge, while the involuting epithelial column is reduced to a secondary germ [15]. This is accompanied by cessation of melanin production and apoptosis of some follicular melanocytes, eventually resulting in depigmented club hairs during telogen [16]. Telogen is characterized by relative proliferative rest. The mechanism of transition back to the active anagen phase is not completely worked out, but likely involves interactions between the secondary germ, the bulge, dermal papilla, and various signal molecules [17–19].

The duration of anagen determines the length of the hair shaft. Catagen phase is relatively constant throughout different locations and usually lasts around 3 weeks. On the other hand, telogen and, especially, anagen phases vary significantly between different body sites (Table 2.1). As will be discussed below, this may have potential implications not only for optimal frequency of laser treatments, but also for determination of permanency of laser hair removal at a given site.

Body site	Duration of anagen (months)	Duration of telogen (months)	Percentage of hair in telogen
Scalp	48–72	3–4	10–15
Eyebrows	1–2	3–4	85–94
Moustache	2–5	1.5	34
Beard	12	2–3	15–20
Axillae	3–6	3–6	31–79
Arms	1–3	2–4	72–86
Pubic area	3–6	0.5	65–81
Thighs	1–2	2–3	64–83
Lower legs	4–6	3–6	62–88

Table 2.1 Hair cycle based on anatomic location [20,21].

Follicular Stem Cells

Originally assumed to be the secondary germ, the location of follicular stem cells was later proposed to be the bulge. Cells within the bulge were found to be slowest-cycling and longest-lived [22]. Most importantly, however, it has recently become possible to conduct sophisticated lineage analysis, which definitively concluded that follicular stem cells residing in the bulge area give rise to all epithelial cell types within the hair follicle and the hair shaft [23]. It was also shown that, unlike the bulge cells, secondary germ cells are transient amplifying cells with a finite proliferative potential [24]. However, recent finding with critical implications for laser hair removal is that following epilation injury to the bulge cells, these transient amplifying cells in the secondary germ are able to "de-differentiate," repopulate the bulge area, and re-express bulge cell markers [25]. As will be discussed below, these findings confirm that permanent and complete hair removal may frequently be difficult.

Follicular Melanocytes, Melanin, and Hair Color

Whereas melanocytes are present in all segments of the hair follicle, only those in the upper part of the hair bulb and in the upper portion of the infundibulum produce pigment under normal conditions. Those in the upper part of the hair bulb transfer their melanosomes to the growing hair shaft [26]. As mentioned previously, melanogenesis ceases during catagen, resulting in depigmented proximal hair shaft of the club hair.

Infundibular melanocytes function similarly to their epidermal counterparts. On the other hand, melanocytes in the outer root sheath of the hair bulb and those in the mid and lower hair follicles are typically amelanotic. They may, however, become activated following injury [27].

Hair color is determined by the amount, the distribution, and the type of melanin contained within the hair shaft. The two types of melanin found in human hair are brown-black eumelanin and red pheomelanin. As could be predicted from its principal role in the prevention of ultraviolet light-induced carcinogenesis, melanin best absorbs light in the ultraviolet region of the spectrum, with gradual decrease in absorption in the visible and near-infrared ranges. However, the absolute absorption by pheomelanin at any wavelength is much smaller than that of eumelanin. For example, at 694 nm, the absorption of light energy by pheomelanin is only 1/30th that of eumelanin [28]. The switch in production between pheomelanin and eumelanin is dependent upon the presence of functional melanocortin 1 receptor. Thus, most redheaded individuals are either compound heterozygotes or homozygotes for mutations in the gene encoding for this receptor [29]. Compared to black or dark brown hair, blond hair results from reduced number and decreased melanization of melanosomes, with eumelanin still being the most prevalent pigment [30]. Gray hair is caused by depletion of melanocyte stem cells, with gradual reduction in the number of pigment-producing melanocytes [31]. Finally, senile white hair demonstrates complete absence of tyrosinase activity [32].

Hair Removal and Laser Biology

The term "hair removal" is quite ambiguous. Patients may believe that all the hair at a given site will be completely and permanently removed. Even in the best candidate with fair skin tone and dark hair color, this may not be feasible. In such patients, permanent hair reduction, rather than complete removal, is the usual outcome. Permanent hair reduction is defined by the FDA as stable decrease in the number of terminal hairs for a period longer than the complete hair cycle at a given site following a treatment regime, which may include multiple sessions [33]. Frequently, regrowing hair is thinner and lighter, as hair follicles are miniaturized. Patients with red, blonde, gray, or white hair may not get permanent hair reduction, but typically experience temporary hair loss, which can be maintained through treatments every 3 months. Although such results are becoming more predictable since the initial reports of laser hair

removal, certain uncertainties in laser biology and physics persist and will be addressed below.

One of the uncertainties in laser hair removal is the exact tissue target. Although not definitively proven, from the above discussion of the hair cycle and follicular stem cells, it appears that complete destruction of hair follicle without regeneration potential may occur when both the germinative cells in the bulb and the stem cells in the bulge area are destroyed. As follicular stem cells appear to be very resilient to thermal damage, this may be difficult to achieve [34]. However, even without coagulation necrosis of the entire hair follicle, laser hair removal may still be accomplished by inducing progression to catagen phase, although the exact mechanism of such induction have not yet been fully worked out. In either case, in order to avoid damage to the surrounding dermis and overlying epidermis, principles of selective photothermolysis have to be employed [35].

Follicular and hair shaft melanin is a convenient chromophore, as it has good absorption in the 600 to 1100 nm optical window, thus allowing for penetration of light to sufficient depth without significant absorption by water. Follicular melanin is also about 2 to 6 times denser than the epidermal melanin [36], with the highest concentration in the hair bulb, one of the areas important for follicular destruction.

Like hemoglobin in blood vessels, melanin absorbs photons of light, becomes activated, and then releases the extra energy in the form of heat. Heat then has to propagate to the tissue target, in this case, the hair follicle. As discussed elsewhere in this book, thermal relaxation time (TRT) is the time required for the target to cool sufficiently through dissipation of heat to surrounding structures. Therefore, if the bulb and the bulge are to be selectively targeted, the duration of light exposure, or pulse duration, has to be shorter than the TRT of the hair follicle. In addition, it has to be longer than the TRT of the hair shaft to prevent the latter from vaporization and subsequent loss of chromophore. TRT is directly proportional to the square of the size of the object. Thus, for an average terminal hair, the TRT is estimated to be between 0.6 ms for fine hair and 9.6 ms for coarse hair [37]. To avoid epidermal damage, pulse duration should also be longer than the epidermal cooling time, approximately 3 to 7 ms.

TRT of the hair follicle, however, represents another uncertainty in laser hair removal. While traditionally thought to be around 20 to 40 ms for a medium-sized follicle[36], it is a matter of some controversy, as well [37,38]. When regarded as a unit, melanin within a hair shaft represents a cylinder of absorbers, with subsequent heat conduction in the outward direction. Heat

then has to diffuse through a non-uniformly absorbing target structure. Physics pertaining to such structures have recently been described in the extended theory of selective photothermolysis [37]. According to this theory, in order for selective photothermolysis to take place, pulse duration has to be shorter than or equal to thermal damage time (TDT). TDT is the time needed for the outermost part of the target to reach damaging temperature by heat diffusion from the absorber. TDT was then calculated to be considerably longer than the TRT, approximately 170 to 610 ms for a medium-sized hair follicle. These calculations have, however, been questioned [38], and the exact mathematical constructs that correspond to observed in vivo behavior have yet to be developed. It appears, however, that longer pulse durations are necessary for thicker-caliber hair and may enhance selectivity, thus allowing for safer treatment in pigmented skin.

Precise timing of treatments is also not certain. It is assumed that early anagen may be more amenable to damage by laser beam. As discussed above, the hair bulb is located superficially during this stage, allowing for adequate light penetration. Telogen hair is also superficial; however, the proximal hair shaft is depigmented and hence does not absorb laser energy well. On the other hand, fat is a better thermal insulator than collagen, so that damage to a hair bulb located in the subcutaneous tissue would be better confined to the hair follicle. Additionally, human hair cycles are not synchronized, which further complicates studies on the influence of hair cycle on laser hair removal. Consequently, results have been contradictory [39–40]. Attempts to correlate effective hair removal with targeting anagen hairs have, in general, failed. Further research in this area is needed; in the meantime, most laser sessions for hair removal are currently carried out in 4- to 8-week intervals, with small, if any, regard as to the body site. There is, however, an apparent difference in response to laser treatment based on location. The upper lip, chin, scalp, and back are generally associated with weakest response, whereas the remainder of the face, chest, legs, and axillae typically demonstrate higher clearance rates.

Further Laser Biology: Wavelength, Spot Size, Fluence, and Cooling Methods

Upon entering a biological tissue, such as skin, photons of energy undergo either scattering or absorption. Since heat is produced only when photons are absorbed [41], it follows that the amount of scattering determines the remaining energy available for biological action. The major cause of scattering in skin is collagen.

This effect decreases with increased wavelength. Thus, light with longer wavelength can penetrate deeper into the dermis. This concept has several implications on laser hair removal. First, in cases of low contrast between skin tone and hair color, such as darkly pigmented individuals or light hair in fair individuals, a significant portion of emitted light is absorbed by the epidermal melanin. This occurs because epidermal melanin absorbs energy not only from direct exposure, but also from backscattering. As wavelengths of light increase, a greater ratio of dermal-to-epidermal deposition of energy results in greater safety in such individuals. Second, because of deeper penetration into the dermis, light with longer wavelength causes greater bulk tissue heating. In addition, since melanin absorption decreases with increasing wavelength, higher fluences need to be utilized. This combination results in greater patient discomfort and should be taken into consideration when performing laser hair removal. As mentioned previously, red hair contains pheomelanin, which absorbs poorly at any wavelength, but especially beyond 800 nm. Therefore, shorter wavelengths, such as those of ruby or alexandrite lasers are needed in these patients.

After being scattered, photons closer to the center of the beam may, in fact, regain the initial direction of travel through their interaction with other photons. On the other hand, if scattered, photons at the periphery of laser beam may not be able to regain it. Therefore, the percentage of light lost to scattering is larger for smaller beam diameter, or spot size, than for a larger one. Two corollaries of this principle are that energy density, or fluence, is lowered for larger spot sizes and that a very small spot size may, in fact, not allow for sufficient depth of penetration, even with longer wavelengths. Thus, the largest spot size accommodated by the size of the treatment area may lead to better efficacy, as well as decreased overall treatment time.

After a spot size is selected, the choice of fluence depends of the amount of chromophore in the target structure, as well as selected wavelength. Higher fluences are needed when the amount of chromophore is reduced, as represented by blonde or thinner-caliber hair. As well, as was previously discussed, higher fluences are used with longer wavelengths due to the nearly linearly decreasing absorption of light by melanin at those wavelengths. In addition, fluences diminish rapidly as a function of the depth of penetration, as progressive absorption and scattering result in decay of the original energy. Therefore, even though temporary hair removal will occur at almost any fluence, higher fluences may result in longer-lasting or more permanent hair reduction. This is limited by the possibility of

epidermal damage with higher fluences, so that signs of such damage, such as whitening or blistering of the epidermis, should prompt a reduction in fluence.

Epidermal cooling during treatment accomplishes two goals. First, it minimizes the risk of epidermal damage due to absorption by epidermal melanin. Such damage may result in blistering, discoloration, and scarring, and is especially important for darker pigmented individuals. Therefore, epidermal cooling allows for use of higher fluences while minimizing the risk of epidermal damage. Second, it has temporary anesthetic effect, thus reducing patient discomfort during treatment. Epidermal cooling can be separated into contact and non-contact. Contact cooling may include cold gel, chilled sapphire window, and cooled copper plate. Non-contact cooling includes cold air convection and dynamic cooling with automatic spraying of liquid cryogen, tetrafluoroethane, immediately prior to laser pulse.

IPL Devices and Hair Removal

IPL devices are based on the same principles of selective photothermolysis as conventional lasers. They are, however, polychromatic or broadband sources of light with emitted wavelengths in the 500 to 1200 nm range. In order to achieve selectivity, a variety of cut-off filters are employed, so that lower frequencies are filtered out. The choice of filtered wavelengths is determined using the same criteria as those described above for lasers. They can thus be altered based on patient's skin type, hair color, and the desired depth of penetration.

Pulse duration is adjustable and may be set to as high as 88.5 ms on some systems. When used with high fluences, the total pulse duration may be split into multiple pulses separated by variable pulse delay to allow for epidermal cooling. A distinct advantage of IPL devices is their very large spot size – 120 to 600 mm^2, depending on the individual system – allowing for deeper penetration and faster treatment [42].

RF Devices and Hair Removal

RF systems do not emit electromagnetic radiation, but are actually high-frequency electrical devices capable of producing alternating current in the range of 0.3 to 40 MHz. In a monopolar system, an electrode is brought into contact with a biological tissue, such as skin, while a large-size grounding electrode is attached to the body at a distance. In a bipolar system, two electrodes separated by a fixed distance come in contact with

the biological tissue, resulting in a current of electrons flowing through an area limited by the electrodes [43].

The flow of electrons is defined by Ohm's law, which states that for a given electric potential, the current will be higher where impedance or resistance is lower. The heat produced by such flow is described by Joule's law, with the amount of heat directly proportional to impedance. Impedance is inversely related to the inherent electrical conductivity of tissue, which increases with increasing temperature. Thus, higher temperature of tissue leads to lower impedance. Mathematical modeling indicates that the heat decreases as a function of depth. Thus, the depth of penetration is estimated at half the distance between the two electrodes [43]. Such penetration results in volumetric heating of tissue and is, therefore, measured in J/cm^3.

When RF current is combined with optical energy of lasers or broadband light, there appears to be synergistic action, known as electro-optical synergy (ELOS). Current devices have electrodes placed on each side of the sapphire window, 8 mm apart. This allows for generation of sufficient heat at a depth of 4 mm, where it can then target the hair follicle. To achieve synergy, the epidermis is first cooled through contact cooling. This results in higher impedance or resistance of this layer. This is then followed by nearly simultaneous optical and RF pulse, with the latter continued for longer duration [44]. As a result of light exposure, the hair shaft, and hair follicle are preferentially heated. Although the hair shaft is a very poor electrical conductor, the surrounding hair follicle is not. When the hair follicle is heated, its impedance decreases further. This causes the RF current to preferentially pass through the follicle, causing thermal coagulation. Such synergy then allows for the use of lower optical and RF current energies, resulting in lower adverse effects, especially in pigmented skin [45]. Since RF current does not rely on tissue chromophores, it can also be used for treatment of blond and white hair, as will be discussed below.

Pearls and Problems

Patient Selection and Pre-Treatment Care

The ideal candidate for laser hair removal has pale skin and dark, thick hair (Figure 2.1). Hair loss occurs in all patients treated with lasers and light sources, regardless of skin or hair color; however, patients with darker skin tones and light or red hair are less likely to experience permanent hair reduction as their dark haired, light skinned cohorts. Several the same degree of additional considerations are important before

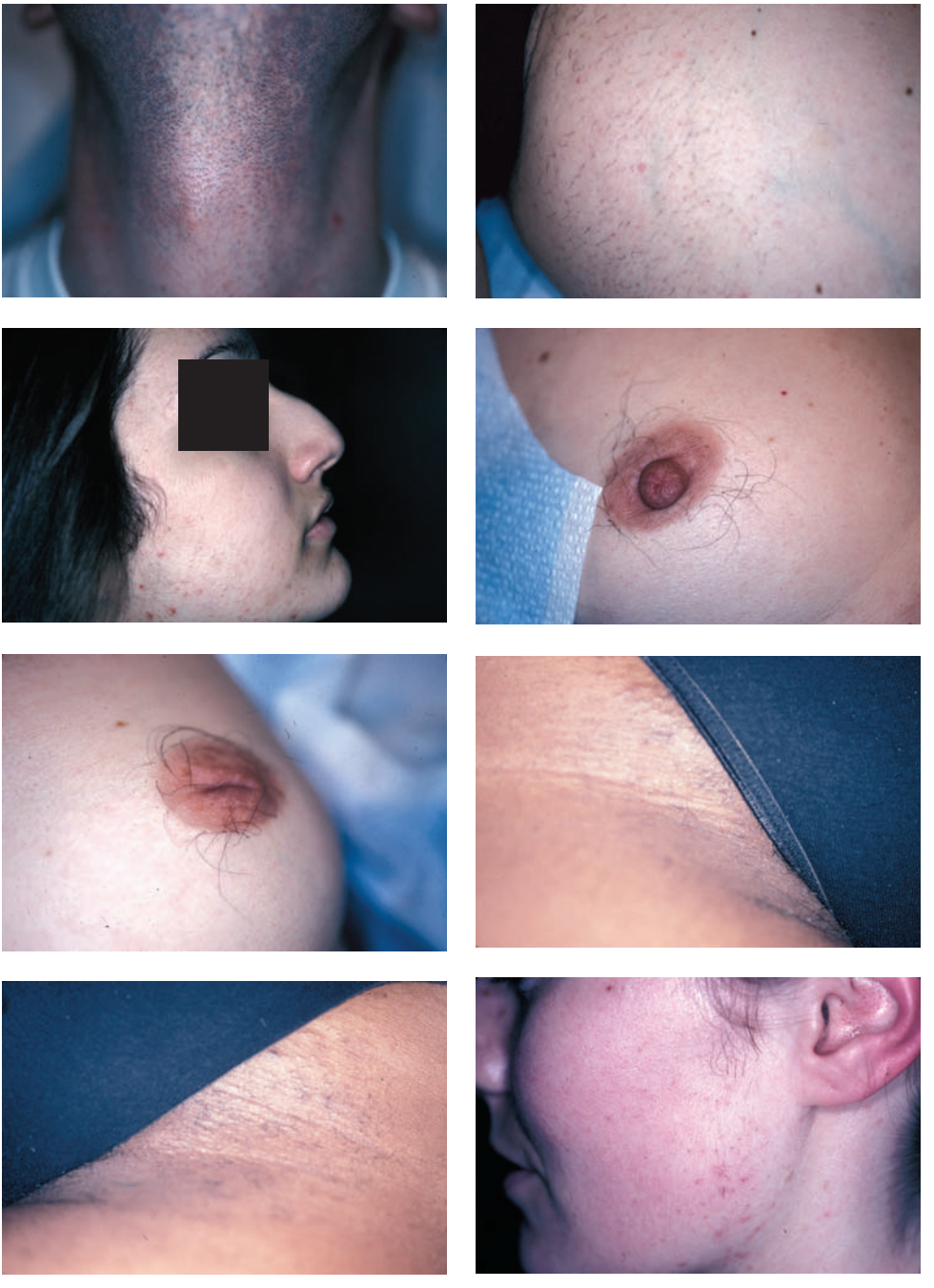

Figure 2.1 Ideal candidate for laser hair removal has light skin and thick dark hair.

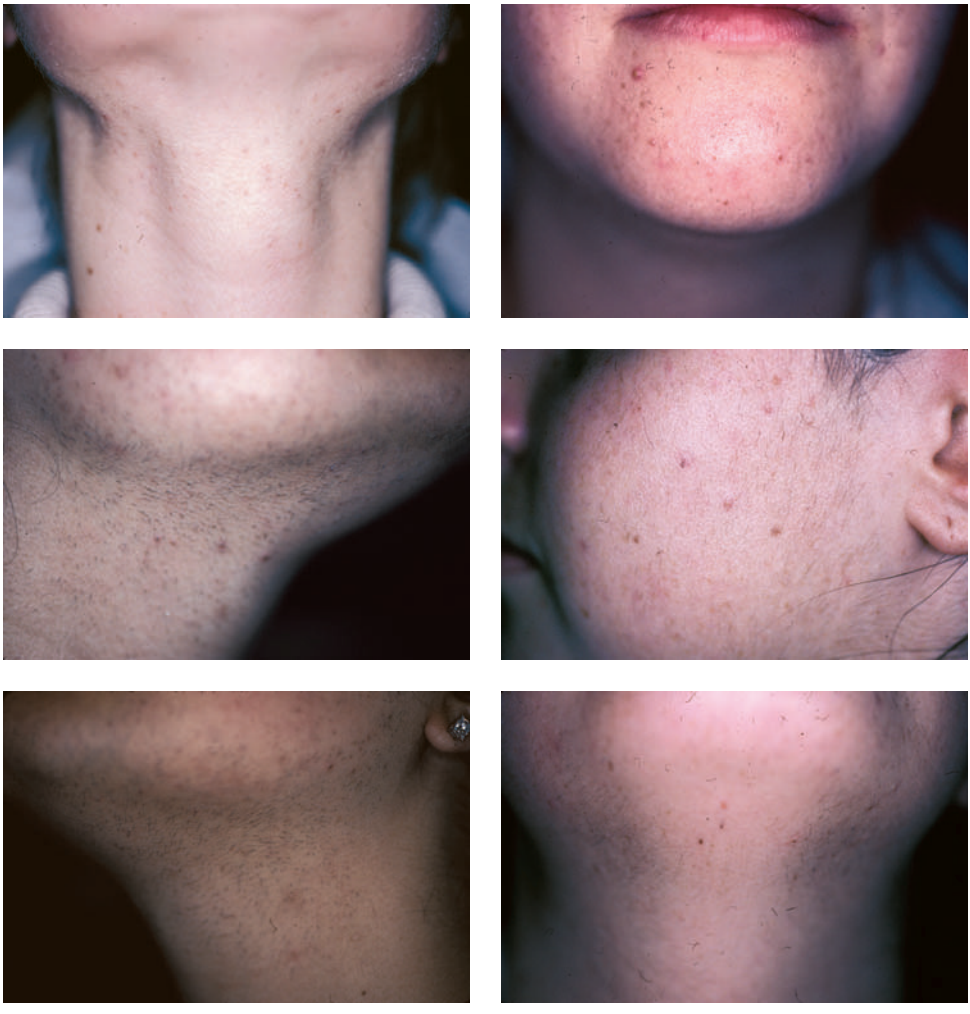

Figure 2.1 (Continued)

undertaking photoepilation. Patients on oral retinoids, such as isotretinoin, should not undergo laser hair removal for at least 6 months following discontinuation of the mediation due to increased risk of keloid formation. Extreme care must be exercised in patients with known history of hypertrophic or keloid scarring. Patients with pigmented lesions, such as ephelids or nevi, may experience lightening or disappearance of these lesions within the treatment area and should be so warned. Finally, although the use of lasers or IPL devices has not been shown to interfere with pregnancy, most laser manufacturers use pregnancy as an exclusion criterion in laser hair removal.

Pre-treatment photographs are recommended to document the improvement following laser therapy. As epidermal melanin absorbs laser energy, patients should have no tan at the time of treatment. To that effect, broad-spectrum sunblocks with sun protection factor (SPF) of at least 15 should be started 4 weeks prior. In individuals with darker skin tones and those with significant suntan, a bleaching cream may be used.

Patients should be advised not to pluck or wax, as these manipulations result in the loss of tissue target. Instead, hairs may be shaved or a depilatory cream may be used. Patients should shave the day before laser treatment; alternatively, treatment areas may be shaved in the office, with cut hairs removed using an adhesive tape to avoid epidermal burns from hair stubs. A topical anesthetic may be applied under occlusion 1 hour before treatment to reduce patient discomfort [46]. Alternatively, tumescent anesthesia may be used in more sensitive areas, such as the axillae [47].

General Treatment Pearls

Immediately prior to each laser hair removal, equipment must be examined for any damage or crust on the handpiece. Cooling system must be turned on and tested. Since lasers and light devices used for photoepilation penetrate deeply and are absorbed by melanin, they have the potential to cause injury to the eyes, especially the retina. To that effect, everyone in the treatment suite must wear goggles designed for the correct wavelength. When working on the face, patients' eyes must be covered with gauze, as goggles frequently permit some light to enter from the sides. If treating near the eyes, the cornea must be covered with metal shields.

In general, all treatment devices may be subdivided into contact and non-contact. As hair is vaporized using non-contact devices, smoke is produced and may be irritating to the airway. Therefore, a smoke evacuation system and adequate ventilation are needed.

For all laser and light systems, the immediate treatment endpoint is vaporization of the hair shaft. This is followed in a few seconds to minutes by mild erythema and perifollicular edema. In general, these should resolve within 10 to 60 minutes. More widespread erythema or confluent edema may indicate epidermal and dermal damage, respectively. If noted, lower fluence, longer pulse duration, or better cooling should be utilized. Gray or white discoloration immediately following laser pulse and lasting a few seconds is an indication of epidermal damage and should be avoided.

During treatment, pressure may be applied to the skin before each pulse. This maneuver leads to decreased depth of the bulb and the bulge, increased penetration of light into the dermis, and decreased amount of hemoglobin, a competing chromophore, in dermal capillaries. Recently, a pneumatic skin flattening device using negative pressure was introduced in conjunction with lasers and IPL devices. This technique may reduce intra-operative pain and post-treatment erythema and edema, while providing more uniform cooling and similar or enhanced efficacy compared to conventional photoepilation [48].

Treatment using each device will now be examined, together with the adverse effects and other problems that may be associated with each laser or light system.

Normal-Mode Ruby Laser

Although ruby lasers were some of the earliest lasers to be used in the treatment of dermatological conditions, they have now fallen out of favor and are only rarely used. This is due to the combination of high laser and maintenance cost, limited clinical applications, and relatively high incidence of adverse effects.

Ruby lasers emit light at 694 nm in the red part of the visible spectrum. Melanin absorption is best for this wavelength compared to all other lasers currently used for hair removal. Unfortunately, high absorption by the epidermal melanin is problematic. Generally, patients with Fitzpatrick skin types I and II without suntan can be safely treated using this laser. Patients with skin type III or those with suntan require efficient epidermal cooling and longer pulse durations, but may still experience post-inflammatory dyspigmentation. It is, thus, recommended that test spots be used in such individuals. Usually, fluence of 20 J/cm^2 is used in an inconspicuous area and may be increased as tolerated, while avoiding signs of epidermal damage, such as graying or whitening, as described previously.

In general, significant hair reduction of around 30% to 35% is noted at 6 months following a single treatment [49,50]. The effect may persist in some patients for up to 2 years [51]. Hair removal is considerably improved following 3 to 4 treatments, with long-term reduction of 55% to 60% noted at 9 months following treatments on the face [50]. The response is poorer on the upper lip, with approximately 6% long-term reduction after 2 treatments and 18% after 3 treatments [52].

When longer, 3-ms, pulse duration is used, apoptosis with subsequent induction of catagen may be seen histologically [40]. Alternatively, shorter pulse durations may result in coagulation within a portion of hair shafts and subsequent inflammatory

response for up to 2 weeks. Depth of laser damage is generally limited to less than 1.5 mm. As well, even in the absence of overt epidermal damage, changes in epidermal melanin may be observed [53].

Because of greater potential absorption by epidermal melanin compared to the other lasers used for hair removal, the ruby laser is associated with a higher incidence of adverse effects, especially in darker skin. As mentioned previously, short-term perifollicular edema and erythema are considered the expected endpoint of treatment, not adverse effects. In skin types I and II, the most common complication is blistering, occurring in 6% of treated patients. Incidence of discoloration, both hypo- and hyperpigmentation, is approximately 2.5% in this population; 4.5% and 2.8% of patients with skin type III may experience blistering and hyperpigmentation, respectively. In skin types IV to VI, the overall incidence of adverse effects is 30%, with 15% of patients experiencing blistering and 10% reporting hyperpigmentation. Around 10% of patients may develop crusting in the treatment areas, with this effect being more prevalent in lighter skin types [54]. On the other hand, atrophic scarring has been reported in up to 3% of patients, usually those with darker skin tones [55]. As would be expected from the earlier discussion of laser biology, the incidence of side effects, such as crusting and dyspigmentation, in darkly pigmented individuals is decreased with longer pulse duration compared to a shorter one [56]. Some of the more rare adverse effects include purpura and erosions in 3% and 2% of patients, respectively [57]. Superficial thrombophlebitis on the chin is an unusual reported occurrence in one patient treated with both the ruby and Nd:YAG lasers. It is, however, not clear which of the two lasers may have caused this adverse effect [54]. Additionally, a case of isomorphic, or Koebner, phenomenon has been described in a patient with lichen planus, so such patients may have to be warned about this possibility [58]. In general, sun-protected sites, such as axillary and pubic areas, have lower overall incidence of adverse effects, whereas extremities are associated with the highest rates of complications [57].

Normal-Mode Alexandrite Laser

Light emitted by alexandrite lasers has a wavelength of 755 nm. At this wavelength there is still very good absorption by melanin, although slightly diminished compared to ruby lasers. Many alexandrite lasers also feature more efficient cooling devices, such as automatic cryogen spraying. Consequently, hair removal using normal-mode alexandrite laser results in

at least as good clearance rates as with ruby lasers and significantly improved hair reduction compared to electrolysis [59]. Slightly diminished absorption by epidermal melanin is also associated with lessened epidermal damage, especially when combined with longer pulse duration.

Patients with skin types I and II can be treated safely using this laser. Patients with skin type III or darker may experience higher risk of hyperpigmentation and require longer pulse duration and efficient cooling. A test spot may be used to evaluate patient response to treatment. The starting fluence for a test spot is usually 15 J/cm^2, lower than that for ruby laser. This is likely due to increased penetration of light with longer wavelengths. If well tolerated, fluence may be increased, with careful avoidance of epidermal whitening during treatment.

In patients with lighter skin tone, no difference in long-term hair reduction after 3 treatments has been found between shorter, 2- or 5-ms, and longer, 10- or 20-ms, pulse durations, with similar incidence of adverse effects [60–62]. This may be explained by the TDT of the hair follicle being significantly longer than all of these pulse durations. Since shorter pulse duration allows for higher scanner frequency, it may be preferred for minimizing overall treatment time. Longer pulse duration of 40 ms may, however, result in lower incidence of adverse effects in skin types IV to VI [63], but may also be associated with increased patient discomfort. Pre-treatment use of bleaching agents and careful post-treatment sun avoidance are critical in this population. As would be expected, larger spot sizes are associated with better long-term hair reduction [64]. As well, at least in Asian patients with skin types III to V, multiple treatments offer significant improvement in long-term hair reduction after 9 months, with 32% reduction after a single treatment, 44% after 2 treatments, and 55% after 3 treatments with alexandrite laser [65].

Histologically, changes in hair follicles following alexandrite laser irradiation are similar to those found with ruby laser. Immediately following treatment, vacuolar degeneration of the inner root sheath with or without vaporization of hair shaft is observed. Increase in apoptosis can be demonstrated 1 month after treatment; foreign body giant cells may also be observed at this time [66]. When a cooling device, such as cryogen spraying, is utilized, epidermis appears completely preserved microscopically [67].

Adverse effect profile depends on patient's skin type. With pulse duration of 10 ms, the overall rate of adverse effects is less than 1% in skin type I, over 9% in skin type III, and nearly 38% in skin type V. Aside from the expected perifollicular edema

and transient erythema, hyperpigmentation lasting an average of 2 months occurs in 19% of all patients, hypopigmentation lasting an average of 3.5 months occurs in 17%, and crusting occurs in 12%, with most complications observed in darker skin tones. The incidence of these adverse effects is also increased during the summer months, suggesting the importance of post-treatment sun protection and avoidance of suntan prior to treatment [57]. It has, however, been suggested that longer, 40-ms, pulse duration may reduce the overall rate of adverse effects to less than 3% [63]. Blistering may be seen in 2% of patients with skin types I and II, but may increase to 10% in those with skin types IV or higher [54]. As with the ruby laser, the incidence of purpura and erosions is low, 3% and 2%, respectively [57]. Scarring is typically not seen following treatment with alexandrite laser, but may be observed in the setting of severe epidermal damage. First reported with IPL devices, paradoxical hypertrichosis following alexandrite laser hair removal has been reported in several patients with skin type IV and black hair. Hypertrichosis occurred on the cheeks in two patients and arms and back in one patient and was not amenable to further laser therapy even at much higher fluences [68]. Recently, several cases of transient erythematous brown or hyperpigmented rings corresponding to the size of the spacing device have been reported [69]. Although their cause is not certain, it has been proposed that either the cryogen spray nozzle may become misaligned during transportation, the nozzle may not be held perpendicularly to the treatment area, resulting in uneven cooling, or carbonized hair debris are deposited on the spacing device, creating hot spots [70,71].

Diode Lasers

By virtue of using smaller-sized semiconductors instead of the more bulky flashlamps to produce laser light, as well as higher internal reflection of the medium resulting in the use of fewer reflecting mirrors, diode lasers are comparatively small and portable. They are also relatively easier to build and, thus, generally cost less than other lasers used for hair removal.

Depending on the semiconductor used in the system, diode lasers can vary widely in their emitted wavelengths. Those manufactured using derivatives of gallium arsenide produce wavelengths between 660 and 900 nm, whereas those utilizing indium phosphide emit light with wavelengths between 1300 and 1550 nm. Diode lasers currently used for hair removal produce 800- or 810-nm light.

Both 800 and 810 nm wavelengths are absorbed by melanin to a slightly lesser degree compared to the alexandrite laser. Absorption is also approximately 30% less than that of the 694 nm wavelength. However, the rates of hair reduction with the diode laser are similar to those observed with the alexandrite laser, likely due to deeper penetration into the dermis [72,73] (Figures 2.2 and 2.3). Treatment with the diode laser can be somewhat more painful, however, at least partly due to greater volumetric heating of tissue. If necessary, pain can be partially alleviated by reducing the frequency of delivered pulses. Decreased absorption by epidermal melanin permits safe treatment in patients with skin types I to IV [74].

Multiple treatments may improve the efficacy of hair removal, with 28% to 33% reduction at an average of 20 months after a single treatment compared to 34% to 53% reduction following 2 treatments [75]. Larger spot sizes result in slightly better clearance rates, at least in the short term, although long-term

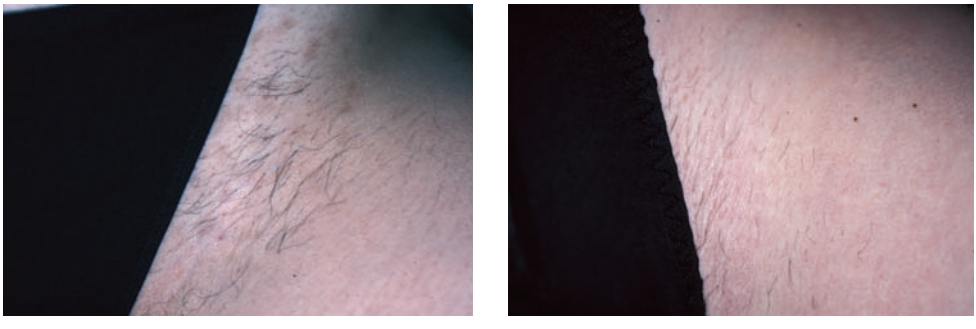

Figure 2.2 Before laser hair removal of the bikini.

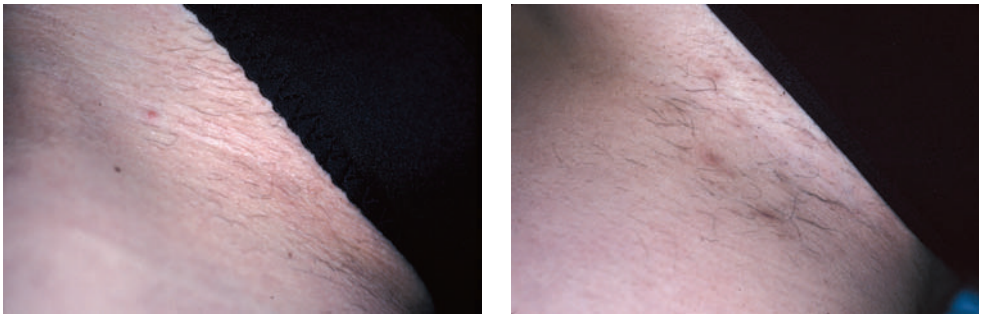

Figure 2.3 Improvement noted after only a single 810-nm diode laser hair removal session. Identical results can be seen with a variety of wavelength systems. Quicker results are seen with the shorter-wavelength systems because of greater melanin absorption.

effect has to be studied further [76]. The new 810-nm diode laser appears to be equally effective to the 800-nm ones in inducing long-term hair reduction at 6 months [77,78].

Since excess hair is a frequent concern in patients with polycystic ovarian syndrome or other patients presenting with severe acne, the contention that oral isotretinoin may not be combined with laser treatments has recently been challenged. A diode laser was safely used in several patients undergoing isotretinoin therapy without increase in adverse effects or long-term sequelae [79,80]. This, however, remains to be tested in larger patient series. Diode lasers also appear to be safe for treatment of eyelashes when metal shields are used to protect the eye [81].

Histologically, fluence-dependent thermal damage to the hair shaft and hair follicle is observed, sometimes with complete destruction of the follicular structure. Significant thermal damage to the hair bulb may also take place, and progression to catagen phase is noted. Mild thermal damage is occasionally noted at the dermo-epidermal junction and the basal layer of the epidermis, especially in darker skin types, but may not result in clinically significant changes [78,82].

As previously mentioned, treatment with a diode laser may result in relatively more patient discomfort compared to lower-wavelength lasers. Blistering, crusting, and transient hypo- and hyperpigmentation are more common in darker patients with skin type IV and higher. Occasionally, hypopigmentation may persist for significantly longer than 6 months and may present as separate circular patterns corresponding to individual laser pulses [83]. Post-treatment folliculitis may be observed in some patients and is likely the result of disruption of hair follicle with subsequent dermal reaction to hair keratins. Unusual adverse effects include terminal hair induction following treatment on the back [84], reticulate erythema similar to livedo reticularis especially in patients with history of chilblains [85], and a case of clinically diagnosed urticarial vasculitis, although histological examination was not performed [86].

Long-Pulsed Nd:YAG Laser

Although significantly less well absorbed by melanin compared to previously described wavelengths, light at 1064 nm is able to penetrate deep into the dermis, up to 4 to 6 mm. Originally used in Q-switched mode with or without topical application of carbon particle suspension, the new millisecond systems appear to offer good results especially for darker skin types, albeit at a price of slightly decreased efficacy in lighter skin [87,88].

Hair reduction is still considerably better in the short term than conventional techniques, such as shaving, with approximately 24% to 29% reduction at 3 months [89]. Higher fluences do not improve short-term results, but may increase the risk of adverse effects, such as blistering [90]. In the long term, substantial regrowth is typically seen after 9 to 12 months following a single treatment. Long-term efficacy is significantly improved after multiple treatments, with 40% of patients reporting at least 50% hair reduction 1 year following 5 treatments [91]. Non-facial skin, such as axillae, may show somewhat better clearance rates compared to facial sites [92] (Figure 2.4).

Histologically, elongation and thermal degeneration of follicular epithelium with complete preservation of epidermis are noted following laser irradiation [93]. In the long term, a reduction in terminal hairs with preservation of sebaceous glands and epidermal pigmentation is observed [92].

Adverse effects encountered with Nd:YAG photoepilation most commonly include blistering, hyper-, and hypopigmentation. Although comparable in lighter skin types (I to III), the incidence of complications in skin types IV to VI is considerably lower with the long-pulsed Nd:YAG than with the other lasers. Overall, the risk of adverse effects in the latter population is less than 10% compared to nearly 30% with the ruby laser. Blistering and hyperpigmentation may occur in 5% and 2% of darkly pigmented patients, respectively [54]. Hair removal using Nd:YAG laser has been found to be considerably more painful than that with diode lasers, likely due to even greater volumetric heating with the former [94]. Although high rates of purpura, up to 18%, have previously been reported following treatment with Q-switched Nd:YAG lasers [57], this does not appear to occur with the long-pulsed lasers. Unusual adverse effects include transient superficial thrombophlebitis in two patients and reticulate erythema similar to that described with diode lasers, although details of both complications have not been elaborated [54,95].

IPL Devices

IPL devices are best reserved for patients with skin types I to IV, although newer models are becoming safer even in darker individuals. A variety of cut-off filters are used to match the patient's skin type and hair color; 515- to 590-nm filters may be used in fair-skinned individuals or those with red hair, as pheomelanin has poor absorption of longer wavelengths. Filters in the 600-nm range may be used in patients with skin types II to III or those with a suntan; 695-nm or higher filters provide for

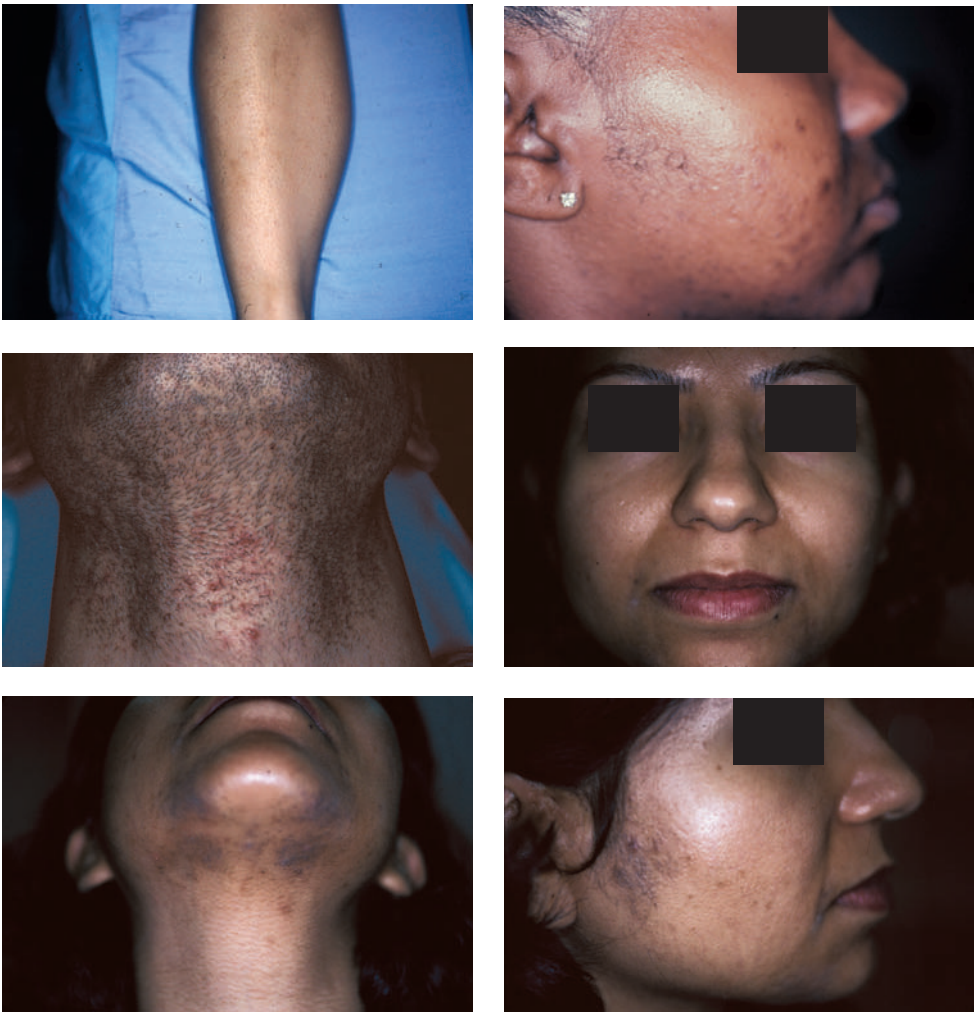

Figure 2.4 Darker-skinned individuals are more safely treated with longer-wavelength systems.

safer treatment in darker skin types. As previously described, longer exposure time is necessary in patients with thicker hair or darker complexion. Light exposure can be delivered as single or multiple pulses. Multiple-pulse mode delivers two to five sequential pulses, depending on the device, and is especially useful in darker complexion. In such individuals, longer interpulse delay is selected to allow for sufficient epidermal cooling. Due to the increased number of parameters used with IPL devices compared to conventional laser systems,

considerable experience is important and novice practitioners are advised to perform test spots prior to initiation of full treatment.

Both short- and long-term efficacy of IPL is difficult to ascertain due to the plethora of devices and treatment settings. It appears, however, that long-term results may be at least as good as those achievable using the alexandrite or the diode lasers [96–98]. Multiple treatments improve clearance rates, with as high as 87% hair reduction at an average of 27 months following a mean of 8 treatments [99]. It is unclear, however, whether performing more than 3 treatments results in added benefit in the long term [100].

Histological studies following IPL hair removal are scarce, especially with the newer devices. Typically, follicular thermal damage, followed by follicular atrophy can be demonstrated with relative preservation of the epidermis [101].

Mild to moderate pain is frequent in hair removal using IPL devices. Additionally, 2% of patients may experience persistent local heat sensation for longer than 24 hours. Transient post-inflammatory hyperpigmentation may be observed in over 16% of patients [102], but may be as high as 45% in patients with skin types IV to VI [103]. Crusting and blistering are moderately common, occurring in 18% and 6%, respectively. Paradoxical effect, as defined by the increase in the number of terminal, pigmented hairs in untreated areas in close proximity to treated sites, can occur in up to 10% of patients and is more common on the neck following treatment of the chin and submandibular area [104]. Transient hypopigmentation may occur in 2% of patients. Scarring is uncommon, but has been reported [102]. Leukotrichia, or the development of white hairs, was noted in several patients treated with an IPL device. The effect persisted for 1 to 4 months in a portion of these individuals, but persisted for longer than 6 months in the majority [105]. Finally, a temporary change from black to yellow hair color was noted in one patient, likely reflecting a switch from eumelanin to pheomelanin production [106].

Combination of RF and Laser or Light Devices

As previously described, RF current is not dependent on tissue chromophores. Thus, devices combining RF current and lasers or broadband light can be used for treatment not only of black and dark brown hair, but also for blond, white, and red hair. As well, by using lower optical fluences, treatment with such devices appears to be safer in darker skin types.

Although a combination with diode laser has also been approved for hair removal, currently published studies mostly utilize IPL with wavelengths between 680 and 980 nm as the source of optical energy. A single treatment using optical energy of 14 to 30 J/cm^2 with pulse duration of 25 ms and RF energy of 10 to 20 J/cm^3 with pulse duration of 200 ms has produced a mean hair reduction of 35% for blond hair at 3 months following treatment [107]. When multiple treatments are undertaken at 8- to 12-week intervals, the average clearance 6 months after 4 sessions is 85% for black hair, 60% for blond hair, 60% for red hair, and 40% for white hair. Lower legs and areas with high hair density require less RF energy. Axillae and legs respond best to treatment, followed by bikini area, trunk, and face [108]. Reduction of facial blond hair after 4 treatments has been found to be 52%, slightly higher than that for facial white hair at 44% [109]. These results are especially impressive, as the treatment areas were the upper lip and the chin, typically resistant to conventional laser hair removal. Vellus hair does not, however, respond to this therapy [110].

Histologically, thermal follicular damage with vacuolar degeneration is noted at the depth of 3.5 mm [108]. Long-term histological studies documenting follicular degeneration or catagen phase induction are currently lacking.

Aside from the anticipated perifollicular edema and transient erythema, adverse effects have been rare and include minimal pain, crusting, transient hyperpigmentation, and hypopigmentation persisting for 3 months [107]. Since this is a relatively new treatment modality, a more complete side effect profile remains to be determined over the next several years.

General Post-Treatment Care

Ice packs applied following hair removal may reduce erythema and swelling. Make-up may be applied immediately following treatment, unless blistering is evident. Mild to mid-potency topical corticosteroids may be used in patients with history of prolonged erythema. In order to minimize the risk of post-inflammatory hyperpigmentation, patients should be instructed on sun avoidance or proper sun protection using sunblocks with SPF of at least 60. Such measures should continue until the next treatment session in order to avoid the appearance of suntan. Patients should also be instructed on possible shedding of the treated hair in the first weeks following treatment, so as not to perceive such occurrence as regrowth. Although treating the unibrow is acceptable, treating eyebrows is not because of the risk of longer-wavelength-induced iris damage (Figure 2.5).

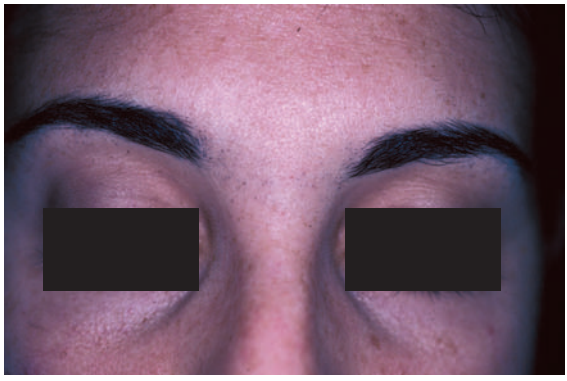

Figure 2.5 Unibrow can be treated. Eyebrows should be avoided.

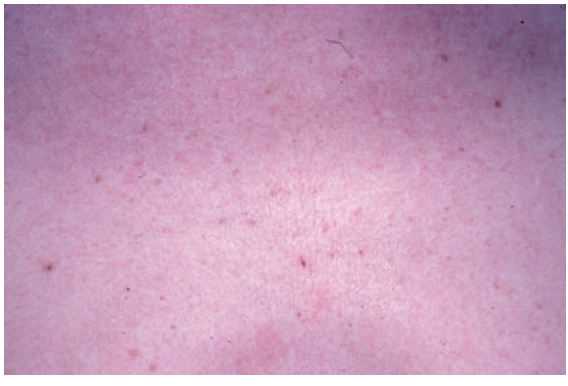

Figure 2.6 Few hair remain after many hair removal treatments. Total removal of all hair remains very unusual.

Although the removal of 100% of treated hair is unusual, it is least likely with longer wavelength, longer pulse duration systems (Figure 2.6).

Additional Clinical Applications

Pseudofolliculitis barbae is a common inflammatory condition resulting from ingrown facial hair. This condition frequently affects African-Americans with skin types V and VI, as well as other individuals with thick curly hair. Long-pulsed Nd:YAG laser has been successfully used to treat this condition [111]. Following 2 treatments in 3- to 4-week intervals, a recent study documented a decrease in the number of papules and pustules of 98%, 87%, and 75% at 1- to 3-month follow-ups, respectively. Of interest, this improvement was significantly higher than was accounted for by hair reduction in the area alone [112]. It is likely that abstinence from shaving adds to decreased

inflammation and subsequent improvement in condition. Since Nd:YAG laser hair removal can be associated with significant pain, attempts have been made to use shorter wavelengths, such as 810 nm diode, in combination with superlong pulse durations of up to 450 ms and contact cooling. Results appear to be promising with good improvement in the number of papules following 3 treatments at 2-week intervals [113].

Pilonidal sinus disease is a chronic condition affecting gluteal cleft typically encountered in young men. Excess hair growth results in inflammation, abscess formation, and eventual appearance of sinus tracts that continue to become inflamed or superinfected. Recently, normal-mode ruby, alexandrite, and 800-nm diode lasers and IPL devices have all been tried in this condition and found to be very efficacious [114–117]. Multiple treatments, usually between 2 and 11, are required at 6- to 8-week intervals and may result in long-term or even permanent remission.

Trichostasis spinulosa is characterized by retention of multiple pigmented hairs and keratinous debris within hair follicles. Clinically, dark spiny papules resembling open comedones are observed, most commonly on the nose, cheeks, and trunk. Recently, an 800-nm diode laser was used for treatment of this condition. Complete clearing for 8 to 12 weeks was noted following 2 monthly treatments, with persistent good improvement for 20 weeks in half of the patients [118].

Folliculitis decalvans and dissecting folliculitis are chromic scarring inflammatory and infectious conditions of the scalp. Successful treatment options are limited and recurrences are common. Normal-mode ruby, diode, and Nd:YAG lasers have been used in these conditions in isolated reports and small series. Following 4 to 8 treatments 4 to 6 weeks apart, patients were able to achieve long-term remission at 6 months [119–122].

Conclusions

Over the years, specific treatment techniques have been refined, yet certain fundamental questions persist. Even so, laser hair removal has become an accepted treatment modality for unwanted and excessive hair. Future advances in this field promise more efficacious devices with further reduced risks of adverse effects.

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3 Pigmented Lesions, Tattoos, and Disorders of Hypopigmentation

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3 Pigmented Lesions, Tattoos, and Disorders of Hypopigmentation

KEY POINTS

- Melasma, traditionally refractile to laser and light source treatment, may respond to newer approaches to treatment
- There is no evidence to suggest that laser treatment of congenital nevi leads to an increased incidence of melanoma in these lesions
- Nanosecond lasers may ultimately be replaced by picosecond lasers for more successful removal of tattoos
- Newer laser-susceptible tattoo inks may greatly simplify the future removal of tattoos

Introduction

Pigmented lesions and tattoos result from excessive or abnormally deposited melanin or other pigment and represent an interesting, yet sometimes challenging, field in cutaneous laser surgery. As tattooing is becoming more common and accepted in society, the popularity of laser tattoo removal continues to grow. This chapter describes the development of lasers emitting ultrashort pulses of light in the nanosecond range that provided laser surgeons with an important treatment modality for such lesions.

In addition, laser treatment options for disorders of hypopigmentation, including vitiligo and striae distensae, will be examined in this chapter. Although relatively recent, laser treatments for such conditions have become a welcome addition in the field where few therapeutic modalities have proven effective.

Essential Concepts

Melanin and Pigmented Lesions: Classification and Implications for Laser Biology

Melanins are not a single compound, but rather represent a class of negatively charged, hydrophobic pigmented polymers.

Melanin synthesis begins with tyrosinase-mediated conversion of tyrosine to 3,4-dihyroxyphenyalanine (DOPA) and dopaquinone. Yellowish-red pheomelanin is produced when cysteine is added to dopaquinone; otherwise, the brownish-black eumelanin is synthesized [1]. In addition to skin and skin appendages, human melanin is produced in such structures as the retina, cochlear stria vascularis, adrenal glands, and parts of the central nervous system. Function of human cutaneous melanin is not completely elucidated, but appears to include absorption of reactive oxygen species and protection of cellular DNA from at least some forms of ultraviolet (UV) radiation [2]. Recent evidence indicates a possible additional function in binding toxic compounds, including metal ions and various medications [3,4].

Once synthesized, melanin is packaged into melanosomes, oval to round lysosome-like intracytoplasmic organelles. In the epidermis, melanosomes are then transferred to keratinocytes from dendritic processes. The exact mechanism is not clear, but is postulated to involve either phagocytosis of released melanosomes or cytophagocytosis of dendritic tips, a process known as apocopation [5]. Once incorporated into the keratinocyte, melanosomes undergo gradual degradation, which parallels terminal differentiation of the keratinocyte.

The size of a melanosome depends on its stage of development, as well as the individual's skin type, with darker skin having larger melanosomes that are more evenly dispersed throughout the cytoplasm. Thus, melanosomes vary from approximately 0.5 to 1 μm.

As described elsewhere in this book, melanin has a broad absorption spectrum from UV to near-infrared wavelengths. Although longer wavelengths are less avidly absorbed by this chromophore, they are also able to penetrate deeper into the dermis due to decreased scatter. Once the laser light reaches the chromophore, it results in the destruction of melanosomes, as demonstrated by membrane disruption and intra-organelle structural changes [6,7].

According to the theory of selective photothermolysis [8], duration of light exposure must be less than the thermal relaxation time (TRT) of the target to cause confined damage. TRT is the time required for the target to cool sufficiently. TRT is directly proportional to the square of the size of the target and can be quickly approximated, in seconds, as the square of the target size in millimeters. Thus, for melanosomes between 0.5 and 1 μm in diameter, TRT varies between 0.25 and 1 μs. It follows, then, that heat confinement can be achieved using laser pulses with durations in the nanosecond (ns) range. Lasers capable of producing such short light bursts are called quality-(Q-) switched.

The mechanism underlying the disruption of melanosomes by a Q-switched laser appears to be photoacoustic in nature [9]. Photoacoustic effect results from the generation of shock waves following laser irradiation. Such waves then cause vibrational damage to cellular structures and rupture membranes.

As the melanosome is rapidly heated, steam is formed, resulting in vacuole formation and subsequent dispersion of pigment to the periphery of the melanin-containing cell [7]. Intracellular steam formation also causes a sudden change in light scattering properties, manifested clinically as whitening of the irradiated skin.

The choice of utilized wavelength depends on the depth of pigment in the skin, as well as patient's skin type. As previously mentioned, longer wavelengths penetrate deeper into the skin, an important consideration when treating dermal pigmented lesions. As is now well established, wavelengths between 600 and 1100 nm represent an optical window, where the light beam is able to penetrate into the dermis without significant absorption by competing chromophores, such as hemoglobin and water. On the other hand, shorter wavelengths are more avidly absorbed by melanin and would be appropriate for superficial, epidermal lesions. For the same reason, patients with darker complexion require longer wavelengths, as less absorption by the epidermal melanin results in lower risk of pigmentary alterations.

Selection of proper beam diameter, or spot size, is important in the treatment of pigmented lesions. Although larger spot size results in decreased peripheral scatter and, subsequently, higher percentage of energy delivered to the target, it should not exceed the size of the lesion being treated so as not to cause pigment changes in the surrounding skin. This is especially important for darker skin types. Thus, the largest size accommodated by the treated lesion should be selected.

In addition to Q-switched lasers, long-pulsed lasers, and intense pulsed light (IPL) sources have also been used for pigmented lesions. The physical basis for such therapy may be similar to that seen with laser hair removal. That is, when a larger structure, such as a lentigo, is examined in its entirety, heat generated from the absorption of incident photons by the chromophore can propagate within the larger structure and cause coagulation damage. Although melanosomes are not damaged, as the pulse duration exceeds their TRT [10], intracellular proteins may be heated sufficiently from conducted thermal energy to cause permanent denaturation and subsequent cellular apoptosis. Exposure time must then be limited to just below TRT of the target. In the case of the lentigo, the

tissue target is the epidermal basal layer with TRT values estimated between 1.6 and 2.8 ms [11]. Additional evidence indicates that subsequent to light pulses in the millisecond range, there may be stimulation of accelerated differentiation of basal keratinocytes, resulting in rapid upward transfer, degradation, and elimination of melanosomes [12].

For the purposes of laser therapy, pigmented lesions are best classified according to their depth in the skin. They are usually subdivided into epidermal, dermal, and mixed epidermal/dermal lesions, although such divisions are somewhat arbitrary. Depth of the lesion may influence the selection of laser, but, as will be shown later, does not predict the response to treatment.

Epidermal pigmented lesions that may be amenable to laser therapy include ephelid, lentigo simplex, lentigo senilis, also known as solar or actinic lentigo, pigmented seborrheic keratosis and dermatosis papulosa nigra, and café-au-lait macule (CALM) and related nevus spilus. Mixed epidermal/dermal pigmented lesions that are sometimes treated with lasers include Becker's nevus, melasma, post-inflammatory hyperpigmentation, and nevocellular nevi. Finally, dermal pigmented lesions include nevus of Ota, nevus of Ito, acquired bilateral nevus of Ota-like macules (collectively known as dermal melanocytoses), blue nevus, and drug-induced hyperpigmentation (Figures 3.1–3.15).

It is important to note that lasers should not be used for treatment of malignant melanoma or most cases of lentigo maligna. A biopsy must be performed prior to initiation of laser treatment for any pigmented lesion where a possibility of malignancy is entertained.

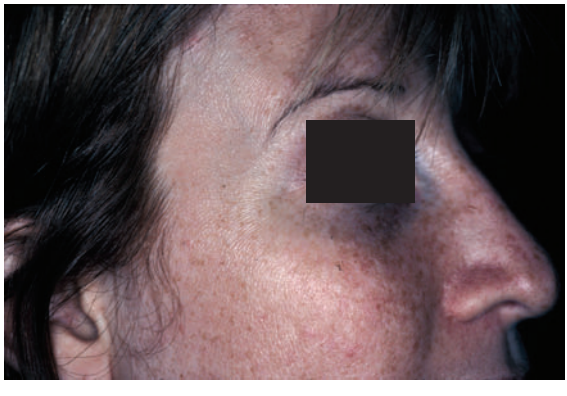

Figure 3.1 Photodamage prior to treatment with IPL source.

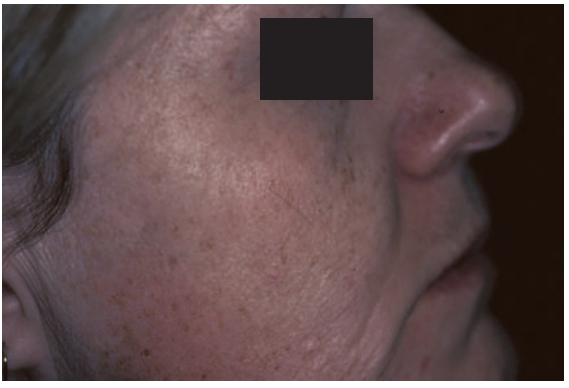

Figure 3.2 Lentigines and photodamage prior to Q-switched Nd:YAG laser treatment.

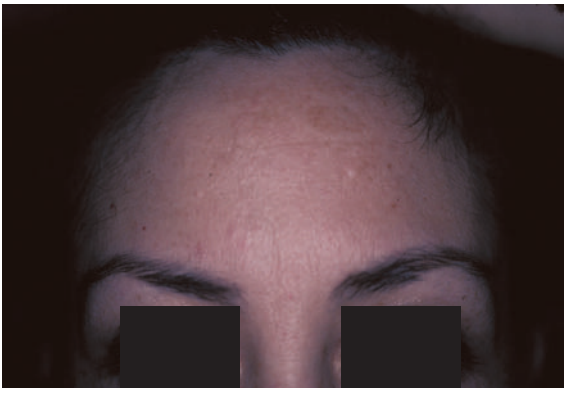

Figure 3.3 Photodamage prior to treatment with IPL source.

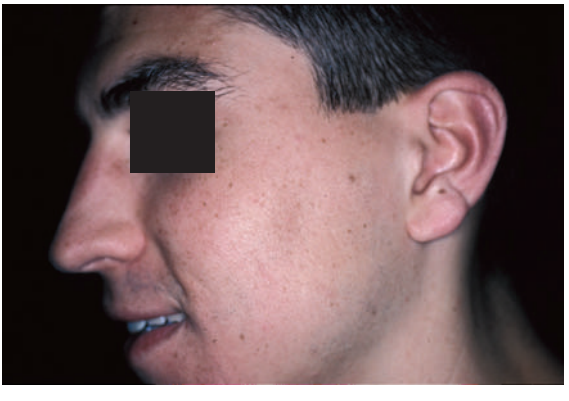

Figure 3.4 Lentigines prior to Q-switched Nd:YAG laser treatment.

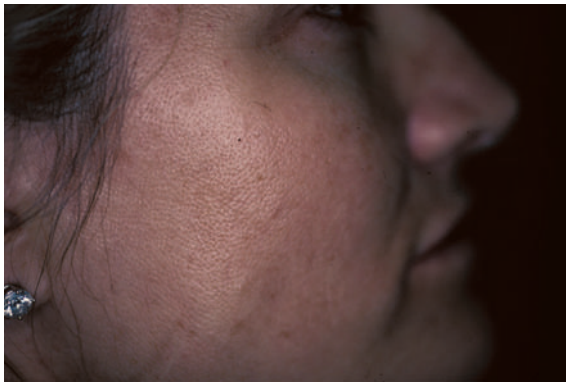

Figure 3.5 Lentigines prior to treatment with IPL source.

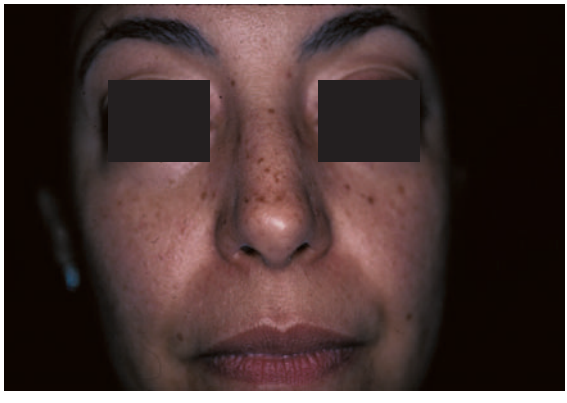

Figure 3.6 Lentigines prior to Q-switched Nd:YAG laser treatment.

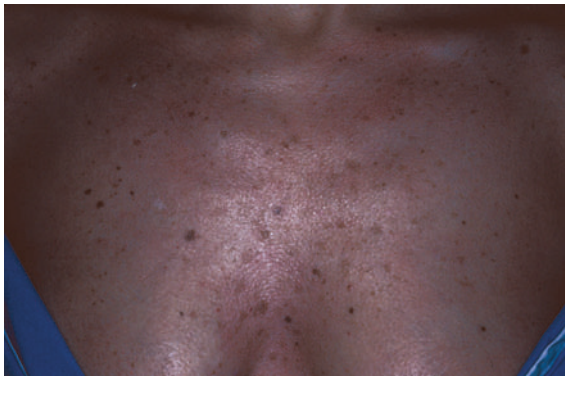

Figure 3.7 Lentigines prior to Q-switched Nd:YAG laser treatment.

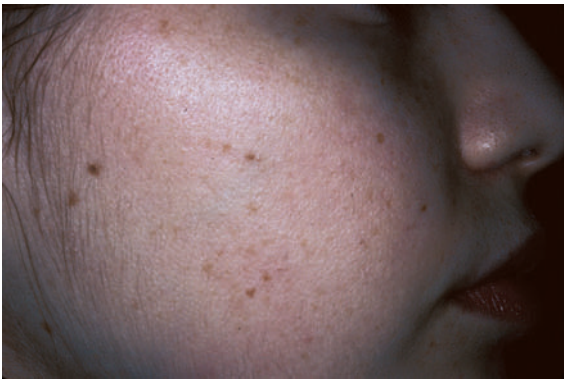

Figure 3.8 Junctional nevi prior to Q-switched Nd:YAG laser treatment.

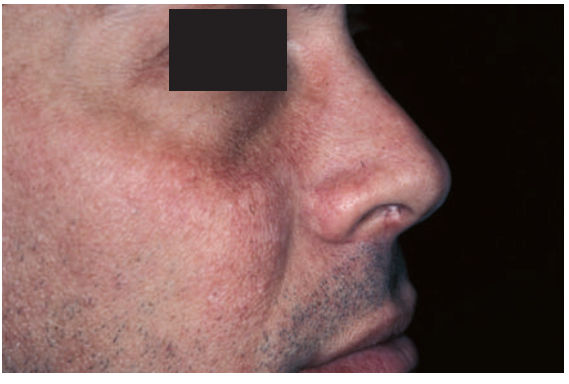

Figure 3.9 Hyperpigmentation prior to treatment with Q-switched Nd:YAG laser.

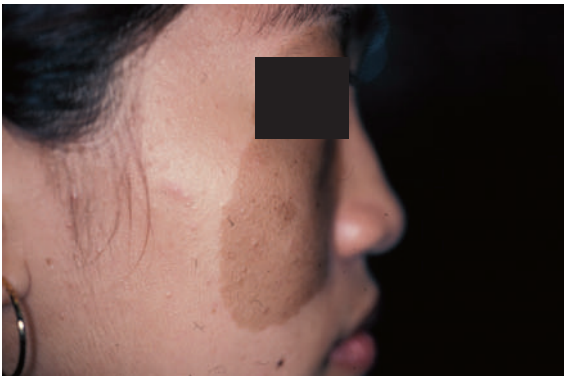

Figure 3.10 CALM prior to Q-switched Nd:YAG laser treatment.

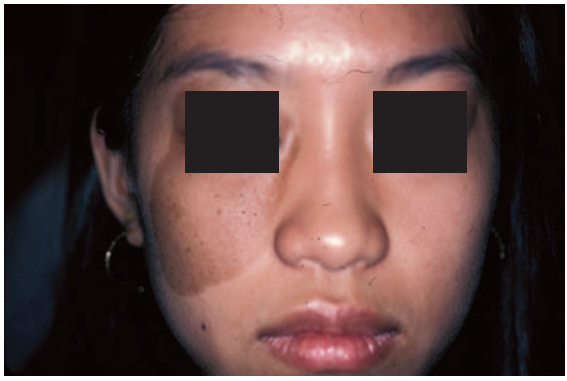

Figure 3.11 CALM prior to Q-switched Nd:YAG laser treatment.

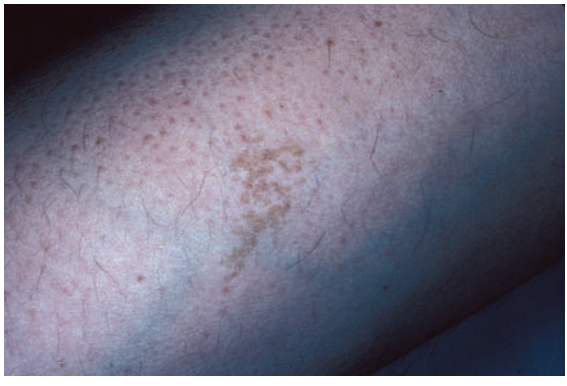

Figure 3.12 CALM prior to Q-switched Nd:YAG laser treatment.

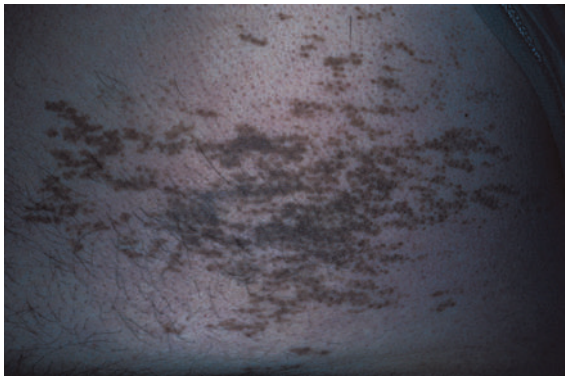

Figure 3.13 Becker's nevus prior to Q-switched Nd:YAG laser treatment.

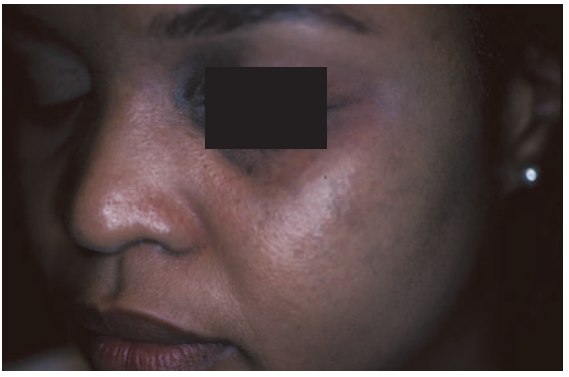

Figure 3.14 Nevus of Ota prior to Q-switched Nd:YAG laser treatment.

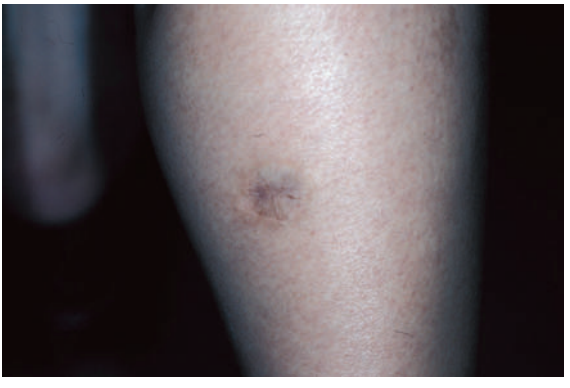

Figure 3.15 Post-inflammatory hyperpigmentation prior to Q-switched ruby laser treatment.

Tattoos: Classification, Chemical Composition, and Implications for Laser Biology

Tattoos may be classified as decorative, cosmetic, traumatic, medical, and iatrogenic (Figures 3.16–3.18). Decorative tattoos are most common and may be further subdivided into professional and amateur. This is an important distinction, as the former are typically placed deeper in the dermis, have a larger quantity of ink, and have more variable composition of inks compared to the latter. Such differences result in greater difficulty of tattoo removal and, frequently, incomplete eradication of some colors, as will be discussed below. Decorative tattoos may incorporate both inorganic and organic compounds. Inorganic pigments may be composed of such elements as cadmium, chromium, mercury, iron, titanium, aluminum, silica,

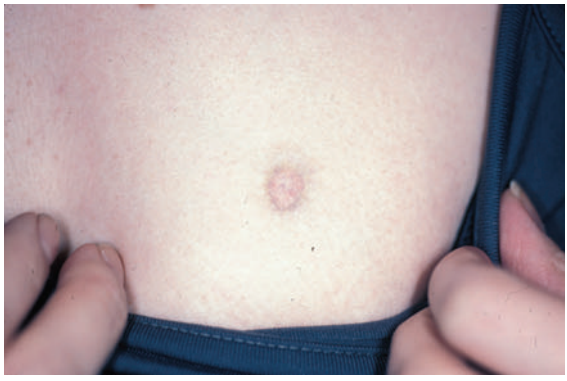

Figure 3.16 Amateur tattoo prior to Q-switched Nd:YAG laser treatment.

copper, chlorine, bromine, sulfur, carbon, and magnesium [13]. The number of organic materials used in tattoos is even higher, with most classified as either azo or non-azo, or polycyclic, compounds [14]. There is also evidence that some pigments or their decomposition products may be toxic or carcinogenic [15].

Cosmetic and reconstructive tattoos are typically placed to improve or create the appearance of normal anatomical structures. Various scenarios may include thinning eyebrows, eyelashes, and vermilion border of the lips, recreation of areola following mastectomy, or camouflage of scars. Cosmetic tattoos, also known as permanent make-up, may also consist of multiple colors and, hence, chemical compounds [16]. As will be shown below, the presence of ferric oxide or titanium dioxide is of particular importance in the treatment of such tattoos.

Traumatic tattoos may result from implantation of small pieces of asphalt and other debris from motor vehicle accidents, graphite from a pencil stab, as well as shrapnel, bullet, fireworks, or other explosive fragments. Additionally, amalgam tattoos are traumatic in origin and typically follow implantation of metal particles into oral mucosa during dental procedures. Medical tattoos are frequently performed to mark radiation sites. Finally, iatrogenic tattoos may result from implantation of pigmented particles into a wound during surgery or other medical procedure, such as with the use of Monsel's solution [17].

The size of pigment particles can vary from less than 10 to 100 nm [18]. Tattoo particles may reside at various depths in the dermis, from 1.1 to 2.9 mm from the granular layer, depending to some degree on whether the tattoo is professional or amateur. In older tattoos, all pigment granules are intracellular

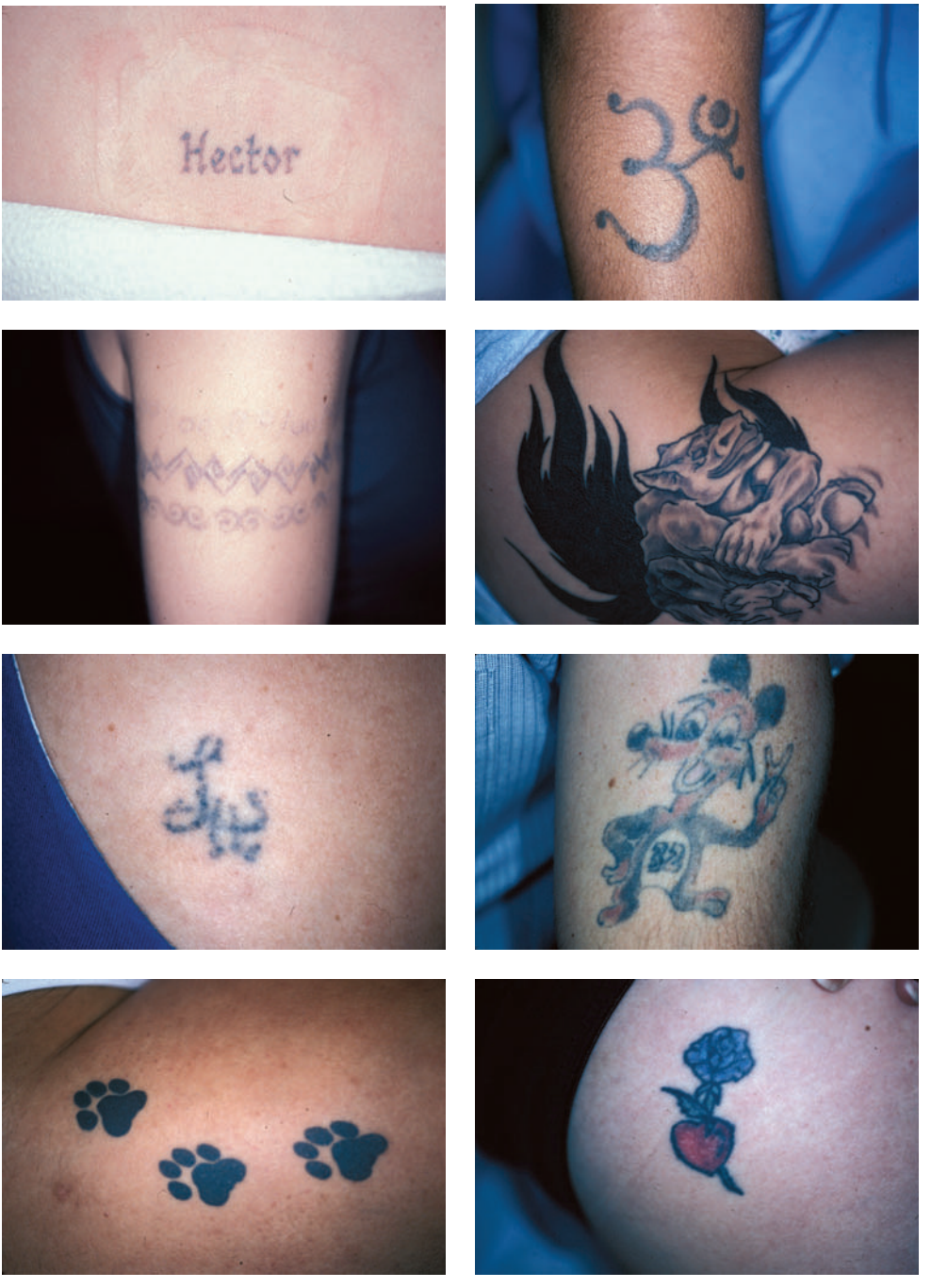

Figure 3.17 Professional tattoos prior to Q-switched laser treatment.

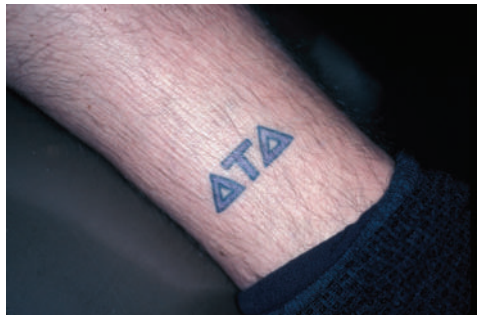

Figure 3.17 (Continued)

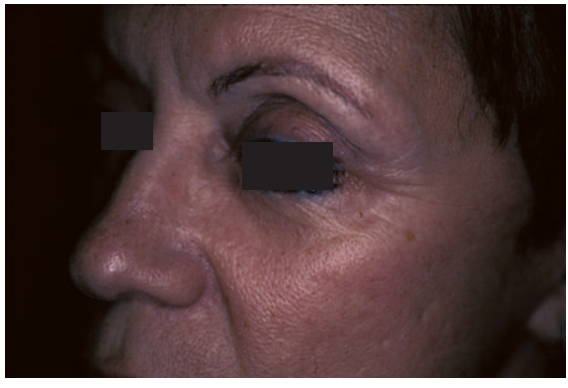

Figure 3.18 Eyebrow tattoo prior to treatment with Q-switched Nd:YAG laser.

and are found within lysosomes of mononuclear cells, such as fibroblasts and macrophages. The distribution of such cells is typically perivascular or periadnexal [19].

TRT of tattoo particles can be calculated from their size and is traditionally approximated at 0.1 to 10 ns. Recently, calculations using formulas for stress-wave generation within carbon particles place these values lower, at 10 to 100 ps [20]. Therefore, lasers with pulse duration in the picosecond range may be more efficient than the current Q-switched lasers at removing small tattoo particles [18]. Previously existing only as prototype models, such lasers may soon become available commercially, as the manufacturing process has been refined over the last few years. Even with picosecond pulse durations, however, it may be difficult to treat tattoo particles smaller than 10 nm, although such small particles may not be clinically apparent.

Photoacoustic destruction of a tattoo particle with a Q-switched laser results in the generation of smaller fragments.

Perceived pigment color	Maximally absorbed wavelength (nm)	Maximally absorbed color
Red	505 – 560	Green
Orange	500 – 525	Green
Yellow	450 – 510	Blue-green
Green	630 – 730	Red
Blue-green	400 – 450 and 505 – 560	Blue-purple Green
Blue	620 – 730	Red
Purple	550 – 640	Green-yellow-orange-red
Black	All	All

Table 3.1 Optimal absorption based on pigment color [23] .

Such fragments may then be eliminated through the epidermis, removed by vascular or lymphatic systems, or become re-phagocytosed by mononuclear cells [21,22].

Absorption spectra of tattoo pigments can be predicted from their perceived color. Color of an object corresponds to that component of the visual spectrum which is reflected by the object, which then absorbs all the remaining visible wavelengths. If all visible wavelengths are absorbed, the object appears black. If all visible wavelengths are reflected, the object appears white. Various tattoo pigments have been tested in vivo and their maximal absorption wavelengths are listed in Table 3.1. Although seemingly simple, this selection of optimal wavelengths for removal of various tattoo inks is complicated by multiple factors in clinical practice, as will be described later in this chapter.

Disorders of Hypopigmentation: Implications for Laser Biology

Acquired disorders of hypopigmentation, or leukodermas, that may be amenable to laser treatments include vitiligo, hypopigmented scars, and striae distensae. Cutaneous hypopigmentation may result from decreased number of melanocytes, decreased production of melanin, or altered optical properties of skin stemming from changes in dermal collagen and vasculature [24].

The exact etiology of vitiligo is not certain. It has long been considered an autoimmune process, although multiple other theories, including neural involvement, impaired redox status, toxic injury, and defective melanocyte attachment, have

also been proposed [25–28]. Whether melanocytes are reduced in number or melanin in amount has also been the subject of a debate, although it now appears that melanocytes are actually destroyed in the disease process [29].

It has previously been shown that narrowband UVB (NB-UVB) light at 311 to 312 nm stimulates both proliferation and migration of melanocytes in vitro [30]. This corresponds to well-documented repigmentation in vitiligo patches following NB-UVB therapy [31–34]. As will be discussed in a later section, xenon-chloride (XeCl) excimer laser emitting 308-nm UV light was subsequently evaluated in the treatment of vitiligo.

Striae distensae are most commonly caused by pregnancy and weight gain, although other conditions, such as prolonged use of high-potency topical corticosteroids, high corticosteroid serum levels, endocrine disorders, and connective tissue diseases may also present with this cutaneous manifestation [35–39]. Initially, erythematous linear dermal scars with overlying epidermal atrophy are noted and are sometimes referred to as striae rubrae. Over time, these are replaced by hypopigmented striae albae. Histologically, the condition is very similar to a scar, with thinned and flattened epidermis, normal or reduced basal melanocytes, and thinned dermis with parallel bundles of collagen [40]. The effect of UVB light appears to be the induction of melanocytes, which become larger and contain increased number of melanosomes. This effect is similar to chronic suntan and thus provides camouflage for hypopigmented striae [41].

The lasing medium in excimer lasers is a mixture of a halogen gas and a noble gas. While various combinations of such gases produce different wavelengths of light, XeCl excimer laser has so far been found to be most useful in dermatology. Following delivery of high electric current, an "*exci*ted di*mer*" is formed, which then returns to the ground state, producing laser light. At higher treatment doses, XeCl excimer lasers cause superficial ablation [42]. At lower doses, their mechanism of action appears to be similar to narrowband UVB light sources [41].

Pearls and Problems

Pigmented Lesions

Patient Selection and Pre-Treatment Care

Prior to undertaking laser treatment of any pigmented lesion, a firm diagnosis must be established. This is especially true if malignancy, such as malignant melanoma, is on the differential

diagnosis. In such cases, a biopsy may help to confirm the correct diagnosis [43].

Patients on oral retinoid therapy should not undergo laser treatment of pigmented lesions for 6 to 12 months following discontinuation of the medication, as they have an increased risk of keloidal scar formation. Since all melanosomes are targeted by Q-switched lasers within the treatment area, hairs within the same area may become temporarily whitened. This is especially true in the beard and moustache area, as well as with hairy melanocytic or Becker's nevi. As well, patients undergoing laser therapy for pigmented lesions should have no suntan at the time of treatment. If significant suntan is present, therapy should be postponed and a bleaching cream may be used to hasten the resolution.

A topical anesthetic may be applied under occlusion 1 hour before treatment to reduce patient discomfort. Although treatment of lentigines is usually well tolerated, anesthesia is important for larger dermal pigmented lesions, such as nevus of Ota. Pre-treatment photographs are recommended prior to initiation of therapy to follow resolution.

Due to their specificity for melanin, as well as ultrashort pulse duration resulting in explosive forces within the target, Q-switched lasers are the most dangerous laser systems for retinal damage. Long-pulsed lasers and light sources used in the treatment of pigmented lesions are also capable of causing permanent retinal damage. Therefore, appropriate eye protection for everyone in the laser suite is critical and should not be removed until the laser is switched to a stand-by mode.

Epidermal Pigmented Lesions

Due to their superficial nature, lentigo simplex, solar lentigo, ephelid, and flat seborrheic keratosis may all be targeted by any of the currently available Q-switched lasers. Treatment with such lasers has been found to be more efficacious than that with either liquid nitrogen, 35% trichloroacetic acid, or glycolic acid peels [44–46]. Additionally, labial melanotic macules, whether idiopathic or associated with Peutz–Jeghers syndrome, and penile melanosis represent variants of lentigo and are also amenable to laser treatments [47–49].

Equipped with a potassium–titanyl–phosphate crystal, the frequency-doubled Q-switched neodymium:yttrium–aluminum–garnet (Nd:YAG) laser emits green light at 532 nm, which is well absorbed by melanin. This wavelength is also well absorbed by hemoglobin, and ultrashort pulses may, therefore, result in purpura from vessel rupture and extravasation of erythrocytes [50].

Q-switched ruby laser and Q-switched alexandrite laser emit wavelengths of 694 and 755 nm, respectively. Light produced by either of these lasers is well absorbed by melanin and both have been successfully used in the treatment of superficial pigmented lesions [51,52].

As mentioned previously, the immediate endpoint of treatment is whitening of treated lesion, frequently associated with an audible popping sound. If significant accumulation of epidermal debris is present, fluence should be lowered. One to two treatment sessions are usually sufficient to clear most freckles and lentigines using these systems, and higher fluences are associated with improved clearance rates [50]. With the exception of freckles, recurrences are uncommon; however, new lesions may arise, especially if patients are not careful about sun protection.

Pinpoint bleeding is typically noted following treatment with Q-switched lasers. Antibiotic ointment should be applied to the treated areas and patients should be instructed in the proper local wound care. If present, pigmentary alterations, such as hypo- or hyperpigmentation, are typically temporary and may last up to 3 months [50]. An additional uncommon adverse effect of Q-switched laser therapy in patients with history of gold therapy is the development of chrysiasis in the treated areas, manifesting as bluish-gray macules reminiscent of purpura [53]. This condition may be amenable to treatment with a normal-mode ruby laser [54].

More recently, long-pulsed lasers and IPL light sources have been evaluated in the treatment of larger epidermal pigmented lesions, such as solar lentigines. As mentioned previously, the basis of such treatments may involve propagation of heat from melanin-containing melanosomes through the larger structure of the lentigo and possible acceleration of differentiation of basal keratinocytes [12]. Care must be taken when selecting pulse duration so as not to exceed TRT of the basal layer, which may result in non-specific dermal heating and potential scarring. Theoretically, due to broad absorption by melanin, most visible-light lasers and IPL sources may be used for such treatments; however, competing chromophores, such as hemoglobin, should be taken into account when selecting the appropriate system. In order to avoid absorption by hemoglobin, compression may be used when delivering laser pulses. Since immediate epidermal damage is not produced when using long-pulsed lasers and light sources, they may be somewhat safer in ethnic skin [55–57]. Following treatment, pigmented lesions darken with subsequent sloughing in 5 to 10 days, depending on location. Compared to Q-switched lasers, long-pulsed systems may require more treatment sessions,

typically 3 to 5, to produce lesion clearance. Treatments are undertaken in 4- to 8-week intervals.

Pigmented seborrheic keratoses and dermatosis papulosa nigra have significant epidermal proliferation with normal or slightly increased number of melanocytes and increased melanization of keratinocytes. They may be treated with any of the ablative lasers, such as ultrapulsed carbon dioxide (CO_2) or erbium:yttrium–aluminum–garnet (Er:YAG) lasers [58,59]. The physical basis of such treatments involves light absorption by water with subsequent evaporation of the treated lesion. Such non-specific ablation will be considered in further detail in the next chapter. Additionally, both Q-switched and long-pulsed lasers that target melanin may be able to treat pigmented seborrheic keratoses and dermatosis papulosa nigra more specifically [60]. Laser spot size should be limited to just below the size of the lesion. Potential adverse effects may include pigmentary alterations, scarring, and recurrence of these common benign lesions.

A CALM may be an isolated finding or, typically when multiple, part of other conditions, such as neurofibromatosis or McCune–Albright syndrome. Histologically, CALM is characterized by slightly increased number of melanocytes that produce giant melanosomes, which are then transferred to basal keratinocytes. The exact pathophysiology of CALM is not completely worked out, but may involve fibroblast-derived stem cell factors or other dermally derived factors [61,62].

Although it may appear that CALMs would be great candidates for laser surgery, in clinical practice they are difficult to treat. Multiple treatments over a period of months or years are usually required, and recurrences are common, occurring in nearly 50% of patients up to 1 year following clearance [63]. It is thought that this may be related to dermal induction of epidermal hyperpigmentation.

Patients with lighter skin tones should be selected for treatment of CALMs, as darker skin types may experience high risk of discoloration. Patients should be warned about risks of incomplete or partial clearance resulting in a speckled pattern, hyperpigmentation, and recurrence. A test spot is recommended prior to initiation of treatment, although it may not predict the final response of the entire lesion. Any of the melanin-specific Q-switched lasers may be used for treatment of CALMs [50,64]; however, due to its greater absorption by melanin, frequency-doubled Nd:YAG at 532 nm is best for lighter lesions with lower concentration of the chromophore.

Nevus spilus, or speckled lentiginous nevus, is a closely related condition, exhibiting dark macules or papules, corresponding

to junctional or compound nevomelanocytic nevi within a lesion of CALM [65]. Although complete or partial clearance of these lesions using Q-switched and long-pulsed lasers and IPL light sources has been described [66–68], our clinical experience has been clearance of the nevus portion with no or minimal improvement in CALM. Care must be exercised when treating these lesions with lasers, as multiple cases of melanoma arising in nevus spilus have been described [69].

Mixed Epidermal/Dermal Pigmented Lesions

With the exception of nevomelanocytic nevi, which are composed of a single type of cells, mixed epidermal/dermal pigmented lesions are generally characterized by their relative recalcitrance to laser treatments. This is likely due to intralesional heterogeneity and interactions between epidermal and dermal components. For these reasons, CALMs can also be included in this category, rather than with purely epidermal lesions.

Becker's nevus, also known as pigmented hairy epidermal nevus, is in fact an organoid nevus with abnormalities in epidermis, hair follicles, and smooth muscle. It typically appears in adolescence as a tan or brown patch with dark coarse hairs. Although previously thought to be more common on shoulders, it may involve any part of the body. Under light microscope, Becker's nevus is characterized by acanthosis, basal layer hyperpigmentation without an increase in the number of melanocytes, and increased number of hair follicles and arrector pili muscles [70]. It thus presents two potential targets for pigment-specific lasers: hyperpigmented epidermis and hair.

Hair removal in Becker's nevus may be accomplished with long-pulsed lasers using techniques described in the previous chapter [71]. Epidermal lightening, on the other hand, may be difficult to achieve and hyperpigmentation is prone to recurrence. Q-switched lasers have been tried with variable success in patients with Becker's nevi [51]. Recently, Er:YAG resurfacing was found to be safe and effective in patients with skin types II to IV. Two years following one session of resurfacing to papillary dermis, patients continued to have 60% to 80% improvement in their lesions. Crust formation and erythema lasting up to 3 months were noted following treatment, but scarring was not observed. Histologically, basal hyperpigmentation did not recur after 2 years [72]. Although promising, these findings need to be verified in larger studies and test spots are recommended before the actual treatment is undertaken.

Melasma is a common pigmentary condition affecting mostly women and characterized by poorly defined tan or brown macules on sun-exposed areas of the face. Pregnancy and oral contraceptives in combination with sun exposure are the most commonly cited etiological factors, although other causes, including genetic predisposition and phototoxic medications, may also contribute to this condition. Melasma is usually subdivided into epidermal, dermal, and mixed types, based on the location of pigment [73]. Although somewhat arbitrary, clinical distinction between the subtypes is usually made with the help of a biopsy or with Wood's light examination, which accentuates epidermal melanin. Histologically, melasma is characterized by a normal number of enlarged melanocytes with prominent dendritic processes, increased epidermal melanin, slightly increased number of dermal melanophages, and mild perivascular lymphohistiocytic infiltrate [74].

Until recently, the only treatment options for melasma-included sun protection, topical bleaching agents, topical corticosteroids, and chemical peels. First lasers to be tried in the treatment of melasma were pigment specific. Thus, both Q-switched and long-pulsed lasers and IPL sources have been evaluated. Although more effective for the epidermal subtype, these systems have limited success in the therapy of dermal melasma. Treatments are further complicated by the frequent incidence of post-inflammatory hyperpigmentation and rapid recurrence upon exposure to sunlight [75–80]. In our experience, the addition of combined red/infrared light emitting diode (LED) therapy for 15 to 20 minutes following each IPL treatment, as well as compulsive sun avoidance, may reduce the risk of such recurrence.

Recently, it has been noted that resurfacing may be effective in the treatment of melasma. This may be accomplished with the use of either the CO_2 or Er:YAG laser, sometimes followed in tandem with a pigment-specific Q-switched laser, thus removing both the epidermal and dermal melanin [81–83]. Because of profound damage to the epidermis, however, melanocytes at the periphery of the treatment area may become stimulated, again resulting in post-inflammatory hyperpigmentation.

Fractional photothermolysis has recently been evaluated in the treatment of melasma and is currently the only FDA-approved laser therapeutic modality for this condition. Although it will be discussed in more detail in a subsequent chapter, important concepts involved in fractional photothermolysis will now be examined. This process utilizes a dermally focused 1550-nm diode laser beam to create columns of thermal

damage, also known as microscopic treatment zones (MTZ), surrounded by uninjured tissue. As MTZ density increases, the distance between adjacent columns decreases by a square root of the amount of change. Thus, for densities of 400 and 1600 MTZ/cm^2, the corresponding inter-MTZ distances are 500 and 250 μm, respectively. The percentage of total surface area treated per session is proportional to MTZ density and to the number of treatment passes. Finally, energy level determines both the diameter and depth of the column of thermal damage. Thus, energy of 6 mJ results in columns with a diameter of 80 μm and depth of 360 μm, whereas 10 mJ corresponds to a diameter of 110 μm and depth of 500 μm [84]. As the dermis is damaged, the stratum corneum is preserved, creating a natural dressing for the subjacent wound. Just below the stratum corneum are thermally damaged epidermal components, also known as micro-epidermal necrotic debris (MENDs), which are subsequently extruded within 7 days [85]. Recent evidence indicates that, in addition to epidermal debris, dermal contents, such as melanin, may also be eliminated through the formed channels [86].

Clinically, treatment area is cleansed and a topical anesthetic is applied for 1 hour, as the procedure is associated with moderate discomfort. Just before treatment, a blue dye (FD&C Blue #1) is applied, followed by petrolatum ointment or ultrasound gel for easier handpiece gliding. The blue dye allows a computer-based tracking device to measure handle velocity, providing for consistent MTZ density independent of operator movement. Following treatment, the blue dye can be removed using a facial cleanser. In a pilot study of fractional photothermolysis in the treatment of melasma, 60% of patients achieved 75% to 100% clearance rates following 4 to 6 weekly or biweekly sessions at 6 to 12 mJ and 2000 to 3500 MTZ/cm^2 [84]. The procedure typically requires no downtime, although erythema may persist for 1 to 3 days. Edema is usually minimal at the above settings, and scarring has not yet been reported [84]. Previous reports of linear abrasions have now been fixed with slightly modified handpiece design. However, hyperpigmentation can still occur following this treatment, so sun avoidance is paramount in any treatment of melasma.

Post-inflammatory hyperpigmentation is somewhat similar to melasma and can also have epidermal and dermal components. Although the epidermal hyperpigmentation may be amenable to treatment with Q-switched lasers and IPL systems, laser therapy for the dermal portion has been mostly disappointing [77]. Following treatment, melanocytes are likely to be further stimulated, potentially resulting in worsened, rather

than improved, hyperpigmentation. If laser therapy is performed on post-inflammatory hyperpigmentation in an attempt to lighten the epidermal component, test spots are recommended but do not guarantee treatment success. A regimen of strict sun protection and the addition of topical bleaching agents may help to prevent recurrence. Similar to melasma, fractional photothermolysis may offer a potential treatment option for this recalcitrant condition, although no such studies have been performed to date.

Although laser treatment of nevocellular nevi has been a controversial topic because of theoretical potential of inducing malignant transformation, a non-excisional therapeutic modality for these lesions would be a welcome addition to laser surgeon's armamentarium. To this end, we have recently conducted a study of changes in melanocytic markers following Q-switched Nd:YAG irradiation. The results showed no change in expression of any such markers (unpublished data), thus validating the contention that laser treatment of nevocellular nevi is safe. Additionally, a long-term histological study of patients with congenital nevi treated with normal-mode ruby laser failed to show any malignant transformation after 8 years [87]. Thus, laser removal of benign nevocellular nevi is warranted, especially in cases where surgical excision is not feasible because of cosmetic or practical considerations. Prior to treatment, patients should be asked about personal or family history of malignant melanoma. Recurrent nevus following laser removal requires a biopsy to rule out malignant transformation.

Nevocellular nevi may be congenital or acquired and may be further subdivided into junctional, compound, and intradermal types. Any of the currently available Q-switched lasers may be used on nevi, although frequency-doubled Nd:YAG at 532 nm may be better suited for the more superficial junctional nevi, whereas Q-switched Nd:YAG at 1064 nm may be somewhat less efficacious compared to ruby or alexandrite due to decreased melanin absorption [88–91]. Since nests of melanocytes may also act as a larger body, longer-pulsed pigment-specific lasers, with pulse durations of up to 3 ms, have also been used in the treatment of nevi [87,92,93]. Care must be exercised, however, as some hair removal lasers may produce much longer pulse durations, which could result in non-specific thermal damage to the dermis and potential scarring. Compared to Q-switched lasers, longer-pulsed systems may have the advantage of des-troying deeper, less heavily pigmented nests by propagation of heat throughout the entire structure. They may thus be more efficacious in the treatment of the deeper components of

congenital nevi. In addition, combinations of Q-switched and subsequent longer-pulsed lasers appear to be most effective in such lesions [94–96]. With any system, multiple treatments, typically between three and five, are generally needed for good cosmetic clearance. Even then, some non-pigmented deep nests may remain [97] and patients should be followed regularly for recurrences.

Dermal Pigmented Lesions

Nevus of Ota, nevus of Ito, and acquired bilateral nevus of Ota-like macules are quite similar conditions and are collectively referred to as dermal melanocytoses. Nevus of Ota typically presents as an ill-defined patch consisting of confluent blue to brown macules in the distribution of the ophthalmic or maxillary nerve. Occasionally, slightly raised papular or even nodular portions may be found within the patch. Typically unilateral, bilateral cases may also occur [98]. Involvement of sclera on the ipsilateral side is common, and other structures, such as the external auditory canal, tympanic membrane, and oral and nasal mucosa, may also be affected. This condition usually starts in the first year of life or around puberty and is more common in patients with darker skin tones, such as Asians, although all races may be affected. Malignant transformation into malignant blue nevus or melanoma has been reported [99,100]. Nevus of Ito is very similar in appearance, but occurs in the scapular, supraclavicular, or deltoid area. Acquired bilateral nevus of Ota-like macules, or Hori's nevus, typically presents in middle-aged Asian patients with bilateral discrete or confluent bluish-brown macules in malar distribution without scleral or mucosal involvement [101,102]. Histologically, dermal melanocytoses exhibit elongated dendritic melanocytes scattered among collagen bundles in the papillary or upper reticular dermis. Nodular areas may be difficult to distinguish from blue nevi [103].

Because of the scattered nature of the dermal melanocytes, Q-switched pigment-specific lasers with adequate penetration into the dermis are best able to treat these conditions. To this effect, Q-switched ruby, alexandrite, and Nd:YAG at 1064 nm have all been used with good clearance rates in the treatment of nevus of Ota [104–106]. However, the Q-switched Nd:YAG laser may be slightly more effective due to deeper penetration of the beam [107]. As well, epidermal melanin absorption is decreased at 1064 nm, resulting in decreased risk of epidermal pigmentary alterations, especially in darker skin types. As for the optimal age for initiation of laser therapy, children may require fewer

sessions and appear to have much lower overall rate of complications compared to adults [108]. In all cases, test spots are recommended prior to initiation of treatment. Topical anesthesia is recommended, as treatments are quite painful. As with epidermal pigmented lesions, immediate treatment endpoint is immediate whitening. Although a single session is occasionally sufficient, more frequently lesions may require 4 to 8 treatments, typically undertaken at least 2 months apart. Blue-green lesions may require more treatments compared to brown-violet and violet-blue lesions [109]. As well, periorbital involvement may be more resistant to treatment [110] and ocular shields are required when using lasers in this area. Patients should also be aware that scleral pigmentation will remain following laser treatments of the cutaneous portion. Most common adverse effects of laser therapy for nevus of Ota include intraoperative pain, hypopigmentation, which may be permanent, in as many as 15% of treated patients, hyperpigmentation, scarring in up to 2%, and recurrence. These are more common with lower wavelengths, such as that of the ruby and alexandrite lasers [105,111]. Pre- and post-treatment skin cooling may improve patient tolerability [112]. Additionally, the use of bleaching agents and sun protection are critical to decrease the risk of pigmentary changes.

Nevus of Hori is treated similarly to nevus of Ota [113,114], although the former may be somewhat more resistant to laser therapy, as complete clearance rates may be slightly lower and adequate lightening may require more sessions [115]. Post-inflammatory hyperpigmentation is also more common following laser treatment of Hori's nevus compared to nevus of Ota and was recently correlated to greater clustering of melanocytes around blood vessels in the former condition [116]. As well, the risk of permanent hypopigmentation may be increased if sessions are not adequately spaced [117]. As with nevus of Ota, the addition of bleaching agents and strict sun protection are important in order to decrease the risk of discoloration.

Blue nevus is a common condition, typically arising in childhood or adolescence. Clinically, a well-circumscribed blue or bluish-black papule is visualized, with the blue color due to Tyndall effect. Histologically, a collection of highly melanized dendritic melanocytes is present in the dermis and may extend into deep dermis or subcutaneous tissue [118]. Although more dense, the presence of dendritic melanocytes is reminiscent of dermal melanocytoses. Consequently, blue nevi may be treated in a similar fashion, usually with Q-switched pigment-specific lasers [119].

Drug-induced hyperpigmentation is a benign condition that may occur with multiple medications. The nature of deposited pigment varies depending on the offending agent and location. Although some drug-induced hyperpigmentation may improve upon discontinuation of the medication, it may persist indefinitely. Lasers appear to be the only effective therapeutic modality for at least some forms of this condition. In general, laser treatments should be undertaken after the medication has been discontinued or, preferably, after sufficient period of time has elapsed following discontinuation to allow for spontaneous fading.

Minocycline is known to cause at least three types of hyperpigmentation: blue-black discoloration of scars, blue-gray pigmentation of normal skin, typically shins, and brown discoloration of sun-exposed areas, such as the face. In addition to cutaneous pigmentation, oral mucosa, sclerae, nails, bones, and teeth may also be involved. Depending on the type, discoloration may result from deposition of iron, hemosiderin, minocycline derivatives, or increased melanin. Several studies have documented the effectiveness of all currently available Q-switched lasers in the treatment of facial and leg minocycline-induced hyperpigmentation, including that of the tongue [120–125]. Complete resolution is typically noted after an average of 4 treatments administered 4 to 8 weeks apart, although treatment with Q-switched Nd:YAG at 1064 nm may require more sessions. No long-term adverse effects have been reported.

Amiodarone typically causes slate-gray pigmentation of sun-exposed areas, such as the face, and demonstrates yellow-brown granules within dermal melanophages. Complete resolution following a single treatment with a Q-switched ruby laser has been reported with no adverse effects [126].

Exogenous ochronosis presents as blue-black or slate-gray hyperpigmentation at the sites of prolonged application of various compounds, most commonly hydroquinone. Histologically, it manifests as yellow-brown, or ocher, banana-shaped fibers in the papillary dermis. Recently, significant lightening was noted following 4 to 6 treatment sessions using a Q-switched alexandrite laser. No adverse effects were noted in this small study. Larger studies of the promising laser treatments are warranted for various types of drug-induced hyperpigmentation, a condition with very few, if any, other therapeutic options.

Post-operative wound care for dermal lesions treated with Q-switched lasers is identical to that following treatment of epidermal lesions described above. Pinpoint bleeding may be noted and antibiotic ointment should be applied to the treated areas. Patients should continue local wound care and exercise

sun avoidance or strict sun protection. Bleaching agents may also be added, if indicated.

Tattoos

Patient Selection and Pre-Treatment Care

The ideal candidate for laser tattoo removal is fair in complexion, without suntan, and with a blue-black monochromatic tattoo present for at least a year. This delay in treatment allows for accumulation of macrophages, which phagocytose the foreign ink material, resulting in a somewhat blurry appearance of tattoos over time. Tattoos in darker individuals may be more difficult to eradicate; similarly, patients with suntan should not be treated until the suntan has completely resolved. Additionally, patients with a recent intake of oral retinoids should not undergo laser tattoo removal until at least 6 months following discontinuation of the medication.

A complete clinical assessment of the tattoo is performed at the initial consultation. This includes visual inspection and palpation for any induration or scarring. Scarring is common following the initial placement of tattoo ink, but may be difficult to discern. If present, it may become more apparent following the removal of tattoo and lead the patient to believe that scarring was caused by the laser surgery. The presence of induration may indicate a potential allergic or granulomatous reaction within the tattoo, thus requiring a different therapeutic approach, as will be discussed below. Different inks within a multi-colored tattoo may not respond in a similar fashion to laser treatments and certain colors, such as yellow, are not amenable to successful eradication at this time.

Compared to the amateur ones, professional decorative tattoos may have deeper placement of larger amounts of ink and multiple pigments with various compositions and additives. Thus, amateur tattoos frequently clear after only 4 to 6 treatments, whereas the professional one may require significantly more sessions, typically 6 to 10, but occasionally as many as 20 or more [127,128]. Finally, patients should also be informed that a blurred outline approximating the shape of the original tattoo may sometimes remain following a successful laser removal.

Laser treatment of large tattoos may require the application of topical anesthesia, although removal of the smaller ones is usually well tolerated by patients. Pre-treatment photographic documentation of the tattoo is recommended. Since tattoos are treated with pigment-specific Q-switched lasers, eye protection is critical to prevent retinal damage. Protective eyewear must

be checked for filtered frequencies to verify adequate blockage of laser light. If eyeliner tattoo is treated, metal shields are required to protect the patient's eyes.

Treatment of Tattoos

As previously mentioned, the development of lasers with ultrashort pulse durations has allowed targeting of the small granules of tattoo ink. Q-switched lasers are the current treatment of choice for all types of tattoos. Conversely, the use of long-pulsed lasers or IPL systems is contraindicated, as they are associated with a high risk of scarring.

Removal of different colors within a tattoo can theoretically be accomplished when lasers are used in accordance with the absorption spectra of the inks, as presented in Table 3.1. This, however, is complicated in clinical practice and additional considerations need to be taken into account. First, certain wavelengths, such as purple and blue laser light, may not be able to penetrate deep enough into the dermis to reach the corresponding pigment particles. Second, the choice of laser beam color is presently limited to the commercially available Q-switched ruby (695 nm, red color), alexandrite (755 nm, red–infrared color), and Nd:YAG (1064 nm, infrared spectrum, and frequency-doubled 532 nm, green color). Third, tattoo color may be produced by a combination of several compounds with different absorption spectra, resulting in competing chromophores. Additionally, certain added pigments may cause significant reflection or scattering of the laser beam. Thus, a given color, when appreciably diluted by other pigments, may not be exposed to sufficient laser energy to cause particle destruction, resulting in tattoo resistance. This is frequently seen with titanium dioxide, a highly reflective material used for brightening of other pigments [129,130]. Fourth, the stress threshold may be not be reached within some ink materials to generate stress waves. Thus, shorter pulse durations or higher fluences may be required for such tattoos, but may be limited by the potential for scarring. Finally, some compounds, such as ferric oxide and titanium dioxide, may undergo chemical alterations when exposed to a laser beam with nanosecond pulse duration. As a result, orange-brown ferric oxide (Fe_2O_3) may be reduced to black ferrous oxide (FeO), and white titanium dioxide (TiO_2) may be reduced to bluish-violet titanium (III) oxide (Ti_2O_3) [131]. This is an important consideration in both decorative and cosmetic tattoos, as will be presented below.

In clinical practice, blue-black tattoo pigment can be removed using the Q-switched ruby, alexandrite, and Nd:YAG

at 1064 nm. Ruby laser is associated with the highest clearance rate in such tattoos, but also results in an increased incidence of long-lasting hypopigmentation [132]. While Nd:YAG may be slightly less effective, it is the preferred method of treatment of blue-black tattoos in darker individuals [133]. On the other hand, the frequency-doubled Nd:YAG laser appears to be considerably less effective, possibly as a result of inadequate penetration into the dermis. By producing green light, it is, however, most effective at treating red inks. Green tattoo pigment is best treated with the red light emitted by the ruby laser [134], but also responds well to the alexandrite laser.

It is recommended that test spots be administered prior to the actual treatment. As with pigmented lesions, the immediate clinical endpoint is tissue whitening, which may be accompanied by a popping sound in lightly pigmented patients. Although higher energies may clear tattoos more effectively [135], they may also be associated with a higher incidence of adverse events. Additionally, novice practitioners frequently reduce spot size to allow for increased fluence. This is a mistake, as it results in the deposition of higher percentage of the total beam energy in the upper layers of skin, resulting in potential scarring. Thus, the largest available spot size that produces tissue whitening should be used for treatment of tattoos [136]. Pinpoint bleeding is frequently noted following laser therapy. An antibiotic ointment and a non-adherent dressing should be applied upon completion. Most importantly, patients should be instructed in the proper local care of their wounds, which may take up to 1 week to heal.

Additional treatment sessions improve the final outcome and should be undertaken at least 6 to 8 weeks apart. This allows for sufficient time for pigment dispersion and elimination, as well as resolution of possible post-inflammatory hyperpigmentation. If the latter is present at the subsequent appointment, treatment should be postponed pending improvement or resolution.

Common adverse effects encountered in the treatment of decorative tattoos include post-treatment bleeding, blistering, infection, hypo- and hyperpigmentation, and textural changes. Hypopigmentation is most common with the Q-switched ruby laser and may be permanent. Hyperpigmentation is usually seen in patients with darker complexion; the use of Nd:YAG laser at 1064 nm may decrease the incidence of this effect. Scarring is not common, but may become keloidal or hypertrophic [137]. One case of acute compartment syndrome of the upper extremity has been reported following Q-switched 1064-nm Nd:YAG laser treatment of a decorative tattoo [138].

Allergic, granulomatous, lichenoid, and photoallergic reactions to various tattoo pigments are well documented [139]. Although mercury-containing red ink is the most common cause of allergic tattoo reactions, cadmium in the yellow ink is known to ellicit photoallergic response [140]. Release of tattoo particles from macrophages following a Q-switched laser treatment may trigger an immediate or delayed localized or systemic allergic reaction in susceptible individuals, even in previously asymptomatic tattoos [141,142]. For this reason, it has been suggested that allergic reactions within tattoos be treated with CO_2 or Er:YAG laser ablation [143,144]. However, generalization of a localized tattoo reaction following such an ablation has been reported, as well [145].

Pigment darkening can occur in decorative tattoos, but is even more common in cosmetic tattoos. As discussed above, ferric oxide and, occasionally, titanium dioxide are responsible for most of such color alterations. Although white, red, tan, and flesh-toned tattoos are typically implicated, other colors, such as yellow, orange, brown, and crimson may also change dramatically following Q-switched laser exposure [146–148]. Additionally, the risk of pigment darkening appears to correlate with the age of the tattoo, increasing as much as sixfold with each decade for some ink colors [149]. Following such color change, pigment may or may not be amenable to subsequent attempts at laser removal. Thus, test spots in the most inconspicuous portions are recommended for all cosmetic or other types of tattoos that contain such colors.

Medical and traumatic tattoos, including amalgam tattoos of the oral cavity, respond well to Q-switched laser treatments, usually in 1 to 6 or more sessions [150–153]. However, if present, fragments of gunpowder or fireworks may explode upon exposure to nanosecond laser pulses, leaving pox-like scars [154,155]. Therefore, if the origin of the traumatic tattoo is unclear, a biopsy is recommended.

Future Developments in Tattoo Removal

As previously described, tattoo particles may require pulse durations in the picosecond range, shorter than the exposure lengths provided by the currently available Q-switched lasers [18]. Such lasers are currently in development and may soon become commercially available.

Recently, the penetration of laser beam in animal skin was significantly improved with the use of topically applied glycerol. It was found to provide moderate reversible cutaneous clearing and to improve tattoo removal by reducing dermal scatter [156].

If confirmed, such findings may have important implications not only for tattoo removal, but other areas of laser surgery, as well.

Finally, a novel concept in laser tattoo removal has recently been introduced. Due to the relative inefficiency of currently available laser systems at removing tattoos, new laser-susceptible tattoo inks have now been developed. The inks are made of various biocompatible pigments encapsulated in polymethylmethacrylate beads. The beads are disrupted upon laser exposure, leading to the absorption of inks by the body and potential complete removal of the tattoo in a single laser session. Studies of the new inks are currently under way.

Disorders of Hypopigmentation

Patient Selection and Pre-Treatment Care

Proper patient selection is important prior to initiation of excimer laser treatments of hypopigmented conditions. Patients with darker skin tones, such as skin type III and above, respond better to this therapy. A prospective patient has to be able to come for treatments at least on a weekly basis, although, as will be shown below, more frequent visits may lead to faster improvement. As a result, treatments require significant time commitment. In addition, as most insurance companies do not cover laser therapy for disorders of hypopigmentation, a large number of frequent treatments may present a significant financial burden for the patient. Thus, patients should have a realistic expectation of the potential number of sessions and associated costs. As well, patients should be informed that laser treatments are aimed at repigmentation, not cure of the condition.

Pre-treatment photographs are recommended and informed consent must be obtained from the patient. As treatments are usually painless, with only minimal, if any, sensation of warmth at the sites of laser exposure, pre-treatment anesthesia is not necessary. UV-protective goggles or glasses must be worn by everyone in the treatment suite. During treatment, unaffected skin is covered by UVB-protective templates, thus preventing unnecessary exposure. Templates are available in various shapes, such as circular or square forms for vitiligo and rectangular or linear ones for striae.

In order to select optimal initial treatment parameters, minimal erythema dose (MED) may first be determined. This can be accomplished by performing several test spots with incrementally increasing fluences. It is important to remember

that selection of fluences should be based on the color of the lesion, not the patient's skin type. Thus, patients with completely depigmented patches of vitiligo may require relatively low doses, around 100 to 150 mJ/cm^2, regardless of their overall skin tone. The minimal dose that produces confluent erythema within 24 hours is then designated as MED.

Vitiligo

Excimer laser therapy is typically initiated at MED or 50 mJ/cm^2 below the MED. The treatment dose is then increased incrementally with each session by about 50 mJ/cm^2 to produce erythematous response. Treatment areas have been divided into UV-sensitive and UV-resistant, depending on overall response. The former group includes face, neck, trunk, arms, and legs, whereas the latter includes elbows, knees, wrists, ankles, and dorsa of hands and feet [157,158]. Multiple treatments are needed for any location, but the ultimate rate of repigmentation appears to depend more on the total number of treatments than on frequency. Still, more frequent treatments, such as 3 times weekly, typically result in faster improvement compared to weekly or twice weekly regimens [159].

Repigmentation usually starts around hair follicles, resulting in "salt and pepper" appearance, and then spreads to the rest of the affected patch. Ultimately, approximately 25% of patients achieve 100% repigmentation in their UV-sensitive patches, 50% achieve 75% improvement, and 64% achieve 50% or greater improvement. UV-resistant patches fare worse, with only 20% of patients achieving 50% or greater improvement [160]. When supplemented by twice daily applications of topical tacrolimus ointment, repigmentation rates appear to increase, with 77% of patients achieving 75% or greater improvement in UV-sensitive areas and 60% in UV-resistant areas [161]. Persistence of pigment for at least 12 months following the completion of excimer laser treatments has also been noted [158,159].

Hypopigmented Striae Distensae and Hypopigmented Scars

Similar to vitiligo, treatments for striae albae and hypopigmented scars are started at MED or 50 mJ/cm^2 below the MED. The dose is then increased at each session to achieve the desired endpoint of erythema. Laser therapy is usually performed twice a week for a total of 10 to 15 treatments, although most patients require 9 or fewer sessions to achieve at least some clinical darkening. Such darkening is noted in 80% of patients [162], with a mean improvement in appearance of 68% in striae albae and

61% in hypopigmented scars [163]. As mentioned previously, histological and ultrastructural studies confirm an increase in the number and size of melanocytes in the basal cell layer, thus providing camouflage for the lesions [41]. Although some persistence of pigment is noted 6 months following the completion of excimer therapy, maintenance treatment is typically needed. Anecdotal evidence suggests that fewer maintenance sessions are required following a complete initial treatment course.

Post-Treatment Care

Mild to moderate erythema is common following excimer laser treatments. Blistering may occur at higher fluences and is similar to a sunburn reaction. Patients should be instructed to use antibiotic or petrolatum-based ointment if any such blistering takes place. Tanning may occur in surrounding exposed normal skin, but is usually temporary. Scarring with excimer laser has not been reported. Overall, this is a well-tolerated and efficacious treatment modality for these typically recalcitrant conditions.

Conclusions

The development of ultrashort-pulsed lasers allowed safe and efficient treatment of multiple pigmented lesions. The list of clinical conditions amenable to therapy with such systems continues to grow. Additionally, long-pulsed lasers and IPL sources, originally created for other indications, have also been found to be helpful in the treatment of some pigmented lesions. Newer technologies may offer additional effective therapeutic options for conditions currently regarded as recalcitrant. An interesting twist on such technologies is the development of engineered tattoo inks, making them more amenable to treatment with the currently available laser systems.

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Ablative Lasers and Devices

4

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Ablative Lasers and Devices

4

KEY POINTS

- Carbon dioxide and modulated erbium:yttrium–aluminum–garnet laser resurfacing produce the greatest wound while also producing the greatest results
- Fractionated resurfacing is a significant advancement in the compromise between the risk/benefit ratio, between ablative and non-ablative resurfacing
- Plasma resurfacing can produce some of the benefits of ablative resurfacing without the same degree of risk
- Newer fractionated resurfacing techniques will produce increasingly improved results

Introduction

The demand for an effective treatment modality for visible signs of sun damage keeps growing as the population continues to age. Although non-ablative technologies are becoming more popular due to their decreased downtime, ablative lasers are still the gold standard of facial resurfacing. In addition to photoaging, numerous other epidermal and dermal conditions, most notably acne scarring, are also amenable to treatment with ablative lasers and will be discussed in this chapter.

More recently, numerous new developments in the field of laser-assisted cutaneous resurfacing have resulted in improvements in the older systems. As well, new concepts, such as fractional resurfacing, are being introduced and promise to deliver impressive results with considerably decreased healing time and reduced risk of complications.

Essential Concepts

Changes Associated with Intrinsic and Extrinsic Aging

Numerous changes are known to occur in skin over time. These changes may be due to normal, or intrinsic, aging processes,

or to extrinsic factors, most notably chronic sun damage. Some of the major ultrastructural components associated with cutaneous aging and important in laser resurfacing will now be examined.

Collagen is the main determinant of the skin tensile strength and represents approximately 70% of the dry weight of the dermis [1]. In chronically photodamaged skin, collagen fibers are fragmented and thickened [2]. The ratio of collagen III to collagen I increases by as much as 30% after the age of 65 years [3]. As well, compared to the tight bundles of collagen in young skin, fibers in the aging skin are significantly more loosely woven and straight, providing for decreased potential for stretching [4].

Elastic fibers consist of various amounts of elastin and fibrillin and, as the name implies, are responsible for skin elasticity. Chronic photodamage results in increased synthesis of structurally and functionally abnormal elastic fibers [5], combined with slower degradation and localization within superficial and mid-dermis [6]. Histologically, these changes are responsible for the findings of solar elastosis; clinically, they account for decreased skin elasticity.

Glycosaminoglycans, most notably hyaluronic acid, and proteoglycans are major components of the dermal ground substance. Through their extensive binding of water molecules, they are the major determinant of dermal hydration. Although these molecules are increased in photodamaged skin, they are clumped and abnormally localized to the superficial band of elastotic material, resulting in inefficient water binding [7].

Dermal water is essential for the proper structural configuration and function of proteins and is extensively bound in younger skin. Although the total dermal water content increases with photodamage, it is present in unbound, or tetrahedron, form and is thus unable to interact with other dermal structural components [2,8].

Clinically, such ultrastructural changes manifest as dry, wrinkly skin with a yellowish hue. Additionally, multiple telangiectases may be present. Skin fragility results from decreased dermal matrix and reduced elasticity of dermal blood vessels, leading to complaints of easy bruising and senile purpura. Premalignant and malignant neoplasms may also arise on ultraviolet (UV) light-damaged skin.

Carbon Dioxide Laser Resurfacing: Laser–Tissue Interactions

Short-pulsed and scanned carbon dioxide (CO_2) lasers continue to represent the gold standard of facial rejuvenation. Originally

considered to be mainly due to ablation of superficial skin layers, the mechanism of action of this laser is now thought to be more closely related to heat-induced collagen denaturation and neocollagenosis.

Skin ablation results from desiccation of tissue. Both CO_2 and erbium:yttrium–aluminum–garnet (Er:YAG) lasers utilize specific absorptive characteristics of the water molecule. Light absorption by water is very low throughout the visible and near-infrared spectrum. Absorption starts to increase with wavelengths longer than 1200 nm, with the largest peak occurring at approximately 2935 nm. At 10,600 nm – the wavelength of the currently available CO_2 lasers – the absorptive coefficient is high at over 800 cm^{-1} [9]. Higher absorption of the laser beam results in lower optical penetration depth (OPD). OPD is defined as the depth at which the fluence is reduced to 1/e, or approximately 37%, of the original value. The OPD for CO_2 laser beam is approximately 20 μm [9].

Precise tissue ablation is governed by the theory of selective photothermolysis [10]. In order to decrease thermal diffusion, sufficient fluence of adequately absorbed wavelength must be delivered in less than the thermal relaxation time (TRT) of the irradiated tissue. TRT is the time required for a given tissue to cool sufficiently from its peak temperature. For the planar geometry of skin ablation, TRT is proportional to the square of the OPD [11]. Thus, for a CO_2 laser, TRT of the epidermis has been calculated to be approximately 1 ms. This value, however, is a topic of debate, as some experimental evidence suggests TRT as high as 20 to 40 ms [12]. The ablative threshold of CO_2 laser is usually quoted as 5 J/cm^2 for 1-ms pulse duration, but may be higher or lower depending on the exposure time [13]. Because of wide variability in pulse durations – also known as dwell time for scanned systems – of different CO_2 lasers, power, measured in watts (W) and equal to energy divided by pulse duration, or power density, also known as irradiance and measured in W/cm^2, is frequently utilized instead of fluence.

At typical settings just above the ablative threshold, CO_2 lasers with 1-ms pulse duration vaporize 30 to 70 μm of tissue per pass, essentially removing the epidermis in one pass [14]. On the other hand, lasers with shorter pulse durations in the microsecond range require higher energy and more passes to achieve a similar depth of ablation [15]. Rapid succession of pulses, known as pulse stacking, does not result in further ablation, but may lead to heat accumulation, as will be shown below. Additional passes with the laser result in continuous ablation until a plateau is reached following three passes at a depth of approximately 150 to 250 μm. Further passes do not

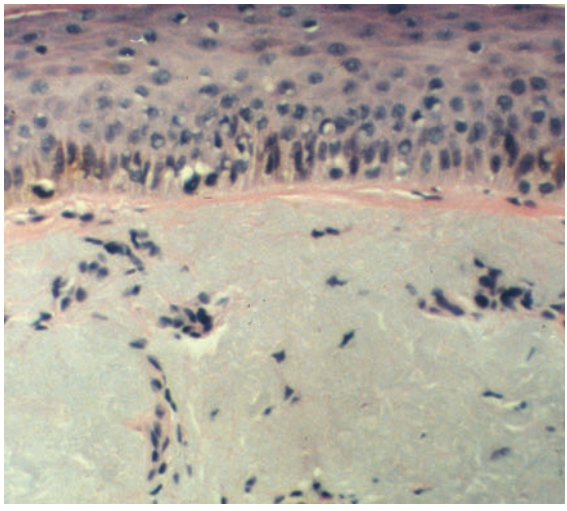


Figure 4.1 Post CO_2 laser-induced fibroplasia.

cause significant ablation, thereby serving as an inherent safety mechanism [14,16]. Due to lower water content of charred debris following an ablative pass, the amount of absorption by the tissue chromophore is considerably reduced unless the debris is removed. This is accomplished by wiping between passes. In the absence of wiping, the debris has been shown to act as a heat sink, allowing for an increase in peak surface temperature on a subsequent pass by as much as 50°C [17,18].

While the clinical improvement following CO_2 laser resurfacing was originally thought to be associated with epidermal and dermal ablation, histological analyses found only limited dermal ablation past 50 μm [19,20], much less than would be required for correction of rhytids. Cosmetic enhancement following skin resurfacing has thus been proposed to be closer related to thermal diffusion, also known as residual thermal damage (RTD), resulting in collagen denaturation and fibroplasia (Figure 4.1).

Although the theory of selective photothermolysis predicts thermal confinement, propagation of heat to deeper tissues occurs even when the pulse duration is below the theoretical TRT of the epidermis. This suggests that the calculated value of TRT may, in fact, be too high. As a result, the total depth of injury by the CO_2 laser is the sum of the depth of ablation and that of RTD. The depth of RTD is described by the Beer–Lambert law, which predicts an exponential decrease in light intensity or fluence with increasing depth in tissue. This implies that an increase in fluence produces only a small increase in RTD. Subsequently, thermal necrosis underlying

the base of ablation is predictably limited to 70 to 100 μm in depth for 1-ms pulse duration, resulting in coagulation of small blood vessels and providing hemostasis for the procedure. RTD remains essentially unchanged for multiple passes; however, pulse stacking or prolonged exposure time significantly increases cumulative thermal injury to unacceptable levels and may result in scarring [14,21].

In order to avoid pulse stacking, it is important to understand the structure of the beam of a typical CO_2 laser. Since the distribution of fluences within the laser beam is Gaussian, or bell-shaped, there is a significant variation in ablative depths between the center and the edges of the beam [22]. This may lead to an erroneous conclusion that beam overlap may provide for a more consistent depth of injury. However, according to the above discussion, the depth of RTD is essentially constant throughout a range of fluences and, subsequently, within most of the beam with the exception of far edges. Therefore, minimal or no overlap during treatment with a CO_2 laser is critical to prevent potential scarring. Instead, a consistent ablation depth may be achieved with multiple passes.

In order to understand tissue tightening induced by dermal heating, the process of collagen denaturation must now be examined. Collagen exists as a right-handed helix with three polypeptide chains held together by hydrogen bonds. Upon heating, hydrogen bonds rupture, allowing the chains to assume a random-coil configuration [23,24]. Although sometimes quoted to take place at 63°C to 64°C [25], collagen denaturation actually occurs over a range of temperatures and pulse durations, with higher temperatures required to achieve similar contraction for shorter exposure times. Thermal denaturation then leads to irreversible shortening and thickening of the collagen fibrils. Once a sufficient number of fibrils have been denatured, this process produces clinically observable tissue contraction. The amount of immediate contraction following CO_2 laser resurfacing is related to the depth of dermal RTD [26]. Subsequently, as with RTD, the immediate surface area contraction reaches its maximum after three passes at approximately 38%, with minimal further contraction afforded by additional passes [27].

Both histologically and ultrastructurally, thermal denaturation results in observable changes in staining and structural characteristics of collagen fibers. Immediately below the charred debris, a layer of intense basophilia with loss of birefringence, also known as the coagulative zone and most often identified as RTD, reflects complete denaturation of collagen, which has been confirmed by electron microscopic studies. Subjacent to that, a thin zone of mixed denatured and native fibrils is identified

and presents with an overall decrease in collagen birefringence. Finally, a hypereosinophilic zone, also known as the transition zone, with normal birefringence and slightly thickened collagen fibrils can be discerned under both light and electron microscopes [22,28,29].

When an occlusive dressing is used following CO_2 laser resurfacing, the basophilic zone of collagen denaturation remains intact, later becoming integrated into the developing granulation tissue and serving as a template for new collagen deposition. Within this zone, necrotic fibroblasts are replaced within 1 to 2 days and are surrounded by granulation tissue within 7 days [22]. Keratinocytes begin migration from hair follicles over the surface of the basophilic zone 2 days following resurfacing and complete re-epithelialization by 5 to 7 days. In the absence of an occlusive dressing, most of the basophilic zone sloughs off within 2 days, thus releasing the tethering mechanism behind the initial wound contraction. As well, epidermal re-epithelialization is significantly delayed under such conditions [30]. An additional contraction occurs 5 to 10 days following laser resurfacing, thought to derive from the action of myofibroblasts. Although some of the initial contraction is reduced by 2 months following resurfacing [22], the dermis continues to exhibit progressively increasing collagen content with horizontal alignment of fibers noted 1 year following the procedure [31]. In addition, decreased solar elastosis [32], increased neoelastogenesis, and improved three-dimensional structure of the elastic fiber network [33] add to the clinical improvement in rhytids following CO_2 laser resurfacing.

Er:YAG Laser Resurfacing: Laser–Tissue Interactions

With all the benefits and undisputable effectiveness of skin resurfacing using CO_2 lasers, these systems are associated with prolonged healing time and difficult wound care regimens. In addition, they may be complicated by infections and dyschromias, as will be discussed below. Subsequently, an Er:YAG laser was introduced in an attempt to ease the recovery process and to improve on the side effect profile of the CO_2 laser. While the original results with this laser were soon found to be inferior to those obtained with a CO_2 laser, newer modulated systems offer solid treatment options for skin resurfacing.

The wavelength of light produced by the Er:YAG laser, 2940 nm, is near the largest absorption peak by the water molecule. As a result, its absorption coefficient is nearly 16 times that of the CO_2 laser, while its OPD is significantly reduced compared to the latter, at only 1 μm [34]. This leads to explosive

vaporization of tissue with a characteristic audible popping sound. As well, the ablative threshold of the Er:YAG laser is significantly lower than that of the CO_2 laser and is estimated at between 0.5 and 1.7 J/cm^2 for pulse durations between 250 and 350 μs [35,36].

Due to the high absorption of laser light by water, the traditional Er:YAG laser operates in a nearly pure ablative mode, with only a thin layer of thermal damage of 10 to 50 μm [36,37]. Each pass of the laser predictably removes 2 to 4 μm of tissue per J/cm^2 of fluence. This is in contrast to the CO_2 laser, where an ablative plateau is achieved after only three passes. As well, wiping between passes is not necessary, as the charred debris has sufficient water content to be ablated during the subsequent laser pass.

A relatively low RTD associated with the Er:YAG laser allows the safe use of fluences well above the threshold, also in contrast to the CO_2 laser. Older systems were equipped with small spot sizes and generated low fluences and repetition rates, requiring at least three passes for complete epidermal ablation [38]. Newer, more powerful laser systems are able to remove 70 to 100 μm of tissue per second [36]. The improved pace of epidermal ablation is, however, limited by poor hemostasis afforded by the traditional Er:YAG lasers, as the depth of RTD does not provide for blood vessel coagulation.

In contrast to the CO_2 lasers, there is no immediate wound contraction with the older Er:YAG lasers and only mild linear contraction with the newer, more powerful systems. Contraction peaks at approximately 14% at 16 weeks post-resurfacing [39]. Healing time is reduced compared to CO_2 lasers, with re-epithelialization complete by 3 to 5 days.

Several modifications on the traditional Er:YAG laser have allowed for better tissue tightening and hemostasis during resurfacing. From the experience with CO_2 lasers, the depth of the RTD determines the amount of immediate and long-term contraction, as well as new collagen deposition. To that effect, modulated Er:YAG systems have been developed to deliver increased thermal energy to the dermis. This entails the abolition of thermal confinement to the epidermis and the use of sub-ablative laser pulses. This can be accomplished with low fluences and long pulse durations, allotting sufficient time for thermal conduction to the underlying dermis. Such use of Er:YAG lasers has been termed thermal, or coagulative, mode and is associated with greater immediate tissue contraction and long-term collagen remodeling. In practice, this has been accomplished in several different ways. A variable-pulse Er:YAG laser allows manipulation of exposure time for various degrees

of ablation and coagulation. A dual-mode Er:YAG laser utilizes a process termed optical multiplexing for delivery of either ablative or a combination of ablative and coagulative pulses simultaneously or in tandem. Finally, a hybrid system utilizing Er:YAG laser for ablation and CO_2 laser for coagulation has also been developed.

Fractional Photothermolysis: Laser–Tissue Interactions

Fractional photothermolysis has recently been introduced as an alternative to both ablative resurfacing and non-ablative photorejuvenation, to be discussed in the next chapter. The first commercially available system utilizes a focused 1550-nm erbium-doped fiber laser to form arrays of columns of thermal damage, also known as microscopic treatment zones (MTZs). Laser light of this wavelength is absorbed mostly by water; however, its low coefficient of absorption, about $10.5\,cm^{-1}$ [9], allows much deeper penetration into the dermis compared to CO_2 or Er:YAG lasers.

The columns of thermal damage are surrounded by uninjured tissue. Thus, the percentage of surface area treated during a laser session is related to the total MTZ density, a product of per pass density displayed on the computer screen and the total number of passes. Both the width and the depth of the MTZ increase almost linearly with increasing energy levels. Thus, the setting of 6 mJ per MTZ results in columns of thermal damage approximately 80 μm in width and 360 μm in depth, 10 mJ is associated with columns that are 110 μm wide and 500 μm deep, and 12 mJ causes damage limited to approximately 125 μm in width and 560 μm in depth. Due to the clinical relevance of this information for the practitioner, the newest model of this laser system displays the corresponding depth of thermal injury alongside the energy level. The newer model also verifies the delivery of adequate total energy based on MTZ density, number of passes, and linear dimensions of the treatment area.

Immediately following laser exposure, lower epidermal and dermal thermal damage is evident on histological sections, as are subepidermal clefting, preservation of the overlying stratum corneum, and coagulation of dermal blood vessels. One day following treatment, thermally damaged epidermal components, also known as micro-epidermal necrotic debris (MENDs), are formed immediately below the granular layer and contain large amounts of epidermal melanin, resulting in the clinical appearance of bronzing. MENDs continue to

migrate up through the epidermis and are progressively eliminated starting on day 3 post-treatment, manifesting clinically as flaking. Extrusion is usually complete by 7 to 14 days. In the dermis, a wound healing reaction occurs following treatment, with gradual replacement of denatured collagen with newly formed collagen fibers, as well as the documented presence of myofibroblasts at 7 days following laser treatment [40,41]. Additional evidence indicates active incorporation of dermal solar elastotic material into MENDs, with subsequent transport and elimination through the columns of thermal damage [42], possibly contributing to the clinical improvement in photodamaged skin.

Due to decreased downtime following laser treatment with the delivery of columns, rather than layers, of thermal damage, fractional photothermolysis is an attractive concept. Initial fractionated lasers use erbium:glass. Newer fractionated Er:YAG and CO_2 lasers are currently in the late stages of development.

Plasma Skin Resurfacing Device: Energy–Tissue Interactions

Plasma is generated when an ultrahigh-frequency electrical current is applied to nitrogen gas. As nitrogen returns to the ground state, it releases thermal energy, accompanied by a burst of golden-yellow light, also known as Lewis–Rayleigh afterglow. Thermal energy is delivered in pulses with duration in the millisecond range. When the handpiece is brought into close proximity to skin, heat is delivered to the epidermis and is subsequently conducted to the upper dermis. Unlike previously described ablative lasers, no tissue chromophore is necessary for the plasma skin resurfacing device.

Energy levels vary from 1 to 4 J/cm^2, with higher settings resulting in superficial ablation and total thermal damage to 317 μm [43]. Ablative settings lead to gradual desquamation following treatment with concurrent subjacent epidermal regeneration. Thus, thermally damaged epidermis serves as a biological dressing during the process of re-epithelialization, typically complete by 7 days [44]. With lower, non-ablative settings, thermal damage is less pronounced, with scaling, rather than full-thickness desquamation, lasting 3 to 5 days.

Similar to ablative lasers, the delivery of thermal energy to the dermis using plasma skin resurfacing device leads to collagen denaturation in papillary dermis with linear skin contraction of 10% to 15% [45]. In addition, long-term stimulation of fibroblasts leads to new collagen deposition for at least 3 months following the procedure [44].

Pearls and Problems

Patient Selection and Pre-Treatment Care

Proper patient and device selection for laser resurfacing is paramount to the overall success of the procedure. As a generalization, the more pronounced or severe conditions to be treated require more aggressive therapies for satisfactory results. This, however, has to be balanced with longer downtime and higher risk of adverse effects associated with such procedures. Thus, moderate to severe photodamage, severe facial rhytids, and deep atrophic facial scars are best treated with the CO_2 laser, with milder conditions amenable to other, less aggressive lasers and devices.

The ideal candidate for laser resurfacing has a fair complexion with Fitzpatrick skin types I to III, expresses realistic expectations about the outcome of the procedure, and is able to follow stringent post-operative wound care protocols. Additional consideration must be given to previous history of excessive or keloidal scarring, poor wound healing, and conditions that may predispose to infections. Patients with recent intake of oral isotretinoin should not be treated with ablative lasers and devices for at least 6 months following the discontinuation of the medication. Patients with history of radiation exposure may have delayed re-epithelialization at exposure sites due to the lack of hair follicles, which normally serve as a source of epidermal stem cells following cutaneous injury. Additionally, the knowledge of variations in wound healing based on anatomical location is critical and will be discussed later. High-quality photographs and informed consent must be obtained prior to the procedure to document pre-existing condition of the skin, as well as post-operative improvement.

Care in the immediate pre-treatment period is important to the overall success and will now be considered in detail. Multiple pre-operative regimens have been utilized in an attempt to decrease the incidence of post-resurfacing hyperpigmentation, especially pronounced in the darker skin tones. However, a rigorous study of several topical agents, including glycolic acid, hydroquinone, and tretinoin found no influence on the rate of hyperpigmentation [46]. On the other hand, the same topical agents may be very beneficial in the post-operative period, as will be shown below.

Antibiotic prophylaxis of wound infection, especially in the context of CO_2 laser resurfacing, is a controversial practice, with some practitioners advertising the use of combinations of several broad-spectrum antibacterial and antifungal agents,

others utilizing only narrow-spectrum anti-Staphylococcal agents, and others still showing no advantage in such indiscriminate use of antibiotics, which may lead to the emergence of resistant strains [47–53]. In our own practice, we agree with the latter group, preferring to treat those patients with clinical evidence of infection based on careful clinical monitoring.

On the other hand, antiviral prophylaxis in the perioperative period is essential to prevent herpetic outbreaks with potential dissemination throughout the physically and thermally injured skin [54–56]. Such prophylaxis is mandatory in full-face or perioral resurfacing, even in those patients without clear history of herpes, as asymptomatic carrier status is not uncommon. Prophylaxis is usually started 2 to 5 days prior to the procedure and is continued for a total of at least 10 days or until full re-epithelialization.

The need for pre-operative anesthesia should be considered for all ablative devices. While topical anesthetic agents and local nerve blocks may be sufficient for Er:YAG, fractional photothermolysis, and plasma skin resurfacing device, CO_2 laser resurfacing may require intravenous sedation or general anesthesia administered by a qualified practitioner. Fractional photothermolysis lasers, currently being used, require the application of a blue dye (FD&C Blue #1) over the treatment area, which allows a computerized tracking device to monitor the linear velocity of the handpiece and to provide real-time feedback for consistent MTZ density. In addition, a petrolatum ointment or an ultrasound gel is applied over the blue dye for easier handpiece gliding. When treating periorbital areas, metal corneal shields are inserted to protect the patient's eyes.

Non-contact ablative lasers and devices create plume, both irritating to the airways and potentially infectious [57–60]. For this reason, all ablative procedures with the exception of the fractional photothermolysis laser must be accompanied by a properly working smoke evacuator. Finally, the ablative device and, if so equipped, its associated scanner, also known as computer pattern generator (CPG), should be tested immediately prior to the procedure, typically using a wet wooden tongue depressor.

Treatment of Photodamaged and Aging Skin Using CO_2 Lasers (Figures 4.2–4.4)

The CO_2 laser is best at reducing the signs of moderately to severely photodamaged and aging skin, including photoinduced dyspigmentation, rhytids, actinic and seborrheic keratoses, and solar lentigines. Entire cosmetic units – and most often the

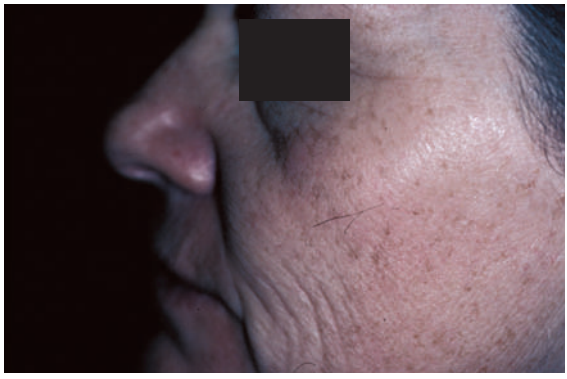
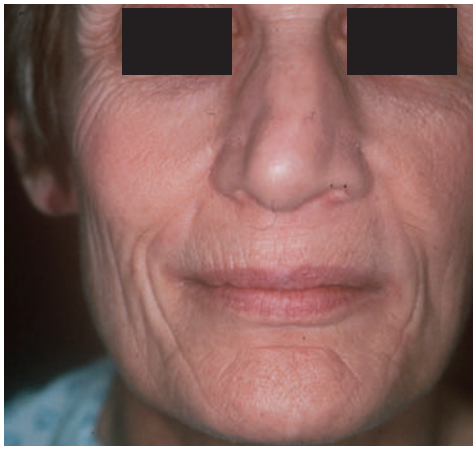
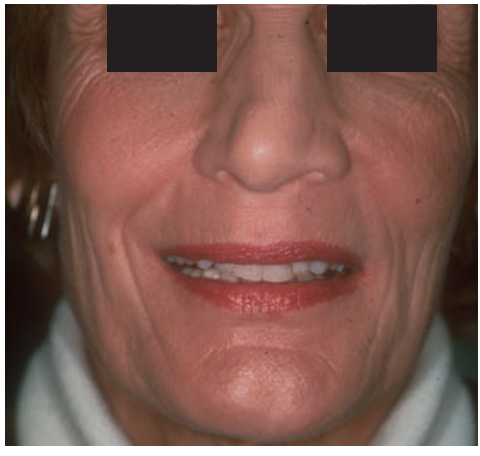


Figure 4.2 Ideal patient for CO_2 laser resurfacing.

(a)





(b)

Figure 4.3 **(a)** Before CO_2 laser resurfacing and **(b)** 2 years after CO_2 laser resurfacing.

entire face – should be treated to prevent obvious lines of demarcation following recovery. As stated previously, the first pass of the laser typically removes the entire thickness of the epidermis. To avoid pulse stacking and achieve even and consistent results, this is best accomplished using the CPG with pattern 3, size 9, and density 5 or 6. Treatment is best started on the forehead, where thicker skin is also more forgiving. Care must be taken not to cross the vermilion border of the lip, as this may blunt its appearance. For milder sun damage and mild rhytids one pass of the CO_2 laser may be sufficient. If no further passes will be undertaken, the grayish-white debris is left intact, serving as a natural biological dressing, preventing tissue desiccation and leading to faster re-epithelialization.

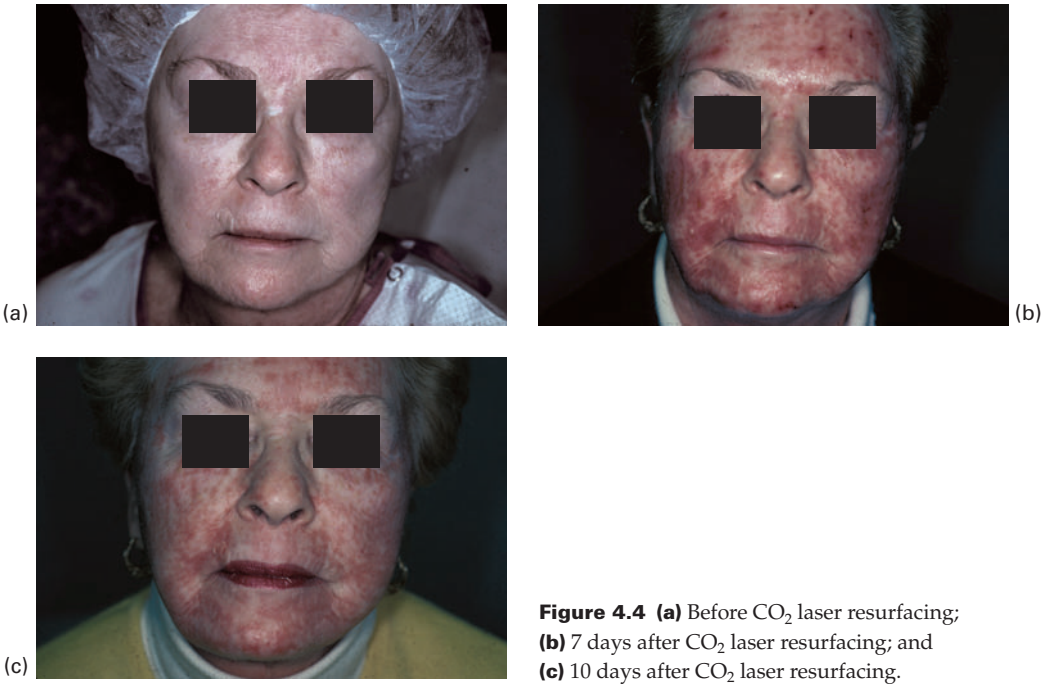


Figure 4.4 **(a)** Before CO_2 laser resurfacing; **(b)** 7 days after CO_2 laser resurfacing; and **(c)** 10 days after CO_2 laser resurfacing.

For moderate or severe sun damage and rhytids, more aggressive resurfacing may be required for good improvement. Additionally, adjunctive botulinum toxin A denervation, administered before or after the laser treatment leads to a prolonged improvement in dynamic rhytids [61,62]. Prior to the second or third pass, the desiccated debris from the previous pass is removed using saline-soaked gauze. Debris is also wiped off following the last pass of the treatment session, as such debris leads to increased inflammation and prolonged healing time. Subsequent passes are performed in a perpendicular direction to the original pass to prevent streaking. As previously mentioned, additional passes with the CO_2 laser beyond the third pass do not offer further ablation and are generally avoided. Clinically, this is evident by the appearance of chamois color, which represents tissue desiccation and indicates the endpoint of treatment [16].

Thermal damage and, as will be discussed below, subsequent post-operative erythema may be reduced by decreasing the density setting of the CPG for the second and third passes. The third pass may be especially useful for the glabellar area, medial cheeks, and the upper lip. The 3 mm handpiece may also be used for precise targeting of problem areas. On the other hand, the periphery of the face, such as the jaw line,

has a higher potential for scarring and for developing demarcation lines. This is prevented by feathering with lower fluence, performing only a single pass at these locations, and leaving the epidermal debris for transition effect.

If available, an Er:YAG laser may also be used following the CO_2 laser passes to sculpt dermal irregularities more precisely, as ablation with the former proceeds unabated without increasing thermal damage. In addition, due to the higher absorption of Er:YAG beam by the water molecule, such use obviates the need to wipe off debris following the last pass of the CO_2 laser and may also lead to reduced duration of erythema, edema, and crusting [63–65].

No more than two passes with decreased fluence and reduced CPG density setting of 4 or 5 should be performed over the eyelids, since both the epidermis and the dermis are thinnest there compared to all other areas of the face. Alternatively, the 3 mm handpiece may be used to deliver individual pulses 3 to 5 mm apart in order to attain significant tissue tightening with reduced thermal damage and healing time [66].

Treatment of the photodamaged or aging neck skin using a CO_2 laser is controversial. From the experience with chemical peels, it has been proposed that the CO_2 resurfacing in this location may lead to increased incidence of scarring due to a decreased number of pilosebaceous units. Indeed, scarring following such resurfacing has been noted in a small study [67]. Several large studies, however, have advocated the feasibility of such treatment, as long as lower settings are used and specific guidelines are followed. It is imperative that a topical anesthetic be applied under occlusion for at least 1 hour prior to treatment to provide epidermal hydration. While thicker-skinned individuals may tolerate treatment with 60 W of irradiance to the entire neck, those with thinner skin require a lower setting of about 20 W on the lower neck as compared to the upper neck [68]. Alternatively, density setting of the CPG is reduced to 3 or lower [69]. A maximum of one pass is undertaken on the neck, leaving desiccated debris intact. Lateral feathering using lower fluence prevents demarcation from untreated posterior neck. Overall, however, we prefer Er:YAG resurfacing of the anterior neck due to shorter healing time and lower risk of scarring, as will be delineated below.

Reports on the use of CO_2 laser resurfacing for rejuvenation of photodamaged or aging dorsal hands are scarce. While lower irradiance, decreased CPG density setting, and a single pass have been advocated as safe and effective in a limited number of patients [66,70], the use of Er:YAG laser, to be discussed below, may be the preferred method of treatment in this area.

Post-operative wound care regimens can be subdivided into open and closed methods. The open method typically utilizes petrolatum-based ointments and similar topical formulations to provide occlusion. The effectiveness of such dressings depends on the patient's diligence in reapplication every 2 to 3 hours. Closed methods promote a moist environment, prevent crust formation, and protect the wound. They are also associated with reduced severity and duration of erythema, decreased pruritus, and reduced post-operative pain [71–73].

Multiple types of closed dressings have been promoted over the last several years and are generally subdivided into composite foams, hydrogels, polymer meshes, and polymer films. Although composite foams are adhesive, easiest for home maintenance, and absorbent, they are opaque and do not allow for direct inspection of skin. Hydrogel dressings are mostly composed of water and are transparent, but must be secured with tape or band net dressing, need additional gauze for absorption, and tend to slide off easily. Polymer meshes and films, including silicone dressings, have slits that allow escape of exudate, but require gauze for absorption. They are also secured with a band net dressing, but are most transparent, allowing visual inspection of the wound [74]. At the end, the choice of the type of occlusive dressing used after CO_2 laser resurfacing usually depends on the practitioner's individual experience.

Although some practitioners change the dressing after 2 days and maintain closed occlusion for a total of 4 to 5 days, many have adopted a combination approach, where the original dressing is removed after 2 days, followed by the open method. Skin is soaked at least 4 to 5 times per day – preferably every 2 hours – using a dilute vinegar solution and gauze while avoiding rubbing. The wound is then covered with a petrolatum-based or similar ointment until complete re-epithelialization. Sun avoidance is crucial after laser resurfacing and sun protection using physical blocking agents is instituted following epidermal healing. The most important method to avoid infections and other potential pitfalls is careful and frequent follow-up in the immediate post-operative period.

Adverse effects and complications following CO_2 laser resurfacing may arise soon after the procedure or may be delayed by as long as a year. The most common adverse effect is erythema, occurring in 100% of treated patients and lasting between 1 and 9 months, with an average of 4.5 months [75]. Erythema is believed to be related to the depth of thermal injury and may also correlate with long-term tissue tightening. As mentioned previously, the use of closed method of post-treatment occlusion may reduce the duration of this side effect. Topical

application of an aqueous solution of vitamin C following resurfacing has also been found to significantly decrease the duration and the intensity of erythema [76]. In addition, implementation of red light-emitting diode (LED) therapy following a combination of blepharoplasty and CO_2 periorbital resurfacing may be effective in accelerating wound healing, including reduction in the duration of erythema [77].

Edema, occasionally quite dramatic, peaks on post-operative day 2 or 3 and may last for up to 1 week. The intensity of swelling may be somewhat alleviated with the help of ice packs or cool compresses following the procedure.

Pruritus is common, occurring in up to 90% of patients in the immediate post-treatment period [78]. Multiple etiologies may contribute to this sensation, with the most common being physiologically related to healing, tissue dryness, and contact dermatitis. Additionally, fungal colonization, especially with Candida species, may lead to prolonged and intense itching [79]. If positive cultures are obtained, appropriate antifungal treatment may reduce this complaint. In the absence of colonization, oral antihistamines may provide adequate pruritus relief.

Various infections have been reported to occur following CO_2 laser resurfacing and may prolong the healing process. Similar to those complicating burn wounds, such infections include bacterial, fungal, viral, and mycobacterial. Bacterial infections occur in 1% to 5% of all resurfacing cases, with the majority due to *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Various other bacterial species, including multiple drug-resistant species, have also been recovered from post-resurfacing wounds [80,81]. Bacterial infections typically occur in the first 10 days, but may be significantly delayed by up to 5 weeks, likely due to patients' contamination of their topical wound care products [82]. Increasing pain, burning, or itching 3 days after the procedure should prompt a search for an infectious agent and appropriate antibiotic coverage. Additional signs may include honey-colored crusting and exudate, pustules, erosions, and may eventuate in scarring. Fungal infections, most commonly Candida species, may occur in 1% to 3% of resurfacing cases, but may not present with beefy erythema or satellite lesions. Instead, persistent erythema, pain, itching, burning, and delayed healing may provide clues to this complication [79]. Thus, a high level of suspicion and appropriate cultures are important for proper diagnosis and treatment. Viral infections, most commonly due to herpes simplex virus, may occur even with antiviral prophylaxis [55]. Dissemination and scarring may occur and the infection must be treated early. As well, as mentioned previously, plume from resurfacing may

be infectious. Thus, an unusual cutaneous dissemination of verrucae with subsequent resolution within 5 days has been described [83]. Finally, the development of an abscess due to an atypical mycobacterial species, *Mycobacterium fortuitum*, 1 month following CO_2 laser treatment has been documented, but, fortunately, is also rare [84].

Dyschromias are a common late complication of CO_2 laser resurfacing. Transient hyperpigmentation is common, occurring in 37% of all patients [75], but nearly universally in those with skin types IV and above [85]. As will be discussed below, Er:YAG laser resurfacing may be associated with less hyperpigmentation in darker individuals. Initial strict sun avoidance and later sun protection using high sun protection factor (SPF) sunblocking agents is critical for reduction of this adverse effect. Post-inflammatory hyperpigmentation typically starts 30 days following laser resurfacing and may be treated with topical bleaching agents, tretinoin, light glycolic or Jessner's chemical peels, and other treatment modalities discussed in an earlier chapter. Hypopigmentation, on the other hand, typically occurs in fair-skinned individuals with skin types I and II, with only rare reports in skin type III. The incidence of this late adverse effect – which may not present for 6 to 12 months – can be as high as 16% in this population [78,86,87]. It is seen more commonly in patients with deeper thermal injury and subsequent prolonged erythema and is currently thought to be secondary to suppressed melanin synthesis [88,89]. Excimer laser, as described in the previous chapter, and topical psoralen and UVA therapy have been tried for this complication with some success [90].

Acne and milia appear to be a complication of topical application of petrolatum-based ointments, although other etiological factors have been proposed, as well. They develop in approximately 10% of treated patients 3 to 6 weeks after resurfacing and are amenable to the standard anti-acne regimens and manual extraction [75].

Contact dermatitis used to be quite common, although its incidence appears to have been reduced over the years. This is likely due to a more consistent use of hypoallergenic topical preparations and the avoidance of sensitizing topical antibiotics [91]. For the same reason, patients should not use their own moisturizers and makeup for at least 2 weeks following laser resurfacing.

Permanent scarring, both atrophic and hypertrophic, typically occurs as a result of post-resurfacing infections or incorrect treatment technique with aggressive settings, pulse overlapping, or excessive laser passes, especially in the sensitive areas of the mandible, chin, and neck. Overall, permanent scarring occurs in less than 1% of treated patients and is more common

in those with history of keloidal or hypertrophic scarring [75]. Developing scars, initially manifested clinically as erythema and pruritus and later as wound thickening, may be treated with topical and intralesional steroids or a combination of intralesional triamcinolone and 5-fluorouracil [92]. Additionally, a pulsed dye laser may also be used for hypertrophic scars.

Laser resurfacing of the eyelids may lead to a specific set of adverse effects, including scleral show, synechia, and various degrees of ectropion. Synechia is the early developing fusion of opposing denuded surfaces, typically occurring on the lower eyelids. This connection may result in webbing and needs to be physically separated, followed by the application of an adhesive patch to prevent recurrence [93]. Patients with excessive eyelid laxity – manifested clinically as poor lid snap – or history of blepharoplasty may be predisposed to developing cicatricial ectropion. Mild ectropion is relatively common and usually resolves spontaneously without sequelae. In cases of more significant ectropion, regular massage of the eyelid, application of topical steroids, or intralesional steroids may be utilized. Surgical intervention may be necessary for correction of persistent ectropion with significant corneal problems.

Uncommon adverse effects following CO_2 laser resurfacing include a rapid development of basal cell and squamous cell carcinomas [94], an appearance of multiple eruptive keratoacanthomas [95], a development of new-onset cutaneous sarcoidosis [96], and a report of ignition of previously injected silicone filler upon exposure to laser light [97].

Treatment of Photodamaged and Aging Skin Using Er:YAG Lasers (Figures 4.5–4.8)

Due to the predictable, relatively constant depth of ablation without plateau with Er:YAG lasers, pre-operative assessment of epidermal and dermal thickness is critical. As mentioned previously, first-generation Er:YAG lasers require multiple passes to complete epidermal ablation. Newer, more powerful systems can perform the same task in one pass and must, therefore, be adjusted according to anatomic location using the ratio of 2 to 4 μm of vaporization for each J/cm^2 of fluence. Eyelid skin is thinnest, with epidermal thickness of 50 to 70 μm. Other facial locations are thicker, with the epidermis extending to the depth of at least 80 to 100 μm. Since the desiccated debris does not need to be wiped off after each pass, ablation is relatively hands-free and rapid.

Dermal ablation is then undertaken to correct dermal irregularities. This process is significantly limited on older systems

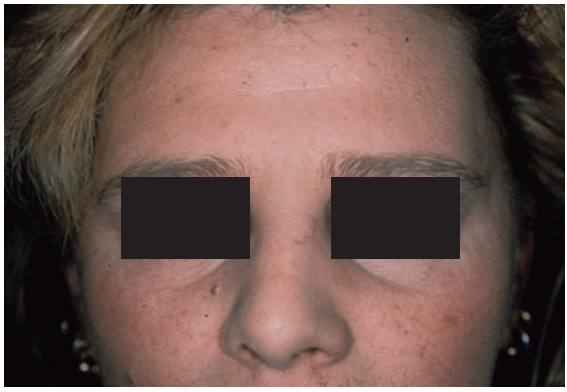
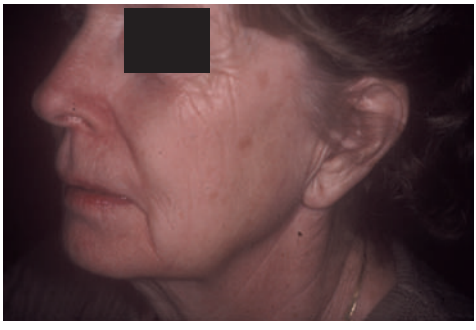
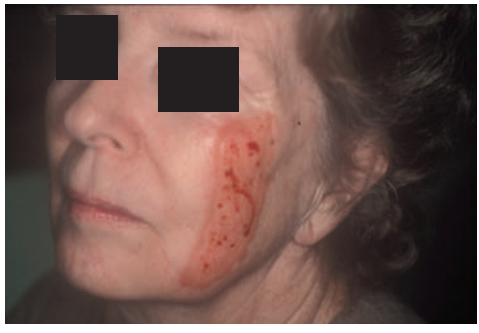


Figure 4.5 Ideal Er:YAG laser resurfacing patient.

(a)





(b)

(c)

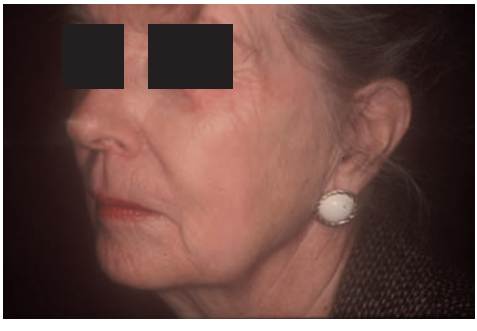


Figure 4.6 **(a)** Before Er:YAG laser resurfacing; **(b)** immediately after Er:YAG laser resurfacing; and **(c)** 6 months after Er:YAG laser resurfacing.

due to poor hemostasis and frequently leads to premature termination of the resurfacing procedure. Newer systems, whether variable-pulsed, dual-mode, or hybrid with a CO_2 laser, may be used in coagulative or mixed ablative and coagulative modes to improve hemostasis and provide thermally induced tissue tightening. Typical coagulative setting of 25 μm is sufficient for eyelid resurfacing, whereas 50 μm of coagulation may be used for hemostasis on the remainder of the face. Dermal ablation is continued until deemed sufficient by the

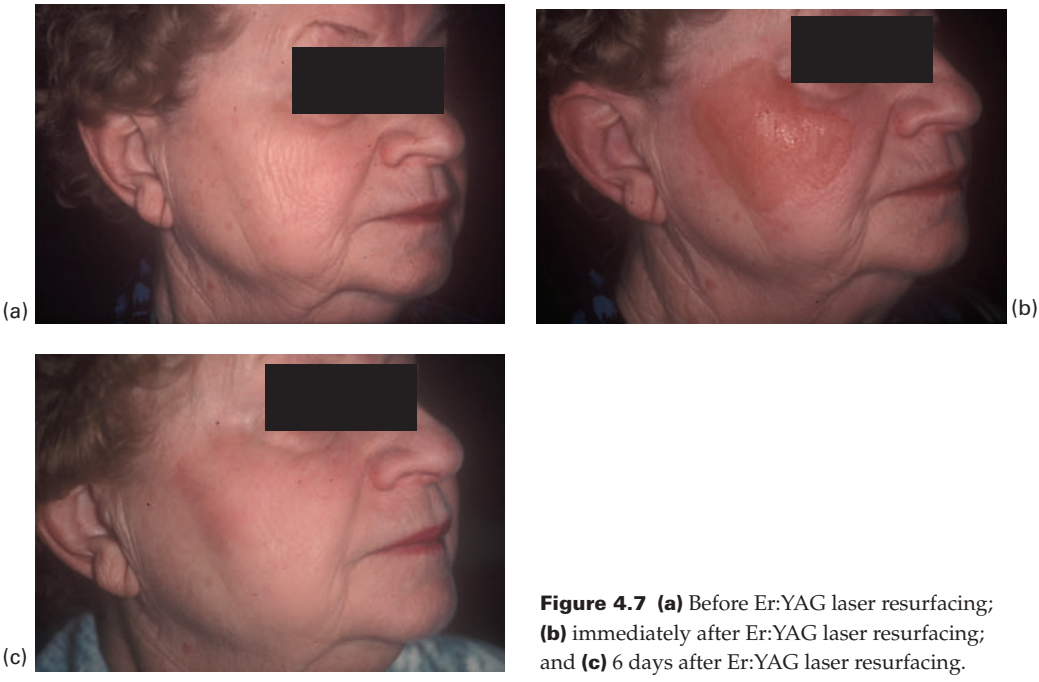


Figure 4.7 **(a)** Before Er:YAG laser resurfacing; **(b)** immediately after Er:YAG laser resurfacing; and **(c)** 6 days after Er:YAG laser resurfacing.

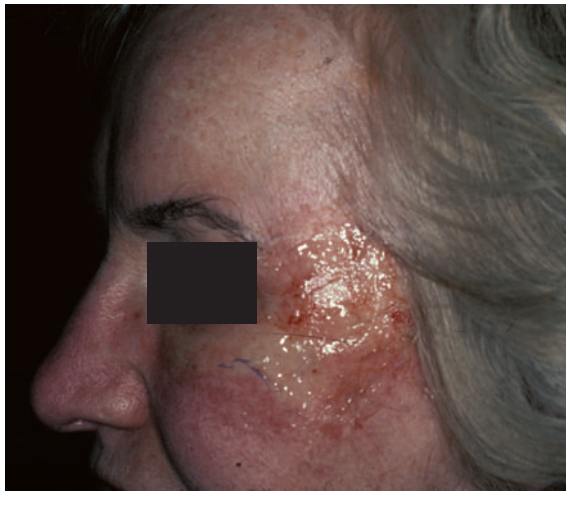


Figure 4.8 Immediately after Er:YAG laser resurfacing.

practitioner without the help of color changes as described for CO_2 lasers. Thus, relatively conservative treatments are recommended for novice practitioners. Peripheral feathering may be accomplished using lower fluence setting or defocused beam. Post-operative wound care regimen using the closed method is

similar to that described at length for post-CO_2 laser resurfacing, but is generally shorter in duration [98].

Although the original, purely ablative systems were associated with modest improvement in photodamaged skin and rhytids, sometimes necessitating additional resurfacing sessions several months later [99], all newer, modulated Er:YAG systems lead to significantly enhanced clinical results. Depending on the aggressiveness of treatment, long-term clinical and histological improvement in photodamaged skin may actually approach that attained using CO_2 lasers with moderate settings [100–104], albeit at a price of prolonged erythema. While the newer systems also display clinically relevant information, such as the depth of ablation and thermal damage, as well as variations in actual fluence based on the degree of pulse overlap, the practitioner must be aware that such information may not always be reliable, as in the case of subsequent purely thermal or mixed thermal and ablative passes using a variable-pulsed Er:YAG laser [105].

More recently, a technique of very superficial intraepidermal ablation using Er:YAG laser, also known as microlaser peels, has become popular due to a significantly improved side effect profile and rapid healing time. Treatment sessions, aimed at ablating just 10 to 30 μm of epidermal thickness, are repeated every month for a total of 3 to 6 treatments and may be combined with non-ablative rejuvenation techniques, such as intense pulsed light (unpublished data). Complete re-epithelialization usually takes only 3 to 4 days and, although results after a single session are fairly unimpressive, the final outcome is significant photorejuvenation [106,107].

Treatment of non-facial skin, including that of the neck, hands, and arms may be accomplished more safely using Er:YAG laser compared to CO_2 laser [108], although the improvement may also be more modest. Hands can tolerate two to three low-fluence passes, whereas the neck is treated with up to two passes for the upper neck and only a single pass for the lower neck. Manual removal of desiccated debris is avoided. Overall, longer healing time, with up to 3 weeks for complete re-epithelialization, is associated with treatment of these areas compared to face [109,110].

The types of adverse effects that occur following Er:YAG resurfacing are very similar to those described above for CO_2 lasers with some important differences in frequency, severity, and duration of several of the complications. Thus, only such differences will now be highlighted. At less than 4 weeks, the overall duration of erythema is significantly reduced with the older, purely ablative Er:YAG systems [111], but may increase to 12 weeks or longer with the newer, modulated systems

depending on the settings [112]. This is not surprising, since, as previously mentioned, erythema is related to the degree of thermal damage of the dermis. Spot bleeding may be noted in the immediate post-operative period secondary to poor hemostasis. Due to faster re-epithelialization, the risk of infections and contact dermatitis following Er:YAG resurfacing may theoretically be somewhat reduced, although this needs to be studied more closely. At 38% and with a mean onset at 3.5 weeks, the rate of transient hyperpigmentation appears to be similar to that following CO_2 ablation, although the study group included significantly more darkly pigmented individuals with skin type III and above [113]. As well, the risk of hyperpigmentation may be lower with short-pulsed compared to long-pulsed, thermal-mode Er:YAG systems [113,114]. Delayed-onset permanent hypopigmentation, on the other hand, appears to be less common than that seen with CO_2 laser, at around 4% [115,116]. Finally, the incidence of scarring with Er:YAG laser appears to be low, but may increase with more aggressive treatment and deep-penetrating thermal damage.

Treatment of Photodamaged and Aging Skin Using Fractional Photothermolysis Lasers (Figures 4.9–4.11)

Following the application of a blue dye and petrolatum ointment or ultrasound gel, as previously described, the energy level and MTZ density are selected based on the clinical indication and level of damage, with higher settings reserved for more severe conditions. As the handpiece is moved over the treatment area, the tracking device monitors the velocity to assure proper placement of MTZs and adjusts the delivery of pulses accordingly. The built-in green light and lower-pitched sound during handpiece gliding indicate proper velocity, whereas orange light and higher-pitched sound announce excessively fast movement. Over the course of a single session, a typical total MTZ density of 2000 to 3000 per cm^2 is delivered using multiple passes in perpendicular directions. The newer model of this laser also indicates when inadequate pulses have been delivered to achieve a desired total energy for a given size of the treatment area. The addition of air cooling may help to reduce pain and to achieve better patient tolerability [117]. Significant improvement in mild to moderate facial photodamage and rhytids has been noted [118,119]. As well, treatments with this laser system have been safely performed on non-facial skin, including that of the neck and chest [120].

Following the completion of a treatment session, the blue dye is removed using a gentle facial cleanser. Post-operative

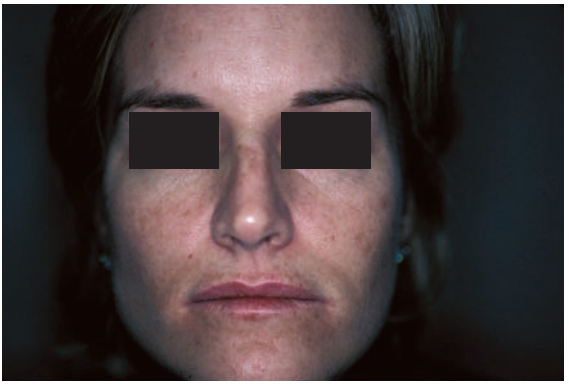


Figure 4.9 Ideal fractionated resurfacing patient with photodamage.

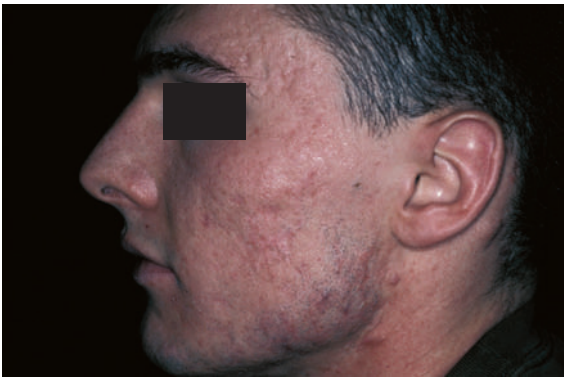


Figure 4.10 Ideal fractionated resurfacing patient with acne scarring.

wound care is minimal and typically consists of applications of topical moisturizer. Since only a portion of the treated skin surface is affected during each session, multiple treatments, typically 3 to 5, may be administered as often as every 1 to 3 weeks, as dictated by complete re-epithelialization.

Adverse effects following laser photothermolysis are generally mild and short-lasting. They include invariable transient erythema, which may last for up to 1 week, frequent edema, typically lasting less than 24 hours [40], bronzing and flaking, starting at 3 days post-treatment and lasting for up to 1 week, and superficial abrasions, a complication that has now been fixed with a slight handpiece modification. Although herpetic recurrences have occurred, bacterial infections, dyschromias, and scarring have not been documented [119]; however, longer experience with this laser is necessary for proper evaluation of potential long-term complications.

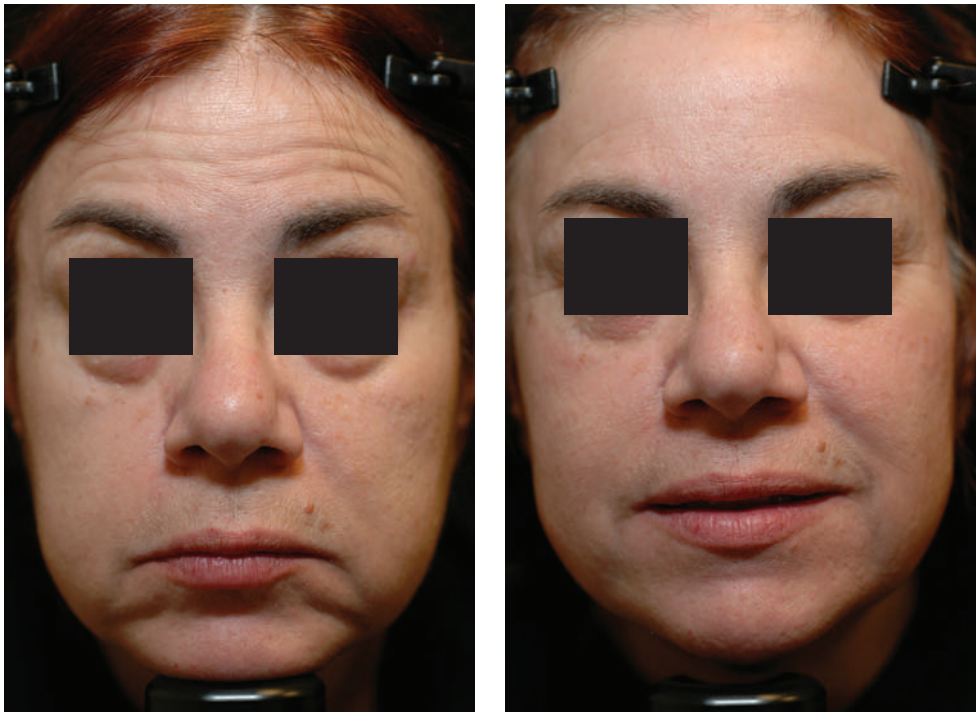


Figure 4.11 **(a)** Before fractionated resurfacing and **(b)** 3 days after fractionated resurfacing. Note slight flaking of skin, but no obvious wound.

Treatment of Photodamaged and Aging Skin Using Plasma Skin Resurfacing Devices (Figure 4.12)

During treatment, the handpiece is brought to within 5 mm of the skin surface. Since the tip of the handpiece is extremely hot, it is imperative that the patient not move during treatment to avoid accidental contact. Adjacent oval-shaped non-overlapping pulses are delivered with the help of a blue illuminator light, which ensures proper placement and consistent distance from the skin surface. In order to avoid excessive heating in any location, once a row of pulses has been completed, the next pulse is aligned with the original starting point. Pulses are then delivered in the same direction, rather than in a zigzag pattern and entire cosmetic units – preferably the entire face – are treated during a single session.

Only a single pass using lower fluence may be undertaken to prevent excessive thermal damage to the dermis. On the other hand, one or two passes with high fluences may be safely administered for treatment of more pronounced

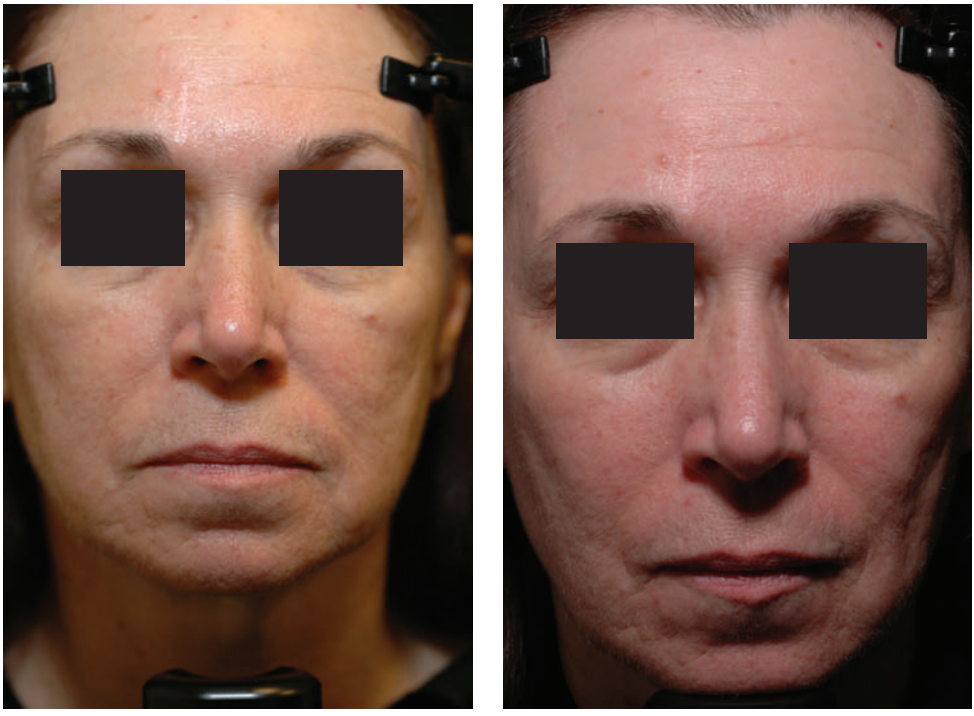


Figure 4.12 **(a)** Before plasma resurfacing and **(b)** after plasma resurfacing.

photodamage [121]. Although counterintuitive, this may be due either to insulation by the previously desiccated tissue or to the formation of transient vapor after the first pass, mitigating the delivery of energy during the second pass. Skin debris is left intact between passes. Alternatively, several treatment sessions with lower fluences administered every 3 weeks lower fluences may be lead to decreased downtime for patients with significant photodamage [122].

The use of this device has also been evaluated for improvement of aging and photodamaged non-facial skin, including that of the neck, chest, and dorsal hands. Significant clinical and histological improvement in neck and chest skin has been noted after one session with lower energy settings, although improvement on dorsal hands was slightly less pronounced [123].

Post-operatively, frequent application of a petrolatum-based ointment appears to be sufficient without the need for a closed method of occlusion. Close patient follow-up is recommended to monitor for development of potential complications. Complete re-epithelialization is typically complete by 10 to 14 days, but may be even sooner for lower settings. Reported adverse effects

following plasma resurfacing device treatment include transient erythema typically lasting from 3 to 7 days, but occasionally as long as 2 weeks, edema, crusting, and mild transient hyperpigmentation that resolved with topical bleaching agents [124]. Scarring has not been reported; however, the incidence of this and other potential short- and long-term complications, such as infections and permanent hypopigmentation, will be better ascertained after prolonged experience with this device.

Treatment of Acne and Varicella Scars

Acne scars may be subdivided into ice-pick, rolling, and boxcar varieties. Boxcar scars may be further subdivided into shallow and deep. Ice-pick scars are usually narrow, sharply delineated tracts extending into deep dermis and subcutaneous tissue. Rolling scars are typically broad based with an undulating appearance. They are formed by tethering action from abnormal fibrous anchoring of the base to the superficial musculoaponeurotic system. Finally, boxcar scars are round or oval and appear punched-out with vertical edges and broad bases, similar to those of varicella [125].

The differentiation between these types and understanding of their pathophysiological factors is important to the selection of proper treatment techniques. Prior to resurfacing, ice-pick scars are best treated with a punch excision. Subcision is a useful technique used to release fibrous adhesions of the rolling scars. Finally, the base of deep boxcar scars may be raised using punch elevation [125]. On the other hand, mild to moderate atrophic scars of the boxcar variety and similar varicella scars may be treated with resurfacing without any pre-treatments.

All previously mentioned ablative lasers have been used for correction of surface irregularities associated with acne scars. As with resurfacing of photodamaged skin, milder scarring may respond satisfactorily to less aggressive treatments with Er:YAG and fractional photothermolysis lasers, as well as plasma skin resurfacing device [126–128]. Moreover, a long-pulsed Er:YAG laser may provide an advantage over the conventional Er:YAG laser in the treatment of rolling and deep boxcar scars [129]. Finally, moderate to severe scarring is best treated using a CO_2 laser at typical resurfacing settings [130,131].

Techniques used for acne scar resurfacing are similar to those for photorejuvenation. Fractional photothermolysis laser can be used on problem areas only, resulting in very short healing time. On the other hand, full-face treatment must be performed using CO_2 and Er:YAG lasers and plasma skin resurfacing device to prevent lines of demarcation. Due to its precise ablation

capability, short-pulsed Er:YAG laser may be used following full-face resurfacing to sculpt and smoothen the edges of the boxcar scars. Post-operative wound care, follow-up, and adverse effect profile are essentially the same as those described previously for each resurfacing device. As with treatment of photodamaged skin, multiple treatment sessions of the fractional photothermolysis laser are typically performed at 1- to 3- week intervals [128].

Treatment of Other Conditions

In addition to the conditions described in this and previous chapters, numerous other exophytic, epidermal, and dermal conditions have been treated using ablative lasers. Thus, viral warts [132,133], syringomas [134], trichoepitheliomas [135], apocrine hidrocystomas [136], angiofibromas [137,138] and periungual fibromas [139] of tuberous sclerosis, epidermal nevi [140], miliary osteomas [141,142], xanthelasma [143], scars from discoid lupus and cutaneous sarcoidosis [144–146], recalcitrant plaques of Darier's disease, Hailey–Hailey disease [147,148], and mycosis fungoides palmaris et plantaris [149], and other conditions have been treated with either CO_2 or Er:YAG laser, although some of these indications require larger case series to establish efficacy and safety. In addition, a focused continuous-wave CO_2 laser beam performs precise bloodless incisions and is occasionally utilized in blepharoplasties [150].

Conclusions

Ablative lasers provide unquestionable improvement in photodamaged skin. However, older technologies are associated with prolonged adverse effects and patient downtime. In response, numerous non-ablative devices have been developed, but, for the most part, have not quite lived up to practitioners' expectations. Newer ablative technologies with fractionated treatments and milder ablative regimens result in faster healing time and fewer complications and appear to provide a viable alternative for today's cosmetic consumer.

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5 Non-Ablative Photorejuvenation and Skin Remodeling

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5 Non-Ablative Photorejuvenation and Skin Remodeling

KEY POINTS

- A variety of non-ablative devices are available. All produce mild improvement in skin quality
- Photodynamic therapy photorejuvenation may produce better results than are seen without the use of a pre-treatment photosensitizer
- Non-surgical skin tightening, used on a variety of skin regions, is based on bulk dermal heating with associated epidermal skin cooling
- A variety of newer devices show some promise in the treatment of cellulite

Introduction

This chapter will deal with some of the latest technologies available today for the improvement of the visible signs of photoaging, as introduced in the previous chapter. With no skin breakage or other readily apparent evidence of treatment, these technologies have become acceptable to those patients who are interested in skin rejuvenation, but are either unable or unwilling to submit to a prolonged downtime of ablative resurfacing or to the risks and costs of the more aggressive surgical treatments, such as facelifts. While clearly easier tolerated, non-ablative lasers and devices lead to clinical improvement that is generally more subtle compared to that produced using ablative technologies introduced in the previous chapter.

One exciting aspect of the new technologies has been their varying approaches to similar clinical tasks. Thus, in addition to monochromatic lasers, other sources of electromagnetic radiation, such as intense pulsed light (IPL) devices and broadband infrared light device (BILD), high-frequency electrical devices, and combinations thereof have been developed for rejuvenation of the aging skin. These advances attest to the willingness to develop therapies based on new physical and biological principles of device–tissue interactions and to test these concepts through rigorous clinical research.

In addition to photorejuvenation, also referred to as dermal or subsurface remodeling and skin toning, this chapter will also deal with photodynamic therapy (PDT) for the aging skin, as well as skin remodeling as it pertains to cutaneous laxity and cellulite, conditions that are typically recalcitrant to most other non-surgical treatment modalities.

Essential Concepts

Photodamage and the Concept of Subsurface Remodeling

The pathophysiology of cutaneous changes associated with photodamage has been extensively covered in the previous chapter. The reader is invited to review the relevant sections at this time. Additionally, a brief summary of the main concepts will now be presented.

Collagen fibers in photodamaged skin appear thickened and fragmented, with higher ratio of collagen III to collagen I compared to younger skin. In addition, fibers are more loose and straight, thus precluding effective stretching [1,2]. Elastic fibers become structurally and functionally abnormal, with slower degradation and gradual accumulation of solar elastotic material in the upper dermis [3]. Due to its abnormal localization and structure, dermal ground substance, composed principally of hyaluronic acid and proteolycans, is not able to maintain efficient dermal hydration [4]. These changes manifest as wrinkly, dry, and fragile skin. Additional clinical features of the aging skin that are relevant in photorejuvenation include irregular pigmentation, telangiectasias, coarse texture, and increased pore size.

Unlike ablative resurfacing and subsequent dermal remodeling, subsurface remodeling can be visualized as heating of skin in an upside-down manner. Although usually used interchangeably with "dermal remodeling," the term "subsurface remodeling" is sometimes reserved for the more superficial heating limited to the upper papillary dermis. Subsequent biological processes, such as stimulation of fibroblasts and neocollagenesis, will be further addressed below.

Cellulite: Pathophysiology and Implications for Treatment

Cellulite, also known as gynoid lipodystrophy, adiposis edematosa, and dermopanniculosis deformans, presents as dimpling of the skin, sometimes likened to the appearance of cottage

cheese. It is most commonly present on the buttocks and thighs of over 85% of women over 20 years of age, but may also be found at other body sites [5]. Of interest, cellulite is not related to body fat index and is very uncommon in males. Staging of cellulite is typically based on its spontaneous presence in the standing or lying positions versus the necessity to apply pressure in order to reveal a predisposition to the condition, a state also known as incipient cellulite [6].

Although no definitive pathophysiological mechanisms have been shown to induce the changes associated with cellulite, it is likely multi-factorial in nature and several theories have been formed based on epidemiological, histological, and radiological studies. These include gender-related anatomical differences, progressive alterations in hypodermal connective tissue, vascular factors, and the role of inflammation. Specifically, herniations of fat into the dermis with a resulting irregular dermo-hypodermal junction is noted on sonographic studies in females, but not males [7], leading to speculations of weaker dermal support in the former [8]. Hypodermal connective tissue, present as fibrous strands or septae separating fat lobules and attaching to underlying structures, appears to become progressively more vertically oriented in females, thus allowing for decreased resistance to fat herniation [6]. Vascular changes, including intrinsic abnormalities leading to progressive edema, vascular compression, and tissue hypoxia, have been proposed to result in sclerosis of the fibrous strands [9]. Finally, a low-level inflammation in fibrous septae, theorized to eventually cause dermal atrophy, has been found in some biopsies of cellulitic skin [10].

Current treatment options for cellulite are few and typically have very limited and only temporary effect. They are usually directed at the above-noted abnormalities in both dermal and hypodermal structures and, aside from lasers and other similar devices, most commonly include subcision, liposuction, mechanical manipulation, mesotherapy, and a variety of topical preparations [11–14]. In a promising development, lasers and radiofrequency (RF) devices, sometimes in combination with mechanical manipulations, have recently been added to the treatment armamentarium. While multiple factors may contribute to the clinical improvement and will need to be further elucidated in future studies, proposed mechanisms of action of these devices include increased local circulation and fat metabolism, mechanical damage to the adipocytes and fibrous bands, and deep dermal heating and subsequent collagen deposition and remodeling. These systems will be presented in further detail below.

Mid-Infrared Lasers: Laser–Tissue Interaction

Mid-infrared lasers typically used for photorejuvenation include the 1320-nm neodymium:yttrium–aluminum–garnet (Nd:YAG) laser, the 1450-nm diode laser, and the 1540-nm ytterbium–erbium:phosphate glass, also known as erbium:glass (Er:glass) laser. Light produced by all three is absorbed by water, with the 1320-nm wavelength absorbed least. As a result, optical penetration depth by this laser is also greatest of the three devices, with effective heating to the depth of 400 μm compared to approximately 300 μm achieved by the 1450-nm diode laser [15]. Additionally, this wavelength is associated with significant scattering, resulting in the deposition of energy outside the laser beam and subsequent effective dermal heating.

As with ablative resurfacing, discussed in the previous chapter, sufficient dermal heating results in collagen denaturation. In the process, the right-handed helical structure of the collagen fibril assumes a random-coil configuration following the rupture of hydrogen bonds [16,17]. This new configuration manifests as shortening and thickening of the collagen fibers, features observable both on light and electronic microscopy. Subsequent wound-healing response leads to the activation and proliferation of fibroblasts and new collagen deposition [18–20]. This dermal remodeling may be employed for improvement of wrinkles, skin tone, and other attributes of aging or photodamaged skin, as well as for acne scars, also to be covered in this chapter.

There is growing evidence that, in addition to collagen denaturation, clinical improvement following mid-infrared laser therapy may be due to additional factors. Vascular damage in the upper papillary dermis follows intravascular coagulation. This, in turn, triggers the influx of neutrophils and the release of numerous inflammatory chemical mediators [21], which stimulate fibroblast neocollagenesis and upregulated production of matrix metalloproteinases, most notably collagenases [22]. This allows deposition of new collagen over the condensed template of the previously denatured collagen with gradual degradation of the latter. Additional evidence implicates mild, subclinical epidermal damage, resulting in histological findings of post-treatment spongiosis and basal cell vacuolization [21]. It is likely that such damage leads to the release of additional cytokines and other inflammatory mediators, further contributing to new collagen deposition.

Clinically evident epidermal damage is an important consideration with mid-infrared lasers, as they are deep penetrating and non-specifically absorbed by both dermal and epidermal

water. Although epidermal cooling may protect the epidermis during the laser pulse, early 1320-nm lasers equipped only with a precooling mechanism resulted in a slightly increased risk of atrophic scarring [23]. Subsequent mid-infrared devices have incorporated continuous or pulsed epidermal pre-, intra-, and post-treatment cooling, typically accomplished with the help of automated liquid cryogen spraying – also known as dynamic cooling – or a chilled sapphire window brought in contact with the skin surface. Additionally, the 1320-nm laser has also been equipped with a thermal sensor to keep the epidermal temperature within a well-defined range, as will be discussed later in this chapter.

Although low throughout the mid-infrared spectrum, laser light absorption by epidermal melanin is approximately 1.6 times lower at 1540 nm compared to 1320 nm [19]. Thus, it has been proposed that the former wavelength may be somewhat safer in darkly pigmented individuals. However, it appears that all mid-infrared lasers may safely be used in such individuals, as long as proper laser parameters and cooling are employed.

IPL Devices: Device–Tissue Interaction

As presented in the previous chapters, broadband or IPL devices can be used for effective treatment of vascular and pigmented lesions that may be seen in photodamaged skin. In addition, an innovative application of these devices has been in the field of full-face photorejuvenation and dermal remodeling.

IPL sources are polychromatic flashlamp-based devices that typically emit light in the 500 to 1200 nm range. In order to act in accordance with the principles of selective photothermolysis and to achieve target selectivity [24], various cut-off filters are employed, effectively removing lower wavelengths. Although each individual device's spectral output is proprietary, most produce less power in the red and infrared spectra and typically only little energy beyond 1000 nm. Pulse duration is adjustable based on the system used, with double- or triple-pulse modes available for longer exposure times or higher fluences, providing for sufficient interpulse delay to allow for epidermal cooling. When combined with effective contact or, occasionally, cryogen spray cooling and spot sizes as large as 6 cm^2, IPL devices can be used for safe and rapid treatment of extensive treatment areas.

Although the exact mechanism of photorejuvenation following IPL treatments is not completely clear, dermal heating likely results from some absorption by water, as well as propagation of heat from the superficial vasculature. Similar to the

mid-infrared lasers, sufficient heating of collagen results in protein denaturation. Stimulation of fibroblasts and subsequent neocollagenesis and dermal remodeling are noted histologically as late as 6 months following treatment and contribute to clinical improvement in many aspects of photodamaged and aged skin, as will be discussed below [25]. Additional histological findings following IPL irradiation include increased epidermal thickness, decreased horny plugs, formation of new rete ridges, and decreased elastosis [26].

PDT: Physical and Biological Principles

With the success of IPL technology, attention has turned to the addition of photosensitizing chemicals in order to stimulate further improvement in the aging and photodamaged skin. Topical 5-aminolevulinic acid (ALA) has been used as part of PDT for treatment of actinic keratoses [27,28], non-melanoma skin cancers [29–31], mycosis fungoides [32,33], acne [34,35], and other cutaneous conditions. ALA-PDT has subsequently been adopted for the purposes of photorejuvenation.

ALA is part of the porphyrin or heme synthetic pathway. When applied topically, this lipophilic compound is preferentially taken up by rapidly dividing epidermal and dermal cells. In itself, ALA is not photosensitizing; however, it is converted into protoporphyrin IX (PpIX) through a series of intracellular reactions. PpIX is photosensitizing, resulting in the formation of singlet oxygen species, which serve as free radicals causing cellular membrane disruption and subsequent death [36].

PpIX has multiple absorption peaks, including 408, 510, 543, 583, and 633 nm [37,38]. Due to the avid absorption by PpIX at 408 nm, a wavelength known as the Soret band, blue light, most commonly produced by blue light-emitting diode (LED) sources, is a commonly used photoactivator in PDT. However, blue light has very limited depth of penetration into the skin; thus, multiple other wavelengths corresponding to the major and minor absorption peaks of PpIX have been employed. These include red LED sources, pulsed dye lasers (PDL), potassium-titanyl-phosphate (KTP) lasers, and IPL devices. While it should be noted that it is not completely clear at this time how the biochemical processes discussed above lead to dermal remodeling, an increase in collagen I formation following IPL-assisted PDT, a process known as photodynamic photorejuvenation [39], has been found to be greater than that noted with the IPL therapy alone [40,41]. This new collagen deposition then contributes to the overall clinical improvement associated with photorejuvenation.

RF Devices and Skin Tightening

As introduced earlier in this book, RF systems are high-frequency electrical devices that produce alternating current in the range of 0.3 to 40 MHz. Bipolar systems consist of two electrodes separated by a fixed short distance. Monopolar systems are equipped with a single electrode used for contact with tissue and a large-size grounding plate attached to the body at a distance. When the handpiece is brought in contact with the skin, both systems produce a flow of electrons, either between the two electrodes or between the electrode and the grounding plate. A recently introduced unipolar RF system is based on different physical principles and will be discussed later in this section.

As described by Ohm's law, the flow of electrons, or current, increases with decreasing impedance. This current is responsible for the production of heat, which is proportional to the impedance as per Joule's law. The depth of heat penetration into biological tissue is estimated to be half of the distance between electrodes in a bipolar system and half the size of the electrode in a monopolar system [42]. Such penetration allows for deep dermal collagen denaturation, new collagen production, and subsequent remodeling and tightening [43]. As well, tissue heating achieved by such devices is volumetric and is, therefore, measured in J/cm^3.

Unlike bipolar and monopolar RF systems, the unipolar technology does not produce electrical current within tissue. Instead, high-frequency electromagnetic radiation at 40 MHz is produced by the device. The resulting rapidly alternating polarity of the electromagnetic field induces high-frequency rotational oscillations in the water molecules. Such ultra-rapid oscillations produce heat, subsequently dissipated to the surrounding tissue. The phase of the electromagnetic waves produced by this device is controlled in such a way as to allow for the greatest heat penetration into tissue, estimated to be around 15 to 20 mm [44]. Thus, hypodermal structures can be effectively heated, resulting in the utility of this device in the treatment of cellulite, to be discussed below.

BILD and Skin Tightening

Not to be confused with broadband light or IPL devices discussed above, a new broad based infrared light device (BILD) or BILD emits light with wavelengths between 1100 and 1800 nm. This spectral output is quite different from that of IPL devices, which have little power beyond 1000 nm. It has been developed as a light-based alternative to RF devices for tissue tightening.

Broadband light emitted by BILD is absorbed by water. If allowed to penetrate into the dermis while protecting the epidermis, the resulting heat would cause collagen denaturation and dermal tightening, as discussed previously. Due to a strong absorption peak by the water molecule between 1400 and 1500 nm, filters are used in this system to lower energy output at these wavelengths in order to increase the overall optical penetration depth. Pre-, intra-, and post-treatment cooling of the epidermis is accomplished through contact with a sapphire tip.

Additional features that allow deep penetration of light into the dermis include large spot sizes of 1.5 and 3.0 cm^2 and pulse durations of up to 11 seconds. Long exposure times allow adequate heat dissipation to deep dermis. As well, lower fluences may be used in that setting, providing for greater epidermal protection and less patient discomfort. Thus, following irradiation, the majority of thermal damage is noted at the depth of 1 to 2 mm. When combined with continuous cooling, lower fluences have also been found to result in little damage above 1 mm in depth, an effect that may be partially overcome at higher settings [45]. As will be shown below, such deep dermal heating and subsequent collagen denaturation and remodeling provides for clinically evident skin tightening.

Pearls and Problems

Non-Ablative Photorejuvenation: Patient Selection and Pre-Treatment Care

While numerous lasers and similar devices have been used in the treatment of vascular and pigmented lesions associated with photodamaged skin, the goal of photorejuvenation is overall improvement in the many aspects of cutaneous changes resulting from exposure to ultraviolet radiation and intrinsic aging processes. As described previously, such aspects may also include rhytids, skin fragility and poor elasticity, coarse texture, and increased pore size.

Proper patient selection is critical to ensuring satisfactory improvement. The ideal candidate is between 35 and 55 years of age with mild to moderate photodamage or rhytids. On the other hand, patients with severe rhytids may only show minimal improvement and are thus better candidates for ablative treatments, as described in the previous chapter. Since epidermal melanin acts as a competing chromophore, the selection of appropriate photorejuvenating technology is also dependent upon the patient's skin type. Longer wavelengths are safer in darkly pigmented individuals, but may also be associated with

adverse effects due to excessive fluences or cryogen spray, as will be further discussed below. As well, the presence of suntan may result in irregular pigmentation when lower wavelengths, such as those emitted by IPL devices, are utilized.

Although controversial, history of excessive or keloidal scarring, recent intake of oral isotretinoin in the past 6 months, active skin disease in the treatment area, or photosensitivity need to be sought prior to initiation of treatment. Of interest, botulinum toxin, even if injected immediately prior to laser irradiation, is not deactivated by the beam and is, therefore, not a contraindication to treatment [46]. High-quality photographs and informed consent should be obtained for every patient before the first procedure and periodically thereafter in order to document improvement. This is especially important with non-ablative technologies, as subtle improvement between sessions may not be apparent to the patient, yet the overall photorejuvenating effect may be quite pronounced when the initial photograph is examined.

Immediately prior to treatment, the patient has to remove all makeup, as it may reflect or absorb laser energy, causing epidermal overheating. Most non-ablative photorejuvenating procedures are very well tolerated, although topical anesthetics may be used based on patient preference. Since most photorejuvenating devices penetrate deeply into the dermis to cause thermal effect, adequate epidermal cooling is paramount to preventing adverse effects and needs to be tested prior to laser pulse discharge. Specific cooling recommendations will be presented when their respective lasers and light sources are examined. Finally, eye protection is afforded by proper goggles for the practitioner and assisting staff members and goggles or gauze for the patient.

Photorejuvenation and Treatment of Acne Scarring with Mid-Infrared Lasers

The 1320-nm Nd:YAG laser is equipped with a handpiece with three portals, consisting of the cryogen spray mechanism, the laser aperture, and a thermal sensor. During the laser pulse, the epidermal temperature is generally allowed to rise to 40–45ºC, although there is evidence to suggest that higher peak temperature of up to 48ºC may lead to improved clinical results [21]. With such epidermal temperature rise, the dermis is estimated to be heated to around 70ºC, sufficient to cause collagen denaturation and subsequent dermal remodeling. This effect is achieved with an adjustable fluence, typically set at 12 to 18 J/cm^2, a fixed 10-mm spot size and a fixed 50-ms pulse duration composed of

six stacked pulses. In practice, a test firing is performed while monitoring peak epidermal temperature displayed on the unit's LCD screen. Fluence can then be adjusted by 1 J/cm^2 to reach the desired temperature range. Three passes with this system have been shown to result in greater post-treatment histological changes compared to a single pass [21]. Cryogen spray is delivered in three pulses to provide pre-, intra-, and post-pulse epidermal cooling. Although designed to provide epidermal protection, cryogen may, in itself, cause cold injury and post-inflammatory hyperpigmentation or atrophic scarring, especially in patients with darker skin types [23]. Thus, the duration of cryogen application should be reduced in such patients.

The pulse structure of the 1450-nm diode laser is slightly different, with four stacked laser pulses totaling 210 ms interspersed with five cryogen spurts, thus also providing for pre-, intra-, and post-treatment epidermal cooling. As well, this device does not feature a temperature sensor and features a 4- to 6-mm spot size. Typical fluences used with this system range from 9 to 14 J/cm^2. Although there is a suggestion of a threshold effect with significantly increased collagen III production above 12 J, no such effect is noted for collagen I or elastin production, with significant production throughout the suggested range of fluences [47].

The 1540-nm Er:glass laser can be utilized in normal, or single-pulse, mode with pulse duration of 3 ms or pulse-train mode with pulses delivered with frequency of up to 3 Hz. The system features a 4-mm spot size and continuous contact cooling with a chilled sapphire tip. Typical fluences range from 8 to 10 J/cm^2 per pulse with a total fluence in pulse-train mode limited to 60 J/cm^2 to prevent epidermal damage [48,49].

All three laser systems require multiple treatment sessions, typically 4 to 6, administered monthly, to achieve moderate long-term improvement in mild to moderate rhytids, skin laxity, thinned epidermis, and other signs of photodamaged and aging facial and non-facial skin [18,50–56]. Overall clinical efficacy, as it pertains to photorejuvenation, appears to be similar among these devices. It is important to note, however, that although histological evidence of new collagen deposition has been documented with the three lasers for up to 6 months [52,57,58], such effect may not directly translate into observable clinical improvement (Figure 5.1).

Mid-infrared lasers generally do not require specific post-operative care and are thus well tolerated by patients. Common adverse effects may include mild transient pain, more common where epidermis is thin and over bony prominences, and mild erythema and edema that resolve within 48 hours [59]. Though

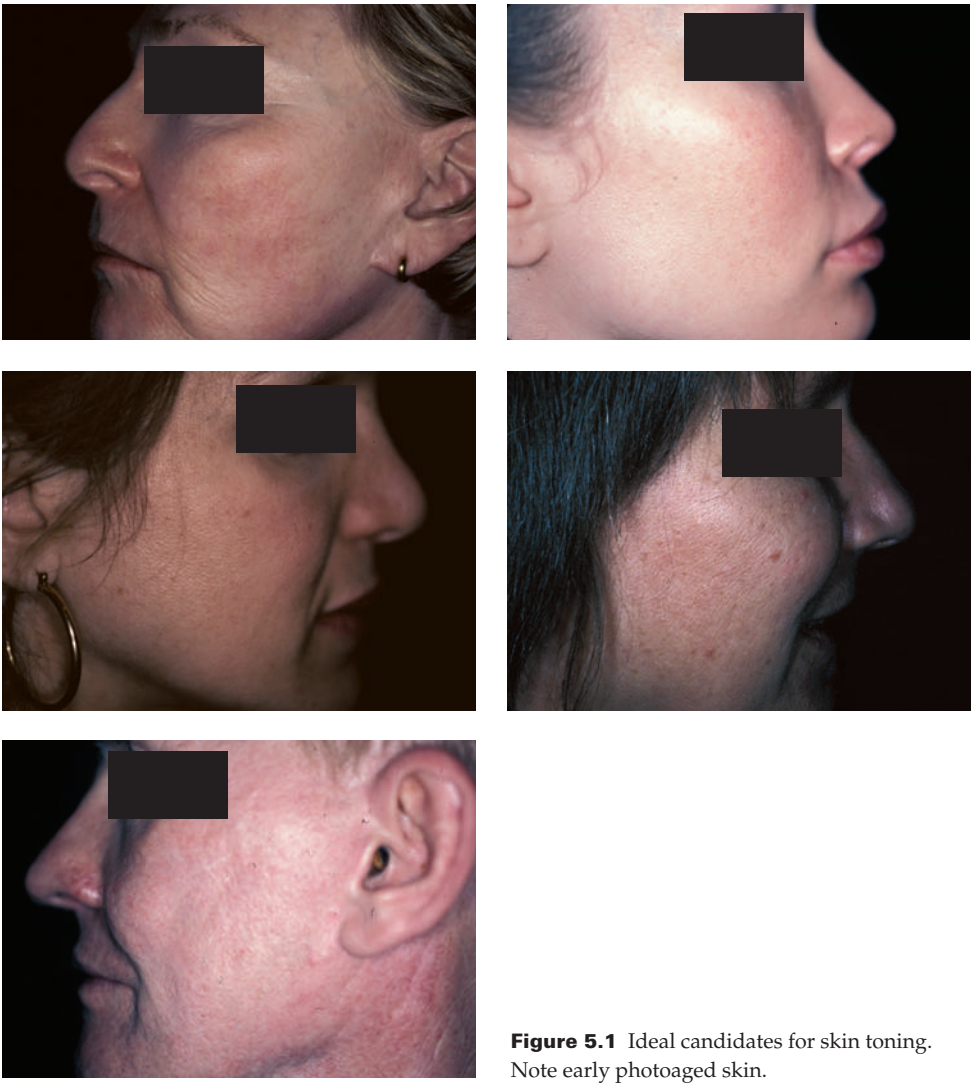


Figure 5.1 Ideal candidates for skin toning. Note early photoaged skin.

uncommon, the occurrence of dyschromia, blistering, and, rarely, scarring, is usually related to the use of excessive fluences or prolonged cryogen cooling [54,60], especially in darker individuals, as described previously.

Additionally, likely as a result of their effect on dermal remodeling, mid-infrared lasers have been found to be safe and efficacious in the long-term improvement in mild to moderate acne and other types of scarring, including that in darker skin types [54,61–64] (Figures 5.2 and 5.3). Classification of acne scarring has been presented in the previous chapter and the reader is

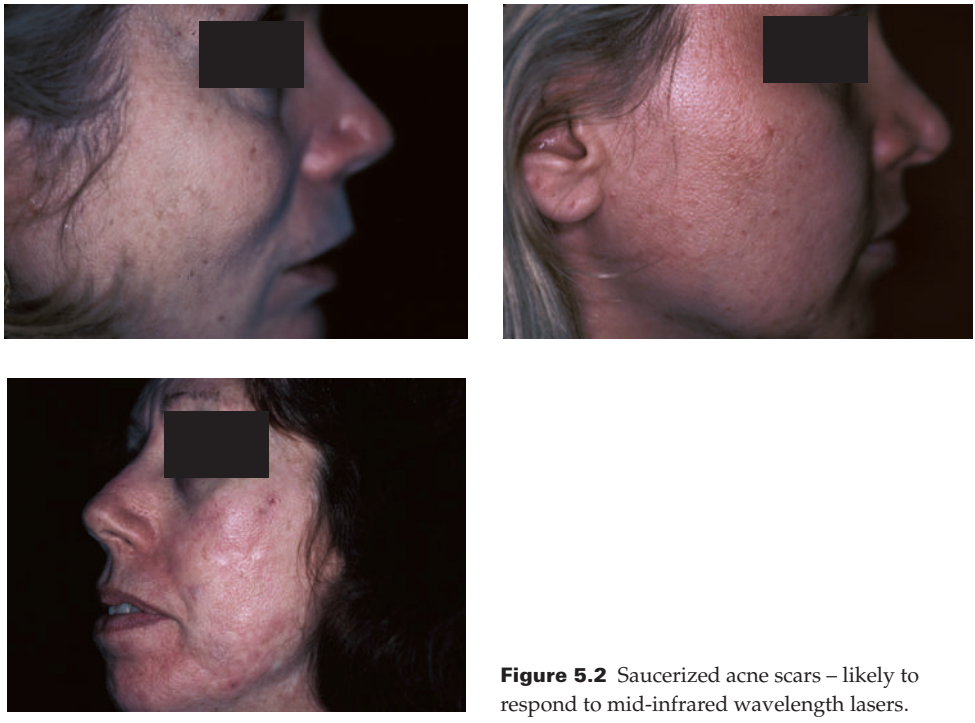


Figure 5.2 Saucerized acne scars – likely to respond to mid-infrared wavelength lasers.

now invited to review that section at this time. While all three laser systems have been used nearly interchangeably for this purpose, a slightly higher rate of improvement in acne scars has been noted with the 1450-nm diode laser compared to the 1320-nm Nd:YAG laser [65]. This difference may, however, have occurred secondary to slightly suboptimal parameters used with the latter. Overall, laser settings, treatment protocols, and adverse effects encountered in the therapy of acne scarring are very similar to those noted above for the correction of photodamaged skin.

Photorejuvenation with IPL Devices

Currently available IPL devices vary significantly in their spectral output, available filters, pulse duration and structure, spot size, fluence, and cooling. Although certain generalizations can be made, treatment parameters may not be interchangeable between different systems. Thankfully, some of the newer devices feature user-friendly menus, providing preset settings

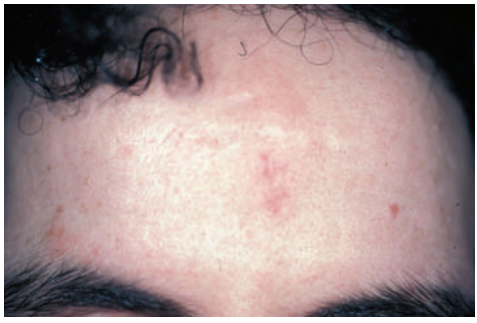
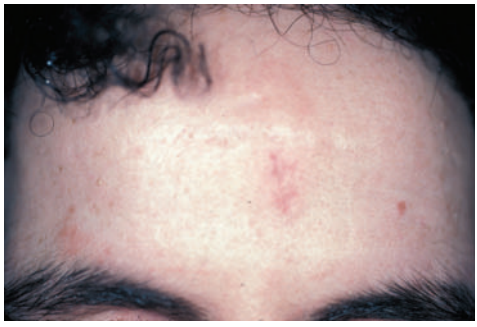
(a)   (b)

Figure 5.3 (a) Non-acne-induced scar – prior to mid-infrared wavelength laser treatment and **(b)** mild improvement in scar after 2 sessions of mid-infrared wavelength laser treatment. Further treatment is required.

for a given clinical indication and patient skin type. In the absence of such presets, the practitioner is advised to consult system manual provided by the device manufacturer.

For the purposes of photorejuvenation, filter selection depends on the patient's skin type, as well as the size, depth, and other characteristics of the specific components of photodamage. Thus, as covered in the previous chapters, telangiectasias and epidermal dyschromia and pigmented lesions respond better to lower-wavelength filters, typically in the 530 to 590 nm range. These wavelengths can also lead to improvement in the other aspects of photodamaged skin, including fine rhytids, coarse texture, and increased pore size [66]. On the other hand, higher filters in the 600- or 700-nm range may also be effective in the treatment of rhytids, yet result in a lower incidence of prolonged erythema or blistering [67]. Care must be exercised in patients with darker complexion or those with suntan, in whom pigmentary alterations are likely following IPL treatments. As a result, higher-wavelength filters should be used with darker skin types, whereas the presence of a suntan may lead to the appearance of hypopigmented rectangular footprints.

Pulse duration and multi-pulse mode selection depends on the size of the specific lesion, fluence, and patient's skin type. Thus, as presented in the previous chapters, larger targets require longer pulse durations. Longer exposure times, typically delivered in a multi-pulse mode, also allow for a more diffuse propagation of heat throughout the dermis with subsequent collagen denaturation and are thus more beneficial for photorejuvenating effect. By allowing epidermal cooling during interpulse delay, the multi-pulse mode is also preferred when higher

fluences are utilized and in patients with darker skin types, such as IV and V, in whom the interpulse delay may be increased to 20 to 40 ms [68].

Spot size is typically constant for a given system, although some devices feature several different heads or interchangeable tips. Since calibration techniques, factory fluence measurements, and changes in power output throughout light pulse may significantly differ between IPL devices, fluences cannot be directly compared and are system specific [69]. Finally, cooling provides epidermal protection and is most commonly accomplished with a chilled sapphire or quartz tip, as well as a cooled gel applied to the skin immediately prior to treatment. The chilled gel also serves as a coupling mechanism, reducing optical refraction by air.

Although well tolerated by most patients, common adverse effects include short-lived burning or stinging pain and transient erythema and edema lasting less than 24 hours in the majority of cases. Blistering may occur in up to 10% of patients but typically does not lead to scarring [70]. Dyschromia – both hyper- and hypopigmentation – may occur in up to 15% of patients according to some sources, but often lasts less than 2 months and is more common in darker individuals [71]. As well, patients with subtle melasma may, at times, experience worsening of the condition, likely as a result of post-inflammatory hyperpigmentation [72]. Purpura may occur in 4% to 6% of treated sites, especially when low-wavelength filters, such as 515 nm, or short pulse durations are used. Such purpura typically lasts 2 to 5 days, less than that associated with PDL treatments [71]. Male patients with facial hair may experience hair reduction in the treatment area and must be properly warned. As well, eyebrow hair must be avoided when treating the forehead. Patients should also be advised that epidermal pigmented lesions, such as lentigos, in the treatment area may turn darker prior to desquamation within 7 days.

Full-face and non-facial IPL treatments are usually performed in 2- to 4-week intervals for a total of 4 to 6 sessions and are associated with high patient satisfaction and significant objective improvement in fine rhytids and other signs of aging and photodamaged skin [66,70,73] (Figures 5.4 and 5.5). Improvement in facial lesions is usually slightly better than that at non-facial sites, such as the neck or the chest. Although the optimal schedule for further maintenance treatments has not been clearly defined, it appears that long-term improvement in skin texture, telangiectasias, and dyschromia persisting for 4 years or longer is possible after a complete course of IPL photorejuvenation [74].

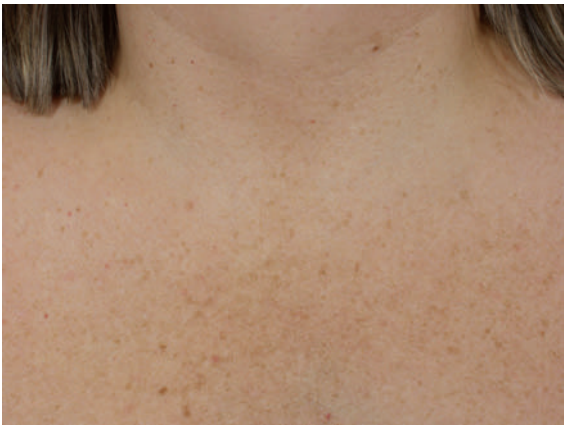


Figure 5.4 Photoaged skin prior to IPL treatment.

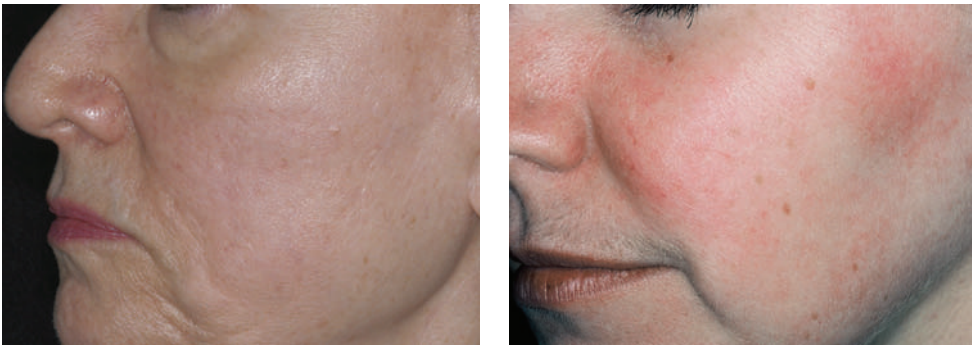


Figure 5.5 Facial erythema prior to IPL treatment.

Photorejuvenation with PDT

In the US, the currently available formulation of 5-ALA used off-label for photorejuvenation is a 20% solution in a single-use applicator (Levulan Kerastick, Dusa Pharmaceuticals, Wilmington, MA). This formulation has been approved by the FDA for the treatment of non-hyperkeratotic actinic keratoses on the face and scalp [75].

Prior to the application of 5-ALA, treatment area is cleansed and, preferably, degreased with the help of an acetone scrub or microdermabrasion. This increases cutaneous penetration of the compound, a concern common to most topical products. 5-ALA is then mixed. First, manual pressure on the outer glass tubing of the applicator results in breakage of the two inner ampoules containing the powdered form of the chemical and liquid ethanol. Next, gentle rotation between fingers for 3 minutes allows

for adequate mixing of the two compounds. Using the roll-on applicator tip, 5-ALA is then painted over the entire treatment area. An additional layer may be applied over the problem areas, such as clinically apparent actinic keratoses.

In order to allow for adequate penetration, the original mode of use included prolonged incubation times of 14 to 18 hours, followed by exposure to a light source. However, shorter incubation of 3 hours and, later, 1 hour has been shown to be just as efficacious for the purposes of photorejuvenation as longer incubation times [39,76]. Thus, 30 to 60 minutes are the most common length of incubation used today.

As previously discussed, multiple light sources, including blue and red LED sources, IPL devices, and pulsed dye or KTP lasers may be used in conjunction with PDT. The selection of the appropriate device depends, in part, on patient's complexion. Thus, LED sources, rather than IPL devices, should be used in patients with skin types IV and above. When IPL devices are utilized as part of PDT, excess 5-ALA needs to be removed prior to treatment, as the chilled coupling gel cannot easily be applied over it. The original FDA protocol for the treatment of actinic keratoses provided for 16 minutes and 40 seconds of blue light exposure. Subsequently, typical exposure time for LED devices for the purposes of photorejuvenation is 15 to 20 minutes. When using lasers or IPL devices, one pass or multiple passes – depending on the desired clinical effect and patient tolerability – with non-overlapping pulses are administered over the entire treatment area. Following sufficient light or laser exposure, any remaining 5-ALA is carefully washed off with a mild cleanser. Alternatively, blue LED source may be used for 5 to 8 minutes to deactivate any remaining compound in a process called photobleaching [77]. Next, a broad-spectrum sunblock is applied to the treated sites. Patients are instructed to avoid direct sun exposure for 24 to 48 hours due to an increased risk of photosensitivity in the immediate post-operative period and to continue regular use of sun-protective lotions thereafter.

Although rare, adverse effects encountered with PDT include those intrinsic to the application of a photosensitizing compound and those associated with lasers and light sources used for the activation of 5-ALA. Most patients tolerate the procedure very well with minimal, if any, discomfort. Those patients who experience mild to moderate pain, burning, or stinging may benefit from post-procedural use of ice packs or mild topical steroids. Additional expected sequelae may include transient sunburn-like erythema and edema typically lasting 48 to 72 hours, as well as crusting or desquamation. Prolonged incubation times may result in a more significant downtime, termed

the PDT effect. Complications associated with the use of activating light and laser devices have been described previously in this and prior chapters.

The current recommendations for PDT treatment of photodamaged skin call for a minimum of 3 treatments administered every 2 to 4 weeks [77]. This regimen compares favorably to a typical course of approximately 5 IPL sessions when used alone. Clinically relevant improvement in the signs of photodamage include a reduction of 55% in fine lines, including crow's feet, 60% to 95% in mottled hyperpigmentation, 55% in skin roughness, 85% in erythema, as well as a decrease in skin sallowness [41,76,78] (Figure 5.6). Most importantly, these rates of clinical improvement, as well as ultrastructural evidence of new collagen production, have been found to be significantly higher compared to those achievable using a laser or light source alone [40,41,78–80]. As for the future of photodynamic rejuvenation, new developments may include improved treatment protocols and the use of other photosensitizing compounds, such as methyl ester of 5-ALA, currently not available in the US.

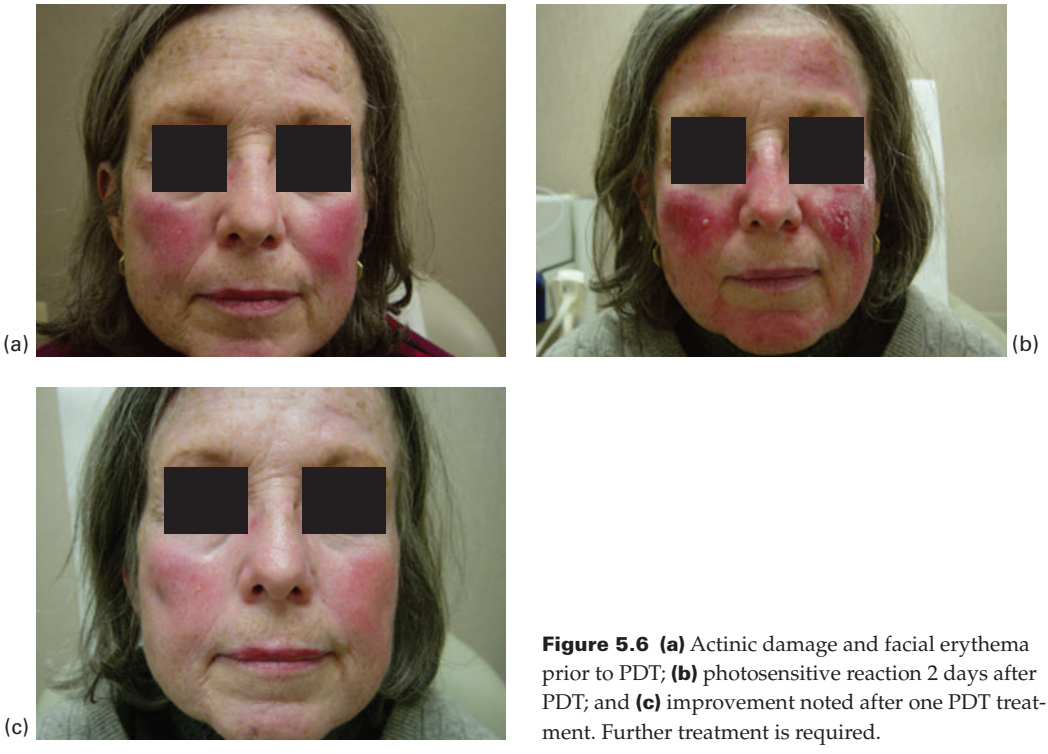


Figure 5.6 **(a)** Actinic damage and facial erythema prior to PDT; **(b)** photosensitive reaction 2 days after PDT; and **(c)** improvement noted after one PDT treatment. Further treatment is required.

Treatment of Skin Laxity

Treatment modalities for facial and non-facial skin laxity currently include a monopolar RF device (ThermaCool TC and NXT, Thermage Inc., Hayward, CA, USA) and a broad-spectrum infrared light device or BILD (Titan S, V, and XL, Cutera Inc., Brisbane, CA, USA). Although the devices and the corresponding protocols have been developed independently, quite similar treatment techniques have emerged over time, likely reflecting the emphasis on the anatomy and function of the underlying support structures. Thus, treatments with both devices have adapted multi-pass, low-fluence approaches with an emphasis on vectors of tension.

The ideal candidate for treatment with either device is a non-obese patient between the ages of 30 and 65 years with mild to moderate skin laxity without extreme cutaneous redundancy or excessive attached fat deposits in the treatment area (Figure 5.7). Improvement in the latter groups has been found to be mostly unsatisfactory for the patient. All skin types are amenable to treatments with either device. While most patients with previous cosmetic or surgical interventions in the treatment areas can be treated, those with a history of silicone filler injections may develop complications, as will be shown below. Additionally, patients with pacemakers should not be treated with the ThermaCool device, which produces a current within the body from the electrode to the grounding plate. Importantly, preoperative high-quality photographs are recommended to assess improvement over time.

Due to moderate discomfort, most patients undergoing therapy with the ThermaCool device require some form of anesthesia, typically achieved with the help of topical creams applied for an hour prior to the procedure. Such use of topical anesthesia has been found not to influence the efficacy of the treatment [81].

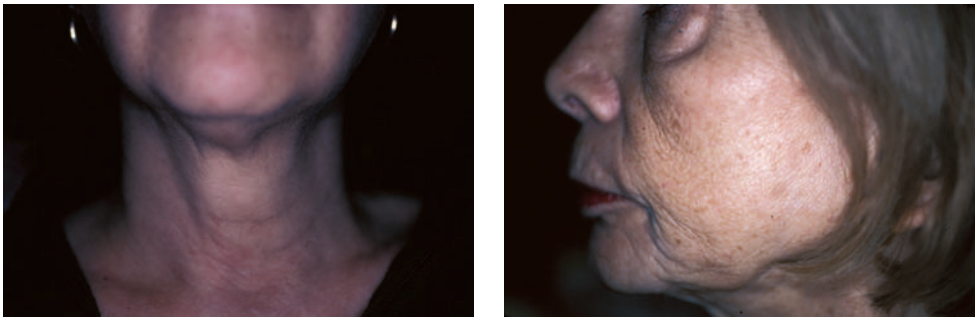


Figure 5.7 Mild skin laxity and jowls. Ideal patient for non-ablative skin tightening.

Although used at times, nerve blocks are usually not recommended, as patient feedback on excessive pain is an important indicator of the need for reduced fluences. Immediately prior to treatment, a proprietary conductive fluid is applied generously to the skin. A grounding plate is attached to a distant site, usually the patient's back. Eye protection is not needed.

A tip is then selected based on the indication and the practitioner's experience. Several different tips are available, which vary in size, depth of penetration, and rapidity of electrical discharge. In addition to the generation of electrical current, the tip also permits the penetration of cryogen to the skin, providing pre-, intra-, and post-pulse epidermal protection. Impedance is also measured by the circuit within the tip, assuring the delivery of proper thermal energy to the skin. Thus, initial impedance is calibrated prior to the first pulse, followed by re-adjustments based on the measured changes.

During treatment, the trigger button is held, followed by the firm application of the entire tip surface to the skin, resulting in the regression of the tip into the handpiece and subsequent delivery of electrical discharge. If tip apposition against the skin surface is not complete, the unit will not fire as a safety mechanism. Although the older system requires manual resetting of the device following such a fault, the newer model performs this action automatically. As a guidance measure, a temporary grid system is supplied by the company and may help novice practitioners to properly position subsequent pulses.

The initial usage of the ThermaCool device advocated single high-fluence pass over the problem areas. This resulted in multiple problems, including second-degree burns and, most importantly, the development of indurated subcutaneous nodules that resolved over several weeks and delayed fat atrophy that occasionally took up to 2 years or longer to improve [82,83]. Newer protocols utilize multiple low-fluence passes combined with the concept of vectors and appear to be better tolerated, effective, and with fewer potential adverse effects [84–86]. In addition, an ultrastructural analysis demonstrates similar changes in collagen with such regimen as compared to a single high-fluence pass [87].

In order to determine the most effective vector of elevation, the skin in the problem area is gently pulled in various directions. This establishes the most effective locations for the application of RF energy. Thus, mid-face elevation requires treatment along the vector extending from the nasolabial fold to the upper external ear, whereas the treatment of jowls is best accomplished with tip application along a more inferiorly placed vector also extending to the upper portion of the external ear. If the

entire eyebrow elevation is desired, the entire forehead medial to the temporal fusion line is treated, whereas only lateral forehead is treated when lateral eyebrow elevation is sought. Additionally, stacked pulses may be utilized for reduction in fat content, but should be avoided over the areas that are predisposed to fat atrophy, such as mid-cheeks or temples, which also require lower overall fluences [86]. Neck is also very commonly treated with the ThermaCool device, though fluences are usually lowered and care must be taken when passing over the thyroid. No post-operative care is needed, but patients should be advised that the clinical improvement may take several months to fully develop.

Aside from those complications described above that were mostly associated with high fluences, other adverse effects noted following treatment with ThermaCool include transient and mild erythema and edema typically lasting less than 24 hours but occasionally persisting for up to 1 week or longer, crusting, bruising, transient acneiform papules, and tenderness and dysesthesia along the jawline and neck lasting several weeks. Less commonly reported complications include transient anesthesia of the earlobe following treatment of posterior neck, trigeminal neuralgia, and short-lasting or persistent headaches [83,88–90]. Silicone granulomas have been noted following RF therapy in a patient with history of such filler injection [83]. However, other filler substances have been evaluated and found not to be affected by this device [91,92]. Scarring and dyschromia are very uncommon with the newer, low-fluence settings.

Although most studies have documented mild to moderate improvement in the lax and sagging skin of the forehead and eyebrows, eyelids and periorbital area, nasolabial folds, jowls, and neck [84,88,90,93–96], other potential indications may include the loose skin of the arms, dorsal hands, legs, abdomen, buttocks, as well as the treatment of acne and acne scarring [97]. The corresponding protocols are currently in development, as various anatomical sites may be associated with differing impedance and, consequently, treatment parameters [98].

Skin tightening with the Titan device is typically associated with minimal or no discomfort; thus, pre-operative anesthesia is usually not necessary unless higher fluences are used. A chilled gel similar to that used with IPL devices is applied to the treatment areas. The sapphire tip is also actively cooled to provide pre-, intra-, and post-treatment epidermal protection. Finally, due to the emitted wavelengths, eye protection is important and is achieved with gauze or goggles for the patient and goggles for the practitioner and staff.

Similar to the newer treatment guidelines for the ThermaCool device described above, vectors of lifting are first identified by pulling the skin of the problem area in various directions with the goal of achieving the most pronounced elevation with the most natural appearance. Once ascertained, these vectors serve as a guide for specific pulse placement. Prior to this targeted therapy, one to two passes of non-overlapping adjacent pulses are delivered to the entire treatment area. Typical fluences are between 30 and 36 J/cm^2, adjusted to achieve a warm to hot, but not uncomfortable, sensation. Pulse duration is adjusted automatically to achieve the desired energy level. Certain locations require reduced fluences. These include the nasolabial folds, where the fluence is reduced by 2 J/cm^2 compared to the rest of the lower face, and temples, where fluences are generally limited to 30 to 32 J/cm^2. Following complete passes, two to six targeted passes are delivered either along the vectors of lifting or to overabundant skin, where pulses may be stacked to induce further tightening. The endpoint of treatment is palpable firming and visible tightening of the problem area [99].

Adverse effects of treatment are few, most commonly including transient erythema and edema occasionally lasting several days, and blistering, especially when higher fluences are utilized [99,100].

Usually, 2 or more treatment sessions scheduled 1 to 3 months apart are recommended for optimal effect. Patients should be reminded that, although some firming is evident after each session, continued tightening may take place for 4 to 6 months following the last treatment.

Titan has so far been used for skin laxity of the forehead and eyebrows, lower face, neck, upper chest, and abdomen (Figure 5.8). Overall, clinical improvement is similar to that seen with the ThermaCool device and is generally described as mild to moderate, and is especially pronounced in those patient, in whom the skin envelope drapes separately from the underlying fat deposits. Recently, a larger spot size of 3.0 cm^2 (Titan XL) has been developed, which will permit faster overall treatment time.

Treatment of Cellulite

Currently, two products on the market are FDA-approved for the treatment of cellulite. One device (VelaSmooth, Syneron Medical Ltd., Yokneam, Israel) combines bipolar RF at 1 MHz, broadband mid-infrared light source with emitted wavelengths between 700 and 2000 nm, mechanical rollers, and suction (Figure 5.9). The other device (TriActive, Cynosure Inc., Chelmsford, MA, USA)

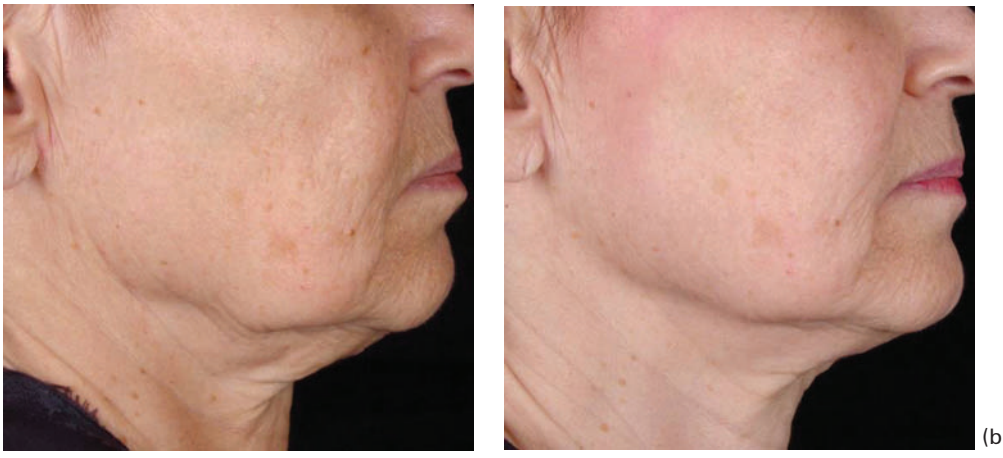


Figure 5.8 (a) Before light-based skin tightening of the neck and **(b)** improvement in neck skin laxity after light-based skin tightening.

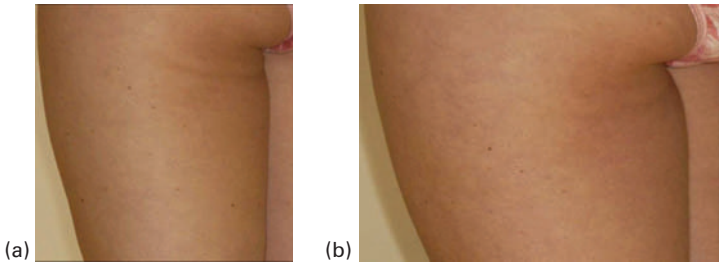


Figure 5.9 (a) Cellulite prior to RF skin tightening and **(b)** improvement in cellulite after RF skin tightening.

incorporates six low-power diode lasers emitting light at 808 nm, contact cooling, rollers, and suction. An additional unipolar RF device (Accent, Alma Lasers Inc., Buffalo Grove, IL, USA) is currently being evaluated for treatment of cellulite and will also be discussed below.

The ideal candidates for these treatments include patients with moderate signs of cellulite on buttocks or thighs, which can be photographed for monitoring of progress. These devices have been tried and found to be safe in all skin types. Patients with scarring or active infection in the treatment area, fluctuating weight, or those with a history of thromboembolic events are generally excluded. Additionally, patients should be assessed for realistic expectations, including the need for multiple treatments and possible maintenance therapy, as well as the clinical goal of gradual and modest improvement. Photographs, body weight, and circumference of each treated area are obtained prior to initiation of therapy.

When using the VelaSmooth device, a conductive fluid is first applied over the treatment area, which also eases handpiece gliding. Eye protection with either goggles or glasses is not needed for either the patient or the practitioner, as the handpiece is applied firmly against the skin. Three preset levels, ranging from 7 to 20 W, for both RF and optical power are available and are typically well tolerated. Vacuum suction of 200 mbar (750 mmHg) can be applied for durations varying from 100 to 300 ms. During treatment, firm pressure is applied while rolling the handpiece back and forth over the treatment area. Multiple passes, typically four to six, are administered to the endpoint of erythema, edema, and subjective feeling of warmth by the patient, which may last for around 2 hours [101]. In addition to these expected effects of treatment, complications may include transient crusting lasting less than 72 hours and bruising for up to a week in approximately 10% of patients [102,103]. Bruising, occasionally extensive, typically occurs following the first 2 to 4 treatment sessions, with no further bruising thereafter. Moderate pain may result from prolonged application of the handpiece to one area for longer than 4 seconds. No scarring or permanent dyschromia have so far been noted with this system. Treatments are usually repeated on a twice-weekly basis for a total of 8 to 16 sessions, with the latter regimen found to be more efficacious [102]. At the end of the treatment course, typical results include a mild to moderate improvement in the visual assessment of cellulite with a mild decrease in the circumference of the treated area.

Similar treatment regimens are utilized with the TriActive system, with a total of 12 to 16 sessions delivered 2 to 3 times per week. Clinical improvement in both clinical appearance of cellulite and hip or thigh circumference achieved with the TriActive system is comparable to that seen with the VelaSmooth device. The incidence of bruising, however, is 30% higher with VelaSmooth compared to TriActive, possibly due to stronger mechanical manipulation [104]. No other adverse effects have so far been reported with the TriActive system.

Although not currently FDA-approved for the treatment of cellulite, the Accent device emits electromagnetic radiation that can penetrate skin for up to 20 mm, as previously mentioned. Due to such deep tissue effect, it has recently been studied in cellulite with encouraging results. When using Accent, mineral oil is first applied to the treatment areas to facilitate handpiece movement. Power may be adjusted to between 100 and 200 W, but is typically used in the 150- to 180-W range. The unipolar handpiece is then moved in a constant circular motion over the area for 30 seconds, with careful avoidance of hot spots. A total

of three to four passes are usually performed, with the endpoint of measured epidermal temperature between 40ºC and 42ºC or patient's intolerance to further heat. Concurrent epidermal cooling is achieved with a chilled tip, which can also be used to reduce temperature in cases of excessive discomfort by applying the handpiece against the skin without pressing the trigger button. Adverse effects encountered to date include erythema, bruising, and occasional blistering, likely related to excessive epidermal temperatures. No long-term complications, such as scarring or dyschromia, have been noted [44]. Treatments are repeated every 2 weeks for a total of 7 sessions. Following this therapeutic course, a significant reduction in the appearance of cellulite and leg circumference, together with histological evidence of dermal fibrosis, have been noted.

Additionally, new ultrasound devices are being developed for emulsification of subcutaneous fat. These systems, however, do not address the issue of skin tightening over the treated areas. Ultimately, future treatment strategies for cellulite will likely include combinations of various therapeutic modalities designed to improve individual components contributing to the condition.

Conclusions

The ever-growing demand for skin rejuvenation with minimal or no downtime has lead to an explosion in the number of various laser-, light-, and RF-based devices. While many of these devices work as intended, in order to practice evidence-based medicine, it is critical to learn whether a system is safe and effective for a given condition. It is, therefore, important for the practitioner to avoid the hype surrounding the device and to explore the physical principles and clinical data available for a given therapeutic modality.

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