David J. Goldberg
Editor

Laser Dermatology

Second Edition

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Preface of Second Edition

The continuing development of cosmetic energy-based technologies over the last 25 years has been nothing short of incredible. It is almost a decade since the publication of the 1st edition of Laser Dermatology. Over the last decade, this field has continued to grow and expand with the appearance of new technology. This book represents the most up-to-date description of the latest in laser and light-source technology. All the initial chapters have been re-written and updated by leading experts from both North America and Europe. After a chapter describing our latest understanding of laser physics, which also covers safety aspects, chapters are dedicated to laser treatment of vascular lesions, pigmented lesions and tattoos, unwanted hair, fractional ablative and non-ablative resurfacing and energy-based treatments for medical purposes.

Each chapter begins with core concepts. These basic points are followed by a history of the use of energy-based technologies for the cutaneous problem under discussion, currently available technology, and indications and contraindications. The chapter authors then provide an example of his/her consent form and approaches to personal treatment.

What has become clear is that a significant understanding of lasers and light sources is required for optimum use of these devices. A basic understanding of laser physics is also fundamental to good laser treatment. Laser safety and minimizing risk to patients is at least as important as an understanding of laser physics. When these concepts, so clearly described in Chap. 1, are understood, cutaneous laser technology can be safely and successfully used for a variety of purposes.

A wide variety of cutaneous vascular disorders can be successfully treated with modern lasers. The pulsed dye laser has enabled treatment of cutaneous vessels by following the principle of selective photothermolysis, a simple physics concept seen throughout laser dermatology. The pulsed dye laser is the most effective laser for treatment of port wine stains but purpura historically limited its acceptability by patients for more cosmetic indications. Both facial and leg vein telangiectasia can also be treated with lasers. Other cutaneous disorders such as psoriasis, warts and scars can be improved by targeting the lesion's cutaneous vessels with appropriate lasers. Chapter 2 describes our latest understanding of the laser treatment of vascular lesions.

When considering treatment of pigmented lesions, accurate diagnosis of the pigmented lesion is mandatory before laser treatment. For some pigmented lesions, laser treatment may even be the only treatment option. Tattoos respond well to Q-switched lasers. Amateur and traumatic tattoos respond

more readily to treatment than do professional tattoos. Cosmetic tattoos should be approached with caution. Treatment of melanocytic nevi remains controversial, but worth pursuing. Chapter 3 describes our latest understanding of the laser treatment of pigmented lesions and tattoos.

A wide variety of lasers can now induce permanent changes in unwanted hair. Hair removal lasers are distinguished not only by their emitted wavelengths but also by their delivered pulse duration, peak fluence, spot size delivery system and associated cooling. Nd:YAG lasers, with effective cooling, are the safest approach for treatment of darker skin. Despite this, complications arising from laser hair removal are more common in darker skin types. Laser treatment of non-pigmented hair remains a challenge. Chapter 4 describes our latest understanding of the laser treatment of unwanted hair.

Ablative and non-ablative fractional laser resurfacing lead to improvement of photodamaged skin. Fractional ablative laser resurfacing produces a more significant wound, but lasting clinical results. Non-ablative fractional resurfacing is cosmetically more elegant, but generally requires more treatment sessions. Visible light non-ablative devices lead to a lessening of erythema and superficial pigmentary skin changes. Mid-infrared laser devices promote better skin quality and skin toning. Chapter 5 describes our latest understanding of ablative and non-ablative fractional laser resurfacing.

Lasers and light sources have become more commonplace in the treatment of dermatological medical diseases. Topical ALA and adjunct light-source therapy (ALA-PDT) is a proven photodynamic therapy for actinic keratoses and superficial non-melanoma skin cancers. ALA-PDT, using a variety of vascular lasers, red/-light sources, and intense pulsed light sources, is also now being used to treat the signs of photoaging. PDT can also be useful therapy for acne vulgaris. Newer lasers and light sources are also now being used to treat psoriasis vulgaris, vitiligo, other disorders of pigmentation, and hypopigmented stretch marks. Chapter 6 describes our latest understanding of photodynamic therapy and the treatment of medical dermatological conditions.

January 2013 David J. Goldberg, M.D.

Contents

Basic Laser: Physics and Safety

1

Holly H. Hare and Ronald G. Wheeland

Core Messages

- A significant understanding of lasers and light sources is required for optimal use of these technologies.
- A basic understanding of laser physics is at the core of safe and efficacious laser treatments.
- Laser safety and minimizing patient risks is at least as important as an understanding of laser physics.

History

What Is Light?

Light is a very complex system of radiant energy that is composed of waves and energy packets known as photons. It is arranged into the electromagnetic spectrum (EMS) according to the length of those waves. The distance between two successive troughs or crests of these waves, measured in meters, determines the *wavelength*. For the visible portion of the EMS, the wavelength determines the color of the laser light. The number of wave crests (or troughs) that pass a given point in a second determines the *frequency* for each source of EMS energy. The wavelength and frequency of light are inversely related to one another. Thus, shorter wavelengths of light have higher frequencies and more energenic photons than longer wavelengths of light which have lower frequencies and less energenic photons.

When Was Light First Used for Medical Purposes?

One must go back to about 4000 B.C. in ancient Egypt to find the earliest recorded use of light. At that time sunlight was coupled with a topical photosensitizer, like parsley or other herbs containing psoralen, to help repigment the skin of individuals suffering from vitiligo, a disorder in which the skin becomes depigmented through a presumed autoimmune reaction. In Europe in the nineteenth century, sunlight was used as a treatment for cutaneous tuberculosis. However, it wasn't until 1961 that Dr. Leon Goldman, a dermatologist at the University of Cincinnati, first employed a ruby laser for the removal of tattoos and other pigmented cutaneous lesions. For his continuous efforts in promoting the use of lasers for medical purposes and for co-founding the American Society for Laser Medicine and Surgery, Dr. Goldman (Goldman et al. 1963) has been called

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the "Father of Lasers in Medicine and Surgery." Since those earliest days, many physicians in different specialties have played key roles in the advancement of the use of lasers in medicine such that today most specialties use lasers in either diagnosing or treating a number of different disorders and diseases (Wheeland 1995).

Who Invented the Laser?

Professor Albert Einstein (Einstein) published all of the necessary formulas and theoretical concepts to build a laser in his 1917 treatise called "The Quantum Theory of Radiation." In this treatise, he described the interaction of atoms and molecules with electromagnetic energy in terms of the spontaneous absorption and emission of energy. By applying the principles of thermodynamics he concluded that stimulated emission of energy was also possible. However, it wasn't until 1959 that Drs. Charles H. Townes and Arthur L. Schawlow (Schawlow) developed the first instrument based on those concepts, known as the *MASER* (*M*icrowave *A*mplification through the *S*timulated *E*mission of *R*adiation). In 1960, the first true laser, a ruby laser, was operated by Dr. Theodore H. Maiman (Maiman). Rapidly the development of additional lasers occurred with the helium-neon laser appearing in 1961, the argon laser in 1962, the carbon dioxide and Nd:YAG laser in 1964, the tunable dye laser in 1966, the excimer laser in 1975, the copper vapor laser in 1981, the gold vapor laser in 1982, and many others since then including the alexandrite laser, pulsed dye laser, erbium laser, holmium laser, diode laser, and titanium:sapphire laser. In addition, modifications to existing lasers have occurred, including Q-switching of the ruby, Nd:YAG and alexandrite lasers; fractionating the carbon dioxide laser; and adding dynamic cooling to the pulsed dye laser.

What Is a Laser?

The word "LASER" is an acronym that stands for *L*ight *A*mplification by the *S*timulated *E*mission of *R*adiation. For this reason, a laser is not just an instrument but also a physical process of amplification (Table 1.1). The last word in the acronym, "radiation," is a common source of patient anxiety since it can be associated with the high energy ionizing radiation often used for cancer radiotherapy. However, in the case of lasers, the word is employed to describe how the laser light is propagated through space as "radiant" waves. Patients should be assured that all currently approved medical lasers are incapable of ionizing tissue and have none of the risks associated with the radiation used in cancer therapy.

All lasers are composed of the same four primary components. These include the *laser medium* (usually a solid, liquid, or gas), the *optical cavity* or resonator which surrounds the laser medium and contains the amplification process, the *power supply* or "pump" that excites the atoms and creates population inversion, and a *delivery system* (usually a fiber optic or articulating arm with mirrored joints) to precisely deliver the light to the target.

Lasers are usually named for the *medium* contained within their optical cavity (Table 1.2). The gas lasers consist of the argon, copper vapor, helium-neon, krypton and carbon dioxide devices. One of the most common liquid lasers, the pulsed dye laser, contains a fluid with rhodamine dye. The solid lasers are represented by the ruby, neodymium:yttrium-aluminum-garnet (Nd:YAG), alexandrite, erbium and diode lasers. All of these devices are used to clinically treat a wide variety of conditions and disorders based on their wavelength, nature of their pulse, and energy.

The excitation mechanism, power supply or "pump," is a necessary component of every laser in order to generate excited electrons and create population inversion (Arndt). This can be accomplished by direct electrical current, optical stimulation by another laser (argon), radiofrequency excitation, white light from a flash lamp or even (rarely) chemical reactions that either make or break chemical bonds to release energy, as in the hydrogen-fluoride laser.

To understand how laser light is created, it is important to recall the structure of an atom. All atoms are composed of a central nucleus surrounded by electrons that occupy discrete energy levels or

Table 1.1 Laser terminology

Absorption – the transformation of radiant energy to another form of energy (usually heat) by interacting with matter.
Chromophore – a targeted component of tissue that absorbs light at a specific frequency.
Coherence – all waves are in phase with one another in both time and space.
Collimation – all waves are parallel to one another with little divergence or convergence.
Electromagnetic radiation – a complex system of radiant energy composed of waves and energy bundles that is organized according to the length of the propagating wave.
Energy – the product of power (watts) and pulse duration (seconds) which is expressed in joules.
Extinction length – the thickness of a material necessary to absorb 98 % of the incident energy.
Focus – the exact point at which the laser energy is at peak power.
Fractional photothermolysis – a concept that employs an array of small laser beams to create many noncontiguous columns of thermal injury, called microscopic treatment zones, within the dermis while maintaining intervening zones of healthy tissue.
Irradiance (power density) – the quotient of incident laser power on a unit surface area, expressed as watts/cm^2.
Joule – a unit of energy which equals one watt-second.
Laser – an instrument that generates a beam of light of a single or narrow band of wavelengths or colors that is both highly collimated and coherent; an acronym that stands for light amplification by the stimulated emission of radiation.
Laser medium – a material or substance of solid, liquid or gaseous nature that is capable of producing laser light due to stimulated electron transition from an unstable high energy orbit to a lower one with release of collimated, coherent, monochromatic light.
Meter – a unit length based on the spectrum of krypton-86; frequently subdivided into millimeters (10^3 m), micrometers (10^6 ms), and nanometers (10^9 m).
Monochromatic – light energy of only a single wavelength emitted from a laser optical cavity.
Optically pumped laser – a laser where electrons are excited by the absorption of light energy from an external source.
Photoacoustic effect – the ability of Q-switched laser light to generate a rapidly moving wave within living tissue that destroys melanin pigment and tattoo ink particles.
Pockels cell – a device consisting of an electro-optical crystal that can be turned on or off very quickly by attached electrodes to allow the build-up of high amounts of energy within the optical cavity of a laser and then released as a single, powerful, extremely short pulse.
Population inversion – the state present within the laser optical cavity (resonator) where more atoms exist in unstable high energy levels than their normal resting energy levels.
Power – the rate at which energy is emitted from a laser.
Power density (irradiance) – the quotient of incident laser power on a unit surface area, expressed as watts/cm^2.
Pump – the electrical, optical, radiofrequency or chemical excitation that provides energy to the laser medium.
Q-switch – an optical device (pockels cell) that controls the storage or release of laser energy from a laser optical cavity.
Reflectance – the ratio of incident power to absorbed power by a given medium.
Scattering – imprecise absorption of laser energy by a biologic system resulting in a diffuse effect on tissue.
Selective photothermolysis – a concept used to localize thermal injury to a specific target based on its absorption characteristics, the wavelength of light used, the duration of the pulse and the amount of energy delivered.
Thermal relaxation time – the time needed for 50 % of heat absorbed during a laser pulse to be dissipated without conduction to the surrounding tissue.
Thermodulation – the ability of low energy light to upregulate or downregulate certain cellular biologic activities without producing an injury.
Transmission – the passage of laser energy through a biologic tissue without producing any effect.

orbits around the nucleus and give the atom a stable configuration (Fig. 1.1). When an atom spontaneously absorbs a photon of light, the outer orbital electrons briefly move to a higher energy orbit, which is an unstable configuration (Fig. 1.2). This configuration is very evanescent and the atom quickly releases a photon of light spontaneously so the electrons can return to their normal, lower energy, and stable inner orbital resting configuration (Fig. 1.3). Under normal circumstances, this

Table 1.2 Types of lasers

Name	Type	Wavelength (nm)
ArFl	Excimer	193
KrCl	Excimer	222
KrFl	Excimer	248
XeCl	Excimer	308
XeFl	Excimer	351
Argon	Gas	488 and 514
Copper vapor	Gas	511 and 578
Krypton	Gas	521–530
Frequency-doubled:YAG	Solid state	532
Pulsed dye	Liquid	577–595
Helium-neon	Gas	632
Ruby	Solid state	694
Alexandrite	Solid state	755
Diode	Solid state	800
Nd:YAG	Solid state	1,064 and 1,320
Diode	Solid state	1,450
Erbium:glass	Solid state	1,540
Erbium:YAG	Solid state	2,940
Carbon dioxide	Gas	10,600

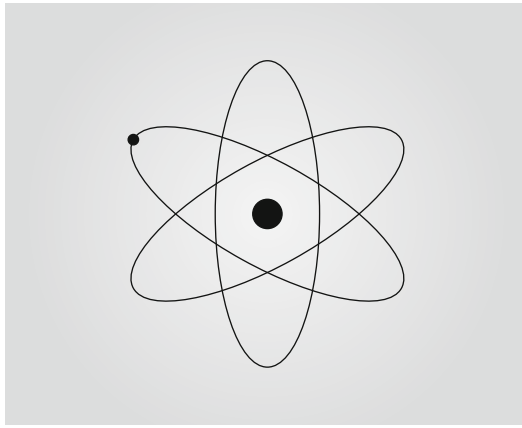

Fig. 1.1 Normal configuration of an atom with central nucleus and surrounding electrons in stable orbits

spontaneous absorption and release of light occurs in a disorganized and random fashion and results in the production of *incoherent* light.

When an external source of energy, usually in the form of electricity, light, microwaves, or even a chemical reaction, is supplied to a laser cavity containing the laser medium, the resting atoms are stimulated to drive their electrons to unstable, higher energy, outer orbits. When more atoms

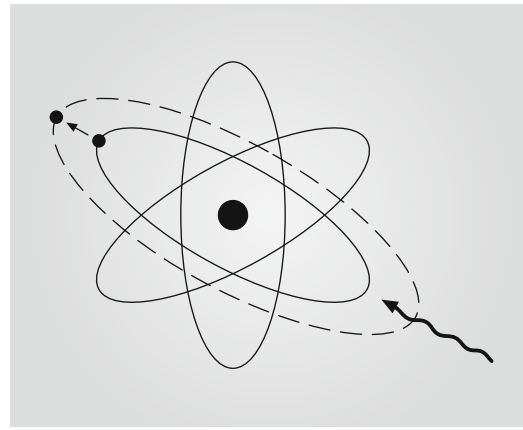

Fig. 1.2 Absorption of energy has briefly stimulated the outer electron into an unstable, but higher energy orbit

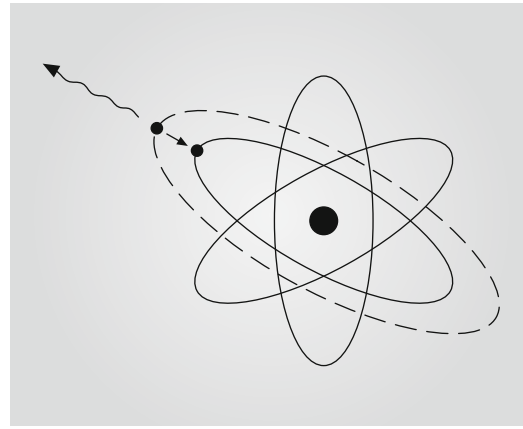

Fig. 1.3 The stimulated electron rapidly drops back to its normal orbit and assumes a stable configuration

exist in this unstable high-energy configuration than in their usual resting configuration, a condition known as *population inversion* is created, and this is necessary for the subsequent step in light amplification (Fig. 1.4).

Amplification of light occurs in the optical cavity or resonator of the laser. The resonator typically consists of an enclosed cavity that allows the emitted photons of light to reflect back and forth from one mirrored end of the chamber to the other many times until a sufficient intensity has been developed for complete amplification to occur. Through a complex process of absorption and emission of photons of energy, the prerequisite for

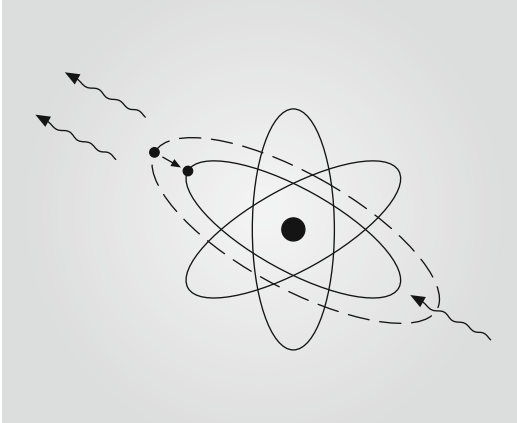

Fig. 1.4 With the stimulated emission of energy, two photons are released in phase with one another as the electron drops back to its normal, stable configuration

the development of a laser beam of light has been met and amplification occurs. The photons are then allowed to escape through a small perforation in the partially reflective mirror. The emerging beam of light has three unique characteristics that allow it to be delivered to the appropriate target by fiber optics or an articulated arm.

What Are the Unique Characteristics of Laser Light?

Laser light has three unique characteristics that differentiate it from non-laser light. The first of these characteristics is that laser light is *monochromatic* or composed of a single wavelength or color. The second unique characteristic is a property known as *coherence* where all the waves of light move together temporally and spatially as they travel in phase with one another through space. The third characteristic is *collimation* where the transmission of light occurs in parallel fashion without significant divergence of the beam, even over long distances.

What Is Irradiance and Energy Fluence?

In order to use a laser to treat any skin condition, it is necessary to understand how the laser can be adjusted to obtain the most desired biologic effects in tissue (Fuller). Two of the factors that are important in this process are irradiance and energy fluence. *Irradiance*, also called power density, determines the ability of a laser to incise, vaporize, or coagulate tissue and is expressed in W/cm^2. It can be calculated based on the formula:

$$\mathrm{Ir} = \frac{\text{Laser output } (\mathrm{W}) \times 100}{\text{pi} \times \text{radius}^2 \,(\text{of the laser beam})}.$$

The *energy fluence* determines the amount of laser energy delivered in a single pulse and is expressed in J/cm^2. It can be calculated based on the formula:

$$\mathrm{EF} = \frac{\text{Laser output } (\mathrm{W}) \times \text{ exposure time } (\mathrm{s})}{\text{pi} \times \text{radius}^2 \,(\text{of the laser beam})}.$$

In regards to irradiance and energy fluence, the higher the number, the greater the effect. For example, high irradiances are needed to incise tissue while only low irradiances are needed to coagulate tissue.

Currently Available Technology

How Does Laser Light Interact with Tissue?

In order to select the ideal laser from the myriad of currently available devices for the treatment of any cutaneous condition, it is important to first understand how light produces a biologic effect in skin. The interaction of laser light with living tissue is generally a function of the wavelength of the laser system. In order for laser energy to produce any effect in skin, it must first be absorbed. Absorption is the transformation of radiant energy (light) to a different form of energy (usually heat) by the specific interaction with tissue. If the light is reflected from the surface of the skin or transmitted completely through it without any absorption, then there will be no biologic effect. If the light is imprecisely absorbed by any target, or chromophore, in skin, then the effect will also be

imprecise. It is only when the light is highly absorbed by a specific component of skin that there will be a precise biologic effect. This reaction may seem difficult to accurately anticipate; however, there are really only three main components of skin that absorb laser light: melanin, hemoglobin, and intracellular or extracellular water. The absorption spectrum of each of these chromophores has been well established. Manufacturers of lasers used this information to develop devices that produce light which is the right color or wavelength to be precisely absorbed by each one of these components of skin. This minimizes collateral injury to the surrounding normal skin.

In 1983, Drs. R. Rox Anderson (Anderson) and John A. Parrish of the Harvard Wellman Laboratories of Photomedicine published their newly developed concept of *selective photothermolysis* (SPTL). This original concept explained how to safely and effectively treat the microvessels in children with port wine stains using laser light. It also led to the first "ground up" development of a specific laser, the pulsed dye laser (PDL), to treat a specific condition, port wine stains in children. This concept has been used more recently to develop more effective treatments for many other cutaneous problems including the treatment of tattoos and benign pigmented lesions and the removal of unwanted or excessive hair. The concept of SPTL defines the way to localize thermal injury to the tissue being treated and minimize collateral thermal damage to the surrounding non-targeted tissue. This is done by choosing the proper wavelength of light that will be precisely absorbed by the specific targeted chromophore without damaging the surrounding tissue. Also important in the concept of SPTL is the thermal relaxation time (TRT), which defines the amount of time needed for a chromophore to dissipate the heat absorbed during the laser pulse. Thus, the delivery of the correct amount of energy with the proper pulse duration will contribute to selective photothermolysis. In large part, the physical size of the target will determine the TRT and, in turn, determine the most desirable duration of the laser pulse.

What Is a Q-switched Laser?

The laser cavity "Q" is a measure of the optical loss per pass of a photon within the optical cavity (Goldman et al. 1965). Thus, the "Q" of a system is a way to characterize the quality of the photons being released so that a high "Q" implies low loss and a low "Q" implies high loss. A "Q-switch" is a physical method to create extremely short (5–20 ns) pulses of high intensity (5–10 MW) laser light with peak power of 4 J. In addition to the normal components (Fig. 1.5) of a laser that were previously described, this system utilizes a shutter which is constructed of a polarizer and a *pockels cell* within the optical cavity. A pockels cell is an optically transparent crystal that rotates the plane of polarization of light when a voltage is applied to it. Together, the polarizer and pockels cell act as the "Q-switch." Light energy is allowed to build (Fig. 1.6) within the optical cavity when voltage is applied to the pockels cell. Once the voltage is turned off, the light energy is released (Fig. 1.7) in one extremely powerful short pulse. Currently available Q-switched lasers include the ruby, Nd:YAG and alexandrite lasers.

The Q-switched lasers and the photons of light released from them have unique characteristics that allow them to be effectively used to treat tattoos (Goldman et al. 1967) and benign pigmented lesions. This is due to their mechanism of action whereby photoacoustic waves are generated within the skin by the released photons of light, and this heats the tattoo pigment particles or the melanosomes. This heating causes cavitation within the cells containing the ink particles or pigment, followed by rupture and eventual phagocytosis by macrophages and removal of the debris from the site. Clinically, this process produces gradual fading of the tattoo with a series of 4–8 treatments at 6–8 week intervals and removal of many benign pigmented lesions with only 1–2 treatments, again at 6–8 week intervals. The precise targeting of subcellular organelles and pigment particles by the Q-switched lasers reduces collateral damage and minimizes the risk of scarring or textural changes. The treatment of tattoos and benign pigmented lesions represents additional examples of how selective photothermolysis can

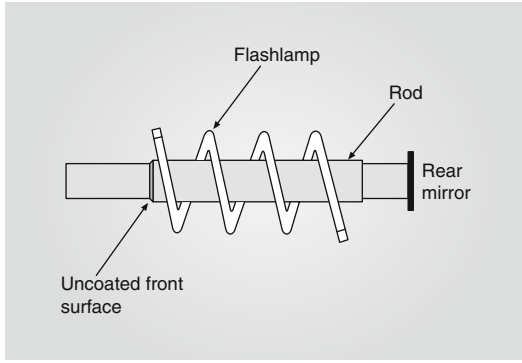

Fig. 1.5 Classic appearance of a solid state laser with central rod that could be ruby, Nd:YAG or Alexandrite crystal surrounded by a flashlamp with emission of light from only one end of the optical cavity

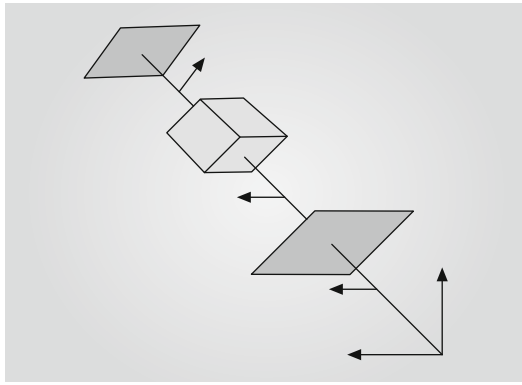

Fig. 1.6 The Q-switched lasers contain a pockels cell that can be made opaque by the application of a voltage and thus allow energy to build within the optical cavity

be effectively applied to more accurately treat conditions other than the microvessels of port wine stains for which this concept was originally developed.

What Is Photodynamic Therapy?

The use of a photosensitizer in conjunction with light is called photodynamic therapy (PDT). PDT is commonly used with the photosensitizer 5-aminolevulinic acid (ALA) or its ester derivative methyl 5-aminolevulinate (MAL), both of which are taken up by epidermal cells (preferentially metabolically active cells) after topical application. The intracellular ALA or MAL is converted

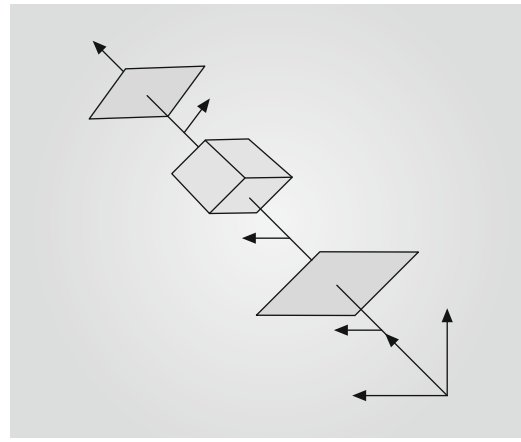

Fig. 1.7 Once the voltage is turned off, the pockels cell becomes optically transparent and the accumulated energy is allowed to be released in a single, short, powerful pulse

to protoporphyrin IX, a photosensitizer. On exposure to a light source, protoporphyrin IX absorbs the light and is excited to a singlet state. Energy is then transferred to oxygen creating excited singlet oxygen which damages cell membranes in the treatment area. This reaction can be stimulated in the epidermis and its appendages but not in the dermis. This is likely a result of inadequate penetration of the drug into the dermis or inability of the light to reach the appropriate depth in the dermis. Several light sources are available for PDT, including the light emitting diode (red or blue light), helium-neon laser, gold vapor laser, pulsed dye laser (PDL), and intense pulsed light (IPL). The initial indication for PDT was to treat actinic keratoses. However, newer studies have shown efficacy in the treatment of superficial basal cell carcinoma, Bowen's disease (squamous cell carcinoma in situ), certain forms of acne vulgaris, acne rosacea, and photodamaged skin (Butani, Goldberg).

Indications

Vascular Lesions

The most common laser used today for the treatment of many different vascular conditions is the pulsed dye laser (Garden and Geronemus 1990).

While initially designed for the treatment of microvessels in port wine stains of infants and children, the initial parameters have been modified to provide longer pulses and wavelengths of light to treat deeper and larger blood vessels and to do this with the addition of epidermal cooling. Cryogen spray or contact cryogen cooling prior to the laser pulse reduces pain while also decreasing the potential for epidermal injury as the light passes through it to reach the deeper blood vessels. Thermal quenching from post-pulse cooling further reduces the risk of collateral thermal injury following delivery of the pulse of light. Cooling devices are now routinely used to treat port wine stains in children and adults, superficial leg veins, solar telangiectasia, angiomas, and other small blood vessel disorders. Long pulses of light from the Nd:YAG laser and the non-laser intense pulsed light (IPL) device have also been used to treat larger and deeper blood vessels. The small beam diameters emitted by the argon and krypton lasers make them of only limited usefulness such as the treatment of small areas containing small caliber, linear blood vessels on the nose or cheeks of adults.

Pigmented Lesions and Tattoos

To treat cosmetically important, but benign, pigmented lesions and tattoos, it is imperative that the risk of scarring and other complications be minimized as much as possible. This is made possible today with the use of short pulses of light from the Q-switched lasers, ruby, Nd:YAG and alexandrite, that deliver pulses of light which approximate the thermal relaxation time of melanosomes and tattoo ink particles. Through their photoacoustic effects, these lasers can produce destruction of melanin pigment or tattoo pigment particles for subsequent removal by macrophages. The most common benign pigmented lesions treated with these devices are solar lentigines, nevus of Ota/Ito, café-au-lait macules, Becker's nevus, post-inflammatory hyperpigmentation, mucosal lentigines of Peutz-Jeghers syndrome and melasma. The variability of the response in congenital or acquired nevocellular nevi makes treatment with Q-switched lasers less desirable. Decorative, traumatic, and cosmetic tattoos can all be effectively treated with the Q-switched lasers. However, multiple treatments are required, and certain colors of tattoos may not respond at all. In addition, there is a risk of darkening of some tattoo colors, especially white and red, that occurs as a result of a chemical reaction following laser treatment, making removal exceedingly difficult.

Unwanted Hair

A number of devices, including the long-pulse ruby, long-pulse Nd:YAG, long-pulse diode and IPL, have been used to permanently reduce the numbers of darkly pigmented hair (Wheeland 1997). This is done by targeting the melanin within the hair shaft and bulb with light energy, which thermally damages the cells and either slows or destroys their ability to regrow. In order to confine the thermal damage to the melanin within the hair follicle without causing damage to the epidermal melanin, the pulse duration must be within the thermal relaxation time of the follicle (generally 10–100 ms for terminal hairs). The theory of thermokinetic selectivity states that smaller structures, such as melanin in the epidermis, lose heat quicker than larger structures, such as melanin in the hair follicle.

At present, treatment of blonde or gray hair with laser light is poor, even with the application of an exogenously applied synthetic melanin solution, and treatment in patients with dark skin (skin types V or VI) or others who have an acquired tan may cause hyperpigmentation, hypopigmentation, scarring, and blistering. A new technology which combines radiofrequency (RF) with optical energy has emerged in attempts to address these limitations. This system, called electro-optical synergy (ELOS), emits optical energy via a light source resulting in increased follicular temperatures through melanin chromophore heating. This creates a temperature differential between the follicle and the surrounding tissues, which allows for directed application of RF energy with less impedance, producing more targeted follicular heating.

The optical energy levels used with ELOS are lower than those used in traditional light-based systems, thereby enabling potentially safer treatments in all skin types. In addition, this combined system can more effectively produce epilation in less melanized lighter hair. However, results still have not been able to parallel those of traditional hair-reduction lasers used on pigmented terminal hair.

Ablative, Non-ablative, and Fractional Facial Resurfacing of Solar Damaged Skin

Over the past decade the short-pulsed carbon dioxide and erbium:YAG lasers have been used to perform ablative skin resurfacing. These devices thermally destroy the epidermis and superficial dermis with minimal collateral damage. However, long healing times and even longer periods of persistent erythema and possibly permanent hypopigmentation, hyperpigmentation, and scarring have greatly reduced the use of these devices.

Since many patients are unwilling to accept ANY downtime from a cosmetic procedure, a number of non-invasive devices have been developed, including the Nd:YAG at 1,320 nm, the diode at 1,450 nm, the pulsed dye laser (PDL) and the IPL, to help restore a more youthful appearance to the skin non-invasively without producing a wound or other visible injury that would keep patients from participating in their normal daily activities. A recent non-invasive technique used for rejuvenation is the light emitting diode (LED). This device delivers intense, non-laser, red- or blue-colored light that can stimulate fibroblasts to produce collagen, elastin, and glycosaminoglycans to help rejuvenate the skin. Sometimes the topical application of a photosensitizer such as aminolevulinic acid (ALA) prior to exposure to the LED will increase the response and cause only minimal crusting and erythema.

The most recent advancement in laser resurfacing is an approach termed "fractional photothermolysis (FP)," which was developed in an attempt to overcome the limitations of posttreatment side effects associated with the ablative and nonablative laser devices (Hantash). The fractional laser devices create microscopic noncontiguous columns of thermal damage called microscopic thermal zones. This avoids the bulk heating of the target tissue caused by other resurfacing lasers and exploits the wound healing effects of the spared viable tissue. Since water is the targeted chromophore, the relatively water-poor epidermis is protected. Downtime is decidedly reduced and side effects are minimal.

Skin Laxity

Another novel, nonablative, noninvasive technique for skin rejuvenation employs a radiofrequency (RF) device to deliver energy in the form of an electrical current deep into the dermis and subcutis. According to Ohm's law, the inherent resistance, or impedance, of the dermal and subcutaneous tissue to the flow of electrical current generates heat. Energy output of the device is calculated using the following formula: Energy (joules) = current^2 × impedance × time. Therefore, heat (joules) is created by the impedance to the movement of electrons relative to the amount of current and time the current is delivered to the tissue. High-impedance tissues, such as subcutaneous fat, generate greater heat and account for the deeper thermal effects of RF devices. An immediate tightening effect is observed due to edema formation and collagen contraction. An inflammatory wound healing response ensues with long-term neocollagenesis. Since RF energy is produced by an electric current rather than by a light source, it is not subject to diminution by tissue scattering or absorption by epidermal melanin. As such, patients of different skin phototypes can be treated and deeper tissue layers can be affected. The handheld tip cools and protects the epidermis before, during, and after RF delivery. RF devices do not produce results comparable to current surgical procedures but they do offer a non-invasive alternative to surgery for mild facial and neck laxity, as well as nonfacial skin rhytides, acne and acne scarring.

Safety

Safety is the most important aspect of properly operating a laser or other optical device since there is always some associated risk to the patient, the laser surgeon, and the operating room personnel whenever a laser is being utilized for treatment. In the outpatient arena, the safe operation of lasers is not generally regulated by the manufacturer, medical licensing board, or other regulatory body. Thus, it is important for the laser operator to understand the risks involved in using lasers and other light sources to develop an appropriate set of standards to ensure that the equipment is being used in the safest fashion possible.

Training – The safe use of any laser begins with appropriate training and familiarization with the indications and uses of each device. This allows the development of the necessary proficiency and concomitant maximal safe use of each device.

Signage – The greatest risk when operating a laser is that of eye injury. To help prevent eye injury, appropriate signage on the laser operating room door should describe the nature of the laser being used, its wavelength and energy. Plus, a pair of protective glasses or goggles appropriate for the device being used should always be placed on the door outside of the laser operating room in case emergency entrance is required. The door to the laser operating room should be locked and all exterior windows closed and covered.

Eye Protection – Inside the operating room, care must also be taken to protect the eyes. If not appropriately protected, the cornea may be injured by either direct or reflected light from the carbon dioxide and erbium:YAG lasers. A more serious injury to the retina can be caused by any of the visible or near-infrared lasers. For the laser surgeon and operating room personnel, there are special optically coated glasses and goggles that match the emission spectrum of the laser being used. The wavelengths of light for which protection is provided by the eyewear as well as the amount of the protection provided in terms of optical density (O.D.) are stamped on the arm of the glasses or the face of the goggles. For most laser devices, the current recommendations are to use eye protection with at least an O.D. of 4.0. The O.D. and wavelengths should be checked and compared with the wavelength of the laser to be used prior to any laser procedure. Correct eye protection should be worn by all operating room personnel at all times when the laser is engaged. For the patient, there are several ways to provide appropriate eye protection. If the procedure is being performed in the immediate vicinity of the orbit, it is probably best to use metal scleral eye shields (Figs. 1.8 and 1.9) that are placed directly on the corneal surface after first using anesthetic eye drops (Nelson). However, if the procedure is being done on the lower part of the face, trunk, or extremities, burnished stainless steel eye cups (Figs. 1.10 and 1.11) that fit over the eyelids and protect the entire periorbital area are probably best. The same eye glasses or goggles used by the laser surgeon and operating room personnel are not recommended for patients since these may leave gaps on the lower edge of the glasses frames near the cheek that permit light to pass beneath them, which could result in injury to the patient.

Laser Plume – Any of the lasers that ablate tissue and create a plume of smoke can potentially harm the laser surgeon, patient, and operating room personnel. Various bacterial spores (Walker) and human papilloma viral (HPV) particles (Garden et al. 1988) have been recovered from carbon dioxide laser plumes. The two best methods to prevent this potential inhalation injury are to use laser-specific surgical masks and a laser-specific plume/smoke evacuator held within 2 in. of the operative site. There is no evidence that HIV or hepatitis C viral particles are transmitted in the laser plume.

Laser Splatter – When treating tattoos or benign pigmented lesions with a Q-switched laser, the impact of the pulses of light can disrupt the surface of the skin sending an explosion of blood and skin fragments flying away from the operative site at a very high speed. The speed of these particles is so fast that it cannot be removed by a smoke or plume evacuator. As a result, most the manufacturers will supply the device with a nozzle or tip that can contain these particles at the skin surface and thus prevent dissemination of these materials into the air. Another technique

Fig. 1.8 The appearance of the concave surfaces of various sizes of corneal eye shields used to protect the eye during laser surgery in the periorbital area

Fig. 1.9 The appearance of the convex surfaces of various sizes of corneal eye shields used to protect the eye during laser surgery in the periorbital area

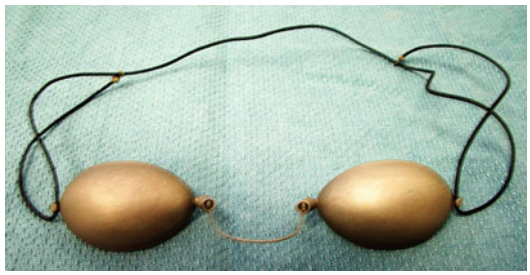

Fig. 1.10 The appearance of the Wheeland-Stefanovsky eye goggles worn over the eyelids for laser surgery not being performed in the immediate periorbital area

Fig. 1.11 The appearance of the externally applied Durette Oculo-Plastik eye cups worn over the eyelids during laser surgery performed closed to periorbital area

that has been successfully used to prevent tissue splattering from the operative site when treating tattoos is to apply a sheet of hydrogel surgical dressing on the surface of the treatment site and discharge the laser through this material to the target. Any extrusion of tissue that occurs with the Q-switched laser pulses will be trapped within the hydrogel and not be allowed to splatter from the operative field.

Fire – Most of the medical lasers used in the treatment of skin diseases do not share the risk of older devices, like the continuous emitting carbon dioxide laser, of igniting a fire. Despite this, it is still recommended that any flammable material, including acetone cleansers, alcohol-based prep solutions or gas anesthetics be restricted from the laser operating room. By following these simple guidelines and using common sense and skill, the risk of using a laser should be no greater than that associated with using older, traditional, non-laser devices to perform the same procedure.

Future

As new concepts emerge to help explain how light can be used to more precisely interact with tissue, it is certain that the development of additional devices based on those concepts will follow soon after. Non-thermal *photoablative decomposition* using the femtosecond titantium:sapphire laser is but one area of recent investigation that

could significantly change the way laser light can be used to ablate tissue with minimal collateral injury. Exciting new research ideas involving the initiation of photochemical reactions with laser light after the topical or parenteral administration of drugs or other photosensitizers are expanding our knowledge of how lasers can be used to effectively treat a number of conditions, like inflammatory, premalignant and malignant conditions, that currently are either poorly treated or untreatable today. Studies on the use of radiofrequency devices to treat many dermatologic conditions are underway. In addition, advances in laser-assisted liposuction are also emerging.

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Laser Treatment of Vascular Lesions

2

Sean W. Lanigan

Core Messages

- A wide variety of cutaneous vascular disorders can be successfully treated with current lasers.
- The pulsed dye laser enabled treatment of cutaneous vessels following principles of selective photothermolysis.
- The pulsed dye laser is the most effective laser for the treatment of port wine stains but purpura limits its acceptability to patients for more cosmetic indications.
- Facial telangiectasias can be treated by a variety of lasers, and purpura can be avoided by appropriate selection of laser parameters.
- Leg vein telangiectasia can also be treated with lasers but sclerotherapy remains the gold standard.
- Other cutaneous disorders such as psoriasis, warts and scars can be improved by targeting lesions cutaneous vessels by appropriate lasers.

History

Port Wine Stain Treatment (Table 2.1)

Argon Laser

The earliest studies on the laser treatment of vascular disorders were on port wine stains (PWS) and published in the 1970s using both the argon and ruby lasers (Goldman and Dreffer 1977). Most work was undertaken with the argon laser. In the 1980s, this was the most frequently used laser worldwide for the treatment of PWS. The argon laser emits light at six different wavelengths in the blue green portion of the visible spectrum. Eighty percent of the total emissions occur at 488 and 514 nm. These two wavelengths of light are absorbed by two chromophores in the skin: oxyhemoglobin and melanin (Fig. 2.1).

Although the argon laser wavelengths do not coincide with the absorption maxima of oxyhemoglobin, there is sufficient absorption to produce thermal damage to red blood cells in cutaneous blood vessels situated superficially within the first millimeter of the skin. Because the argon laser light is delivered in pulses lasting many tens of milliseconds (ms), there is nonspecific thermal damage to peri-vascular connective tissue and beyond. The unfortunate clinical consequence has been textural alteration, scarring, and pigmentary changes (Fig. 2.2).

The continuous wave argon laser beam can be mechanically shuttered to pulses of 50–100 ms or longer. Alternatively the operator moves the beam continuously across the surface of the skin

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Table 2.1 Lasers used for treatment of port wine stains

Laser	Wavelength (nm)	Pulse duration (ms)
Argon (no longer used)	488, 514	50–200
Continuous wave dye	577, 585	50–200
Copper vapor	578	50–200
Krypton (no longer used)	568	50–200
Carbon dioxide (limitations see text)	10,600	50–c/w
Pulsed dye	577, 585	0.45
Long pulsed dye	585, 590, 595, 600	1.5–40
KTP	532	2–50
Alexandrite	755	Varies
Nd:YAG (limitations see text)	1,064	Varies

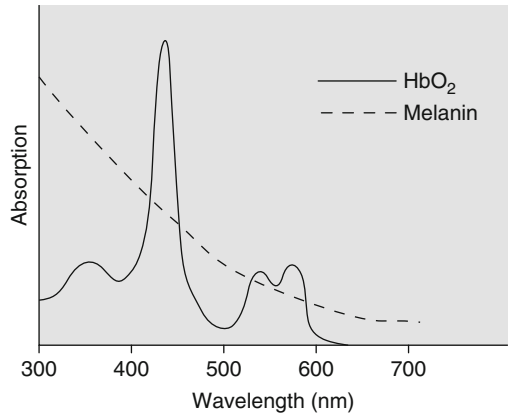

Fig. 2.1 Schematic absorption spectrum of oxyhemoglobin (HbO_2) and melanin

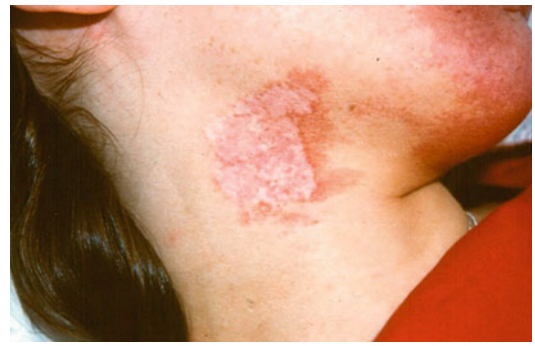

Fig. 2.2 Adverse effects of argon laser treatment (From Lanigan 2000b)

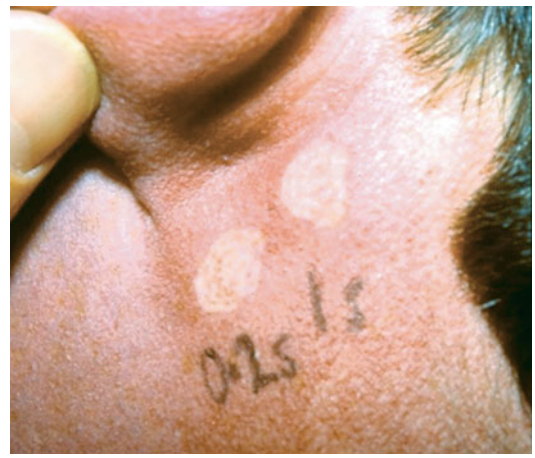

Fig. 2.3 Immediate blanching with argon laser (From Lanigan 2000b)

to reduce the exposure time at each unit area. The clinical end point is minimal blanching. This is a just visible greyish white discoloration of the skin (Fig. 2.3). The operator gradually increases the power until this change is observed. The visible change of minimal blanching inevitably involves non-selective thermal damage, as it is a sign of thermal coagulation of tissue protein. Treatment is far more painful than with current lasers and generally localized areas within a PWS are treated after infiltrational anaesthesia. After treatment the skin invariably weeps and crusts with some superficial blistering. The blanched appearance reverts to a reddish purple color after a few days. Gradually after a period of 4–8 weeks the treated area visibly lightens towards normal skin color. This lightening progresses for more than 6 months after treatment. Because of the high instance of adverse reactions with the argon laser, it is essential to initially perform a small test treatment. The presence of scarring in the test site would normally indicate cessation of treatment or a change to a different laser.

Results of treating PWS with the argon laser were generally better in adults with purple PWS. Hypertrophic scarring after argon laser treatment of PWS was up to 25 %. The results in children were not considered good enough and scarring rates too high to recommend the argon laser for pediatric PWS. The argons laser is rarely used now for PWS.

Continuous Wave Dye Laser

It was recognized from the modeling work of Martin van Gemert and colleagues (1982) that longer wavelengths of light absorbed by hemoglobin, particularly at 577 nm which coincides with the beta absorption peak of haemoglobin would be more appropriate for treatment of vascular lesions (Fig. 2.1). An argon laser can be used to energize a rhodamine dye to produce coherent light at 577 or 585 nm. As with the argon laser the light emerging is continuous but can be mechanically shuttered to produce pulses of light 10's to 100's of milliseconds in duration. Lanigan et al. (1989) reported the results of treating one hundred patients with PWS with a continuous wave dye laser at 577 nm. A good or excellent response was seen in 63 %, with a fair result in 17 %; 12 % of patients had a poor response. Hypertrophic scarring occurred in 5 % and a similar percentage had post inflammatory hyperpigmentation. The best results were seen in older patients with purple PWS. These results were similar to those obtained with the argon laser.

It is likely that any advantage gained by the longer wavelength of light is offset by the long pulse durations employed and the use of minimal blanching as an end point. Dover et al. (1995) treated 28 patients with PWS with the pulsed dye laser and a continuous wave dye laser delivered through a scanning device. Results were better in 45 % of patients treated with the pulsed dye laser and in 15 % of patients treated by the laser with scanner. There was a higher incidence of hyperpigmentation with a continuous wave laser but no differences in the instance of scarring or hypopigmentation.

Robotic Scanning Hand Pieces

The major disadvantage of continuous wave lasers, in the treatment of PWS, is the long pulse duration resulting in nonspecific thermal damage. In addition, manual movement of a continuous wave laser beam over the skin is dependent on the operator's skill not to under or over treat an area. Robotic scanning devices have been developed to try and address some of these difficulties. These hand pieces can be used in conjunction with continuous wave lasers such as the argon laser, and also quasi-continuous systems, such as the copper vapor and KTP lasers.

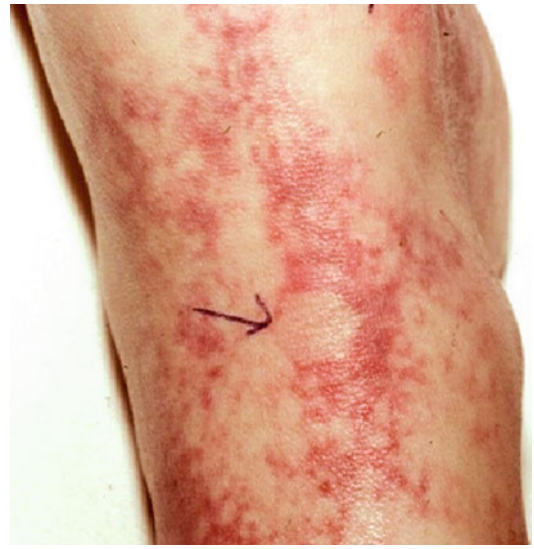

Fig. 2.4 Hexagonal clearance of a port wine stain treated with the KTP laser and robotic scanning hand piece (Hexascan^{R}) (From Lanigan 2000b)

Robotic scanning laser devices have been most widely used in the treatment of PWS. The scanner is connected to the laser output by a fiber optic cable. The automated program places pulses of energy in a precise non-adjacent pattern in the shape of a hexagon (Fig. 2.4). The number of pulses delivered will determine the size of the hexagon, which varies from 3 to 13 mm in diameter. Adjacent hexagons can then be applied to cover the PWS skin. The advantages of automated scanning devices are shorter pulse durations, uniformity of energy placement, faster treatments, and reduced operator fatigue. In a study using scanning devices compared with conventional techniques, the rates of scarring were substantially reduced after scanner assisted laser treatment. Clinical results were also improved in the scanned patients.

Copper Vapor Laser

The copper vapor laser (CVL) is one of two heavy metal vapor lasers used clinically. Results of treating PWS with this laser were reported in the early 1990s. The wavelengths of light emitted by a CVL are 510 and 578 nm. The longer wavelength yellow light is well absorbed by oxyhemoglobin. In contrast to other yellow light lasers, the CVL emits a train of pulses with a duration of 20–25 ns and 10,000–15,000 pulses/s. Because of the very short gap between each pulse of light from the CVL, the biological effect of this laser is similar to that of a continuous wave laser. The CVL is often termed a quasi-continuous laser for this reason.

Good or excellent results have been reported in treating PWS with the CVL (Sheehan-Dare and Cotterill 1993). Best results are seen in predominantly purple or red PWS. Adverse reactions with the CVL are infrequent but most studies have been on small numbers of patients. Textural changes and pigmentary disturbances are most commonly reported.

Carbon Dioxide Laser

The carbon dioxide laser as a treatment of PWS is primarily of historical interest. Yet this laser may still have a role in the removal of hemangiomatous blebs within PWS, resistant to other lasers. The carbon dioxide laser emits infrared light at 10,600 nm which is absorbed by tissue water. In a continuous mode the laser will nonselectively vaporize tissue. It is hypothesized that if the majority of ectatic blood vessels are located superficially within the dermis, vaporization of tissue down to this level, but no further, could result in clinical lightening of the PWS without scarring. Prior to the widespread use of the pulsed dye laser, the carbon dioxide laser was considered of potential value in the treatment of PWS. Lanigan and Cotterill (1990) reported their results using this laser in 51 patients with PWS. Twenty-nine of the patients had failed to respond to argon or continuous wave dye laser treatment. Twenty-two were children with pink PWS. Good or excellent results were seen in 74 % of adults and 53 % of children. Two children (12 %) had a poor result including a hypertrophic scar on the neck in one child. Miralles et al. (1996) treated the tuberous component of 30 patients with PWS unresponsive to pulsed dye laser treatment. In all patients the lesions disappeared, but textural changes were seen in 37 % – with one patient developing hypertrophic scarring. In view of the excellent safety profile for the pulsed dye laser in the treatment of PWS, the carbon dioxide laser cannot be recommended as initial treatment of this vascular birthmark.

Currently Available Lasers for Vascular Lesions

Currently the main lasers used for the treatment of vascular lesions including port wine stains are pulsed dye lasers (PDL) and the KTP laser. Recent work has also demonstrated that long pulsed 755 nm alexandrite and 1,064 nm Nd:YAG lasers may be of value in treatment of both PWS, bulky vascular anomalies and leg vein telangiectasia. The pulsed dye and Nd:YAG lasers can be used together with sequential pulses and Intense Pulsed Light Sources are particularly valuable for diffuse facial redness.

Advantages

These lasers have considerable advantages over earlier continuous wave lasers and other technologies such as radiofrequency and electrolysis. The major advantage is selective vessel destruction with minimal perivascular thermal injury. This is achieved primarily through selective photothermolysis (Anderson and Parrish 1981). By selecting the appropriate wavelength, a chromophore such as oxyhemoglobin can be targeted and thermally injured if sufficient laser energy is absorbed. By control of the pulse duration of the beam, the heat can be confined to the target relating to its size and time to cool (thermal relaxation time). In addition, by using appropriate wavelengths, targets at varying depths in the skin can be selected to a degree. This has resulted in an array of treatment paradigms with very low incidences of adverse events.

Disadvantages

The lasers used currently in the treatment of vascular disease have a low incidence of side effects. Risk of complications is substantially less than that seen with previously used continuous wave lasers such as the argon laser. The major disadvantage of the pulsed dye laser is the development of profound purpura. Using the short pulsed dye laser this occurred in 61 or 62 patients and lasted a mean of 10.2 days (1–21 days) (Lanigan 1995). In this same study, 70 % of patients reported swelling of the treated area which lasted 1–10 days; weeping and crusting occurred in 48 %. Forty-five percent of patients did not go out of their home for a mean of 5.6 days (2–14 days). Longer pulsed PDL treatment leads to less purpura as does treatment with KTP and Nd:YAG lasers and Intense Pulsed Light.

Indications

Lasers currently available can treat a wide range of vascular disorders. Cutaneous ectatic disorders either acquired or congenital can be treated. Particular attention in this chapter will be given to the treatment of port wine stains, capillary (strawberry) hemangiomas, leg vein telangiectasia (Table 2.2) and facial telangiectasia. A number of other disorders of cutaneous vasculature can be treated (Table 2.3). Cutaneous disorders not primarily of vascular origin, e.g. angiolymphoid hyperplasia, adenoma sebaceum, etc., (Table 2.4) can also be treated. Particular emphasis will be given on treating psoriasis, scars and viral warts in this way.

Table 2.2 Lasers used for treatment of leg vein telangiectasia

Laser	Wavelength (nm)	Pulse duration (ms)
KTP	532	1–200
Pulsed dye	585	0.45
Long pulsed dye	585, 590, 595, 600	0.5–40
Alexandrite	755	3–40
Diode	800, 810, 930	1–250
Nd:YAG	1,064	0.3–100

Table 2.3 Some other cutaneous vascular lesions treated with lasers

Spider angioma
Cherry angioma
Venous lake
Angiokeratoma
Pyogenic granuloma
Kaposis sarcoma
Rosacea
Poikiloderma of Civatte (caution see text)
Radiation induced telangiectasia
CREST syndrome

Table 2.4 Some other disorders treated by vascular specific lasers

Angiolymphoid hyperplasia
Lymphangioma
Adenoma sebaceum
Granuloma faciale
Scars
Psoriasis
Warts

Port Wine Stains

Port Wine Stain Treatment with the Flash Lamp Pulsed Dye Laser

The flash lamp PDL was the first laser specifically designed for the selective photo thermolysis of cutaneous blood vessels. It is considered the best laser for the overall treatment of a mixed population of patients with PWS, although some individuals may benefit from other lasers. The laser's active medium is a rhodamine dye selected to produce yellow light at 577–595 nm. Most lasers emit the longer wavelength as this has been shown to have a deeper depth of penetration while also retaining vascular selectivity. The pulse duration is variable and generally used at either 450 μs or 1–2 ms. The other variables are spot size and fluence. The spot sizes available with today's PDL range from 3 to 12 mm. Seven to ten millimeter spot sizes are generally preferred as these will cover larger areas.

There are a number of studies reporting the efficacy of the PDL in the treatment of PWS

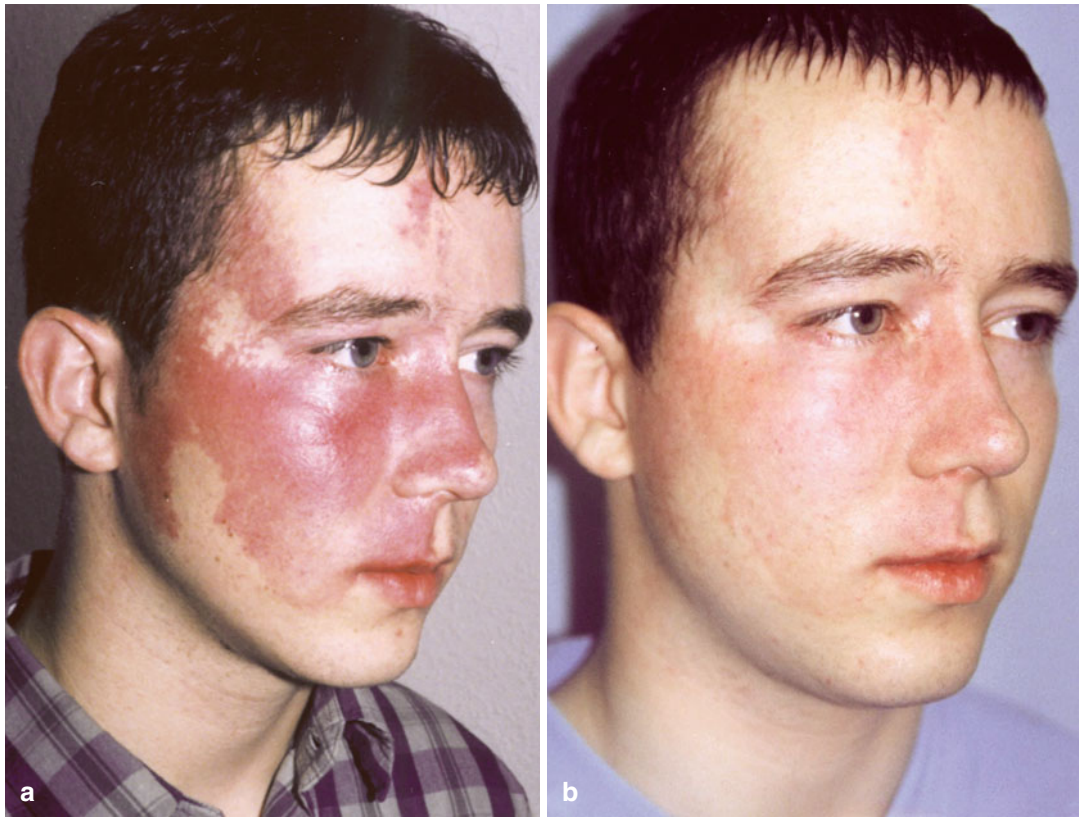

Fig. 2.5 (**a**) Extensive port wine stain on face. (**b**) Near total clearance of port wine stain after course of pulsed dye laser treatment (Courtesy of Lasercare Clinics Ltd)

(Figs. 2.5 and 2.6). Results are generally reported in terms of lightening the PWS rather than the clearance, as complete clearance only occurs in the minority of patients. The vast majority of research papers use subjective criteria for improvement compared with baseline photography. Approximately 40 % of patients with PWS achieved 75 % lightening or more after laser treatment and more than 80 % of PWS lightened by at least 50 %. Several prognostic criteria had been put forward to assist in predicting the outcome of treatment. Some authors reported best results in pink lesions (Fitzpatrick et al. 1994) others report better results in red lesions. In a study of 261 patients treated over a 5-year period (Katugampola and Lanigan 1997), color of PWS was not found to be of prognostic value. Although it is generally considered that younger children will require fewer treatments than adults, some (Alster and Wilson 1994) have reported that younger children may require more treatments owing to the rapid growth of residual blood vessels between treatments. Yet others (Van der Horst et al. 1998) found no evidence that treatment of PWS in early childhood was more effective than treatment at later stage.

Two features that will affect outcome are site of the PWS and size of the birthmark. PWS on the face and neck respond better than those on the leg and hand (Lanigan 1996). On the face, PWS on the forehead and lateral face respond better than those over the middle of the face, particularly those involving the second branch of the trigeminal nerve (Renfro and Geronemus 1993). The chest, upper arm and shoulder generally respond well. PWS less than 20 cm^2 at initial examination cleared more than those greater than 20 cm^2 irrespective of age (Morelli et al. 1995).

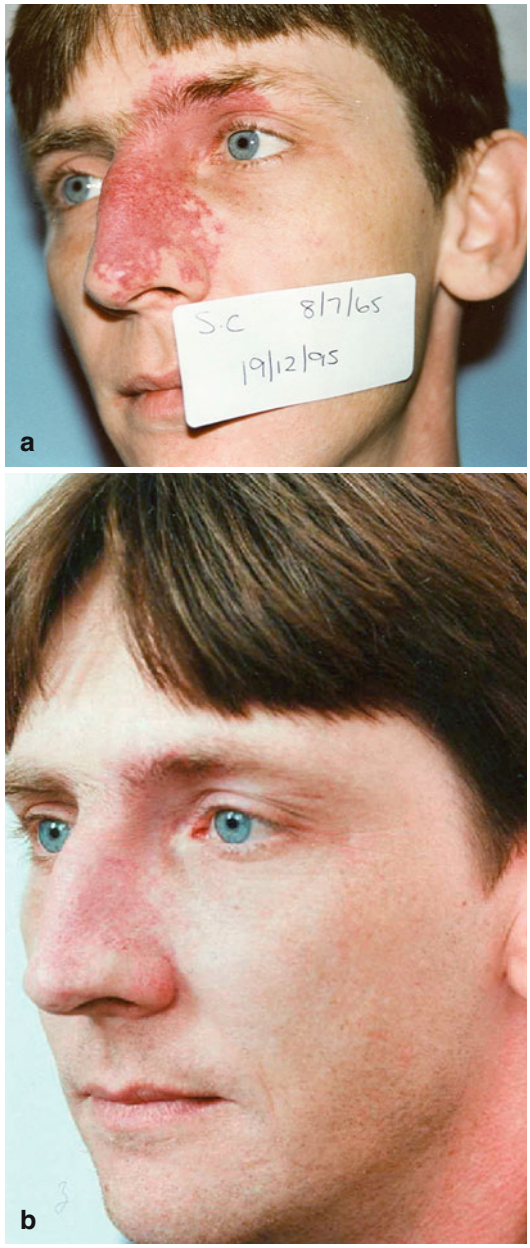

Fig. 2.6 (**a**) Port wine stain on face. (**b**) Complete clearance following course of pulsed dye laser treatment (Courtesy of Lasercare Clinics Ltd)

Second Generation Pulsed Dye Lasers

The pulsed dye laser (PDL) has become the treatment of choice for PWS. Several investigators established the efficacy, and low incidence of side effects, of first generation PDLs operating at either 577 nm or 585 nm wavelengths and 0.45 ms pulse width. However, in the majority of cases, complete clearance was not achieved, and a significant proportion of lesions were resistant to treatment. In recent years, increased understanding of the interaction between lasers and PWS has led to modification of the original PDL design and has given rise to a number of second generation lasers. The most important changes include longer pulse widths, longer wavelengths, higher delivered fluences and use of dynamic cooling devices. Many of these lasers have proved to be useful in the treatment of PWS (Geronemus et al. 2000).

Geronemus et al. used a 595 nm wavelength PDL, 1.5 ms pulse width and fluences up to 11–12 J/cm^2 with a dynamic cooling spray. They obtained greater than 75 % clearing of PWS in 10 out of 16 (63 %) patients after four treatments. All patients were children under 12 months of age. In a study comparing a 585 nm, 7 mm spot, 0.45 ms pulse width PDL with a second generation long-pulsed dye laser (LPDL) with 1.5 ms pulse width, 5 mm spot and wavelength settings ranging from 585 to 600 nm, optimal fading in 30 out of 62 patients was seen with the LPDL compared to only 12 patients with the shorter pulse width laser (Scherer et al. 2001). In 20 patients, there was no difference with respect to wavelength for the LPTDL, 13 patients showed best fading at 585 nm, 3 at 590 nm, 8 at 595 nm and 6 patients at 600 nm. The authors compensated by increasing the fluence for the reduced light absorption at longer wavelengths.

The rationale for the aforementioned alteration in treatment parameters is in part based on an increasing understanding of laser-PWS interactions from non-invasive imaging, mathematical modeling, and animal models. Longer pulse widths, as opposed to the 0.45 ms duration delivered by first generation PDLs, may be more appropriate for larger caliber PWS vessels, based on ideal thermal relaxation times of 1–10 ms (Anderson and Parish 1981; Dierickx et al. 1995b). Longer wavelengths penetrate deeper, allowing targeting of deeper vessels. Higher fluences are needed in part because the newer longer wavelength is further from the peak absorption peak of oxyhemoglobin at 577 nm (Fig. 2.1).

Unfortunately higher fluences also increase the potential for epidermal heating due to competitive absorption by epidermal melanin. This necessitates the use of cooling devices to minimize epidermal damage (and consequent side effects). Cooling methods include liquid cryogen sprays; cold air cooling and contact cooling. The cooling device can be synchronized with laser pulses, or alternatively operated a few milliseconds before or after the pulse. The addition of epidermal cooling allows a reduction in pain and prevention of pigmentary side effects during PWS treatment, even at higher fluences.

Overall, the findings of various studies indicate an improvement over the results with first generation PDLs, where greater than 75 % clearing was noted in only about 40 % of patients. However, with so many variables uncontrolled in the plethora of small studies, it is often difficult to clarify which modification contributed to improved outcomes.

Treatment of Resistant PWS

Further evidence of improved efficacy of second generation PDLs comes from responses in PWS which have proven to be resistant to first generation PDLs. In a case report, PDL treatment with a longer pulse width of 1.5 ms was effective in treating a PWS previously resistant to a 0.5 ms PDL (Bernstein 2000). Work using high fluence long-pulsed dye laser with cryogen cooling) in treatment of resistant PWS has demonstrated that further lightening can be obtained, though this may be at the expense of an increased incidence of side effects (Laube et al. 2003; Mazer and Fayard 2003a).

KTP Laser Treatment

The Nd:YAG laser is a solid state laser containing a crystal rod of yttrium – aluminum – garnet doped with neodymium ions (Nd:YAG). The primary wavelength of this laser is in the infrared at 1,064 nm. A frequency doubling crystal made of potassium titanyl phosphate (KTP) can be placed in the beam path to emit green light at 532 nm. This results in a quasi-continuous laser with individual pulses of 200 ns produced at a frequency of 25,000 Hz. This train of pulses can be shuttered to deliver macro pulses of 2–20 ms. High fluences are available with this laser and the pulse durations may be more appropriate for some PWS.

The KTP laser has been shown to produce further lightening in 30 PDL-resistant PWS lesions (Chowdhury et al. 2001). KTP laser fluences ranged from 18 to 24 J/cm^2 with pulse widths of 9–14 ms. Five (17 %) patients showed greater than 50 % response. In general, patients preferred the KTP laser because it induced less discomfort and purpura. However, two (7 %) patients developed scarring.

A study comparing the PDL with a frequency doubled Nd:YAG laser showed similar response rates among the 43 patients; however, a substantially higher scarring rate with the 532 nm Nd:YAG laser was noted (Lorenz et al. 2003). Another study in Chinese patients showed rather modest benefits using the 532 nm Nd:YAG laser with only 13.6 % of patients showing more than 50 % improvement (Chan et al. 2000).

It would appear that the KTP laser has a role to play in the treatment of resistant PWS. However, the long pulses employed with this laser, and the significant epidermal injury induced by the shorter wavelength of light, may increase the incidence of laser induced adverse effects when this laser is compared with today's PDL.

Infrared Lasers

Longer wavelength lasers such as the alexandrite (755 nm) and Nd:YAG (1,064 nm) may have a role in PWS treatment. In the millisecond mode, these lasers have been widely used for hair removal and leg vein telangiectasia. These lasers may be of value in the treatment of bulky malformations and mature PWSs. Such lesions are typically more resistant to PDL due to the predominance of larger and deeper vessels and higher content of deoxygenated haemoglobin. Noe (Noe et al. 2003) used a 3 ms Alexandrite laser with dynamic cooling to treat three patients with hypertrophic PWS, using fluences ranging from 30 to 85 J/cm^2. All lesions significantly lightened without side effects. Yang et al. (2003) treated 18 patients with PWS, comparing a 595 nm PDL to a long-pulsed Nd:YAG laser with contact cool-

ing. Similar clearances rates were achieved, and scarring was only noted in one patient where fluences exceeded the minimum purpura dose. Patients preferred the Nd:YAG laser because of the shorter recovery period between treatments. Civas et al. (2009) used an Nd:YAG laser to treat a variety of vascular lesions including 19 with PWS. Good to excellent (more than 50 %) improvement was achieved in 63.2 % of patients with PWS.

Non-coherent Light Sources

Intense pulsed light (IPL) has also been used to treat PWS. Unlike laser systems these non-laser flashlamps produce non-coherent broad band light with wavelengths in the range 515–1,200 nm and permit various pulse widths. Filters are used to remove unwanted wavelengths. A study of 37 patients treated with IPL showed a clearance of pink and red PWS, and lightening in purple PWS (Raulin et al. 1999). Direct comparison of an IPL with a PDL source in a study of 32 patients showed that overall the response rate was better with the PDL (Strempel and Klein 1996). However, it was noteworthy that 6 out of the 32 patients had a better response with the IPL. The potential role of IPL for treating PDL-resistant PWS is confirmed by a study showing responses in 7 out of 15 patients previously resistant to PDL, with 6 patients showing between 75 and 100 % improvement (Bjerring et al. 2003).

Faurschou et al. (2009) in a randomized trial involving 20 patients with PWS received one side-by-side treatment with a PDL and IPL. Both PDL and IPL lightened PWS. Median clinical improvements were significantly better for PDL (65 %) than IPL (30 %) A higher proportion of patients obtained good or excellent clearance rates with the PDL (75 %) compared with IPL (30 %). Eighteen of twenty patients preferred to receive continued treatments with PDL.

However, Babilas et al. (2010) performed a split-face comparison of intense pulsed light with short- and long-pulsed dye lasers for the treatment of port-wine stains. There were 11 untreated and 14 previously treated patients with PWS. In previously untreated PWS as well as in pretreated PWS, IPL treatments were rated significantly ($P<0.05$) better than treatments with the PDL. The authors concluded that in PWS resistant to dye laser therapy, IPL showed additional lesion clearance.

The use of IPL increases the therapeutic possibilities in PWS. There is a multiplicity of choices of treatment parameters with non-coherent light sources. Further work is necessary to determine optimum settings.

The current evidence on the technology available to treat PWS has been reviewed by Faurschou et al. (2011) The authors performed a comprehensive review of published randomized clinical trials (RCTs) of lasers or light sources for the treatment of port-wine stains. They included five RCTs involving a total of 103 participants; all trials used the PDL for comparisons. Participants preferred the PDL to intense pulsed light based on the clinical effect. They marginally preferred the Nd:YAG laser to the PDL due to shorter lasting purpura, and PDL in conjunction with cooling was preferred to treatment with PDL alone. The authors concluded that the PDL leads to clinically relevant clearance of PWS. A limited number of RCTs evaluated the efficacy from IPL and other laser types. High-quality RCTs are needed to assess individual efficacy from different lasers and light sources, as well as participant satisfaction.

Capillary (Strawberry) Hemangiomas

Capillary or strawberry hemangiomas are common benign tumors of infancy. Most develop during the first to the fourth week of life. There is an early proliferative phase which usually lasts for 6–9 months. This growth phase is followed by a gradual spontaneous involution which is complete in 50 % by 5 years and 70 % by 7 years of age.

The majority of strawberry hemangiomas are of cosmetic concern. However, the appearance of a large vascular tumor on the face of a baby is not without significance. Some hemangiomas cause problems by interference with organ function, e.g., peri-ocular hemangiomas that lead to problems with vision. Subglottic and intranasal

hemangiomas may cause problems with swallowing and respiration. Bleeding and ulceration can occur particularly in perineal hemangiomas. Most complications occurred during the proliferative phase of the hemangiomas. Once regression is underway the majority of complications associated with the hemangioma will resolve. Unfortunately regression of many hemangiomas is incomplete leaving either a flat telangiectatic patch or an area of redundant discolored skin. If ulceration has occurred, scarring may follow.

Laser treatment of strawberry hemangiomas is performed either to slow or arrest proliferation in early hemangiomas; to correct or minimize complications; or cosmetically to improve residual telangiectatic lesions. A continuous wave Nd:YAG laser can be used; this laser's longer wavelength leads to deep penetration with thermal coagulation of large volumes of tissue. It is useful for debulking large hemangiomas but hypertrophic scarring occurs frequently (Landthaler et al. 1995). Intra oral hemangiomas can respond particularly well to this form of treatment (Dixon et al. 1986). Lasers can also be used intralesionally in the treatment of bulky hemangiomas.

The majority of strawberry hemangiomas currently treated by a laser are treated with the pulsed dye laser. In the first report of a patient treated with the pulsed dye laser, Glassberg et al. (1989) treated a macular hemangioma in a 6 day old infant. This report and other subsequent publications emphasized the importance of *early* treatment of proliferative hemangiomas to obtain most benefit from treatment. Because of the limited penetration depth of the pulsed dye laser (just over 1 mm), it is unrealistic to expect significant alterations in a large mature capillary hemangioma. Fluences of 5.5–6 J/cm^2 with a 5 mm spot are generally used with the 1.5 ms PDL. Treatment intervals have been reduced to every few weeks to achieve optimal benefit when treating hemangiomas. Multiple treatments may be required in small infants.

There is some controversy over the merits of early pulsed dye laser treatment in uncomplicated childhood hemangiomas (Batta et al. 2002; Hohenleutner and Landthaler 2002). Batta et al. in a randomized controlled study of early PDL treatment of uncomplicated childhood hemangiomas found there was no significant difference in the number of children in terms of 1 year complete clearances in the treated vs. the untreated control group. They suggested that treatment in uncomplicated hemangiomas is no better than a wait-and-see policy. This is contested by Hohenleutner and Landthaler who recommend early laser treatment especially in superficial and small childhood hemangiomas. It is likely, based on clinical experience worldwide, that the PDL is of benefit in treating developing strawberry hemangiomas; however, the publication by Léauté-Labrèze et al. (2008) describing the benefits of propranolol for severe hemangiomas of infancy has attracted great interest in using this drug as first line treatment.

The deeper component of the hemangioma may still develop despite successful treatment of the superficial component. For life-threatening proliferative hemangiomas a combination of propranolol, laser therapy, systemic steroids and other agents may be required.

Of note, the complications of bleeding and ulceration respond very well to pulsed dye laser therapy. Usually only one or two treatments are required and often there is a prompt response. Noticeably the pain from an ulcerated hemangioma regresses rapidly after treatment (Barlow et al. 1996). In some patients, the hemangioma will also undergo regression but this is not always the case. The entire hemangioma not just the ulcerated or bleeding area is generally treated.

In the incompletely regressed capillary hemangioma of the older child, superficial ectatic blood vessels can be easily treated with the pulsed dye laser (Fig. 2.7) but scarring or redundant tissue may require surgical repair.

Leg Veins and Telangiectasia

Visible veins on the leg are a common cosmetic problem affecting approximately 40 % of women in the United States; they remain a therapeutic challenge. Sclerotherapy is currently the gold standard of treatment but many vessels less than 1 mm in diameter may be difficult to inject. Work over the last 10 years or more with vascular specific, longer wavelength, longer pulsed lasers,

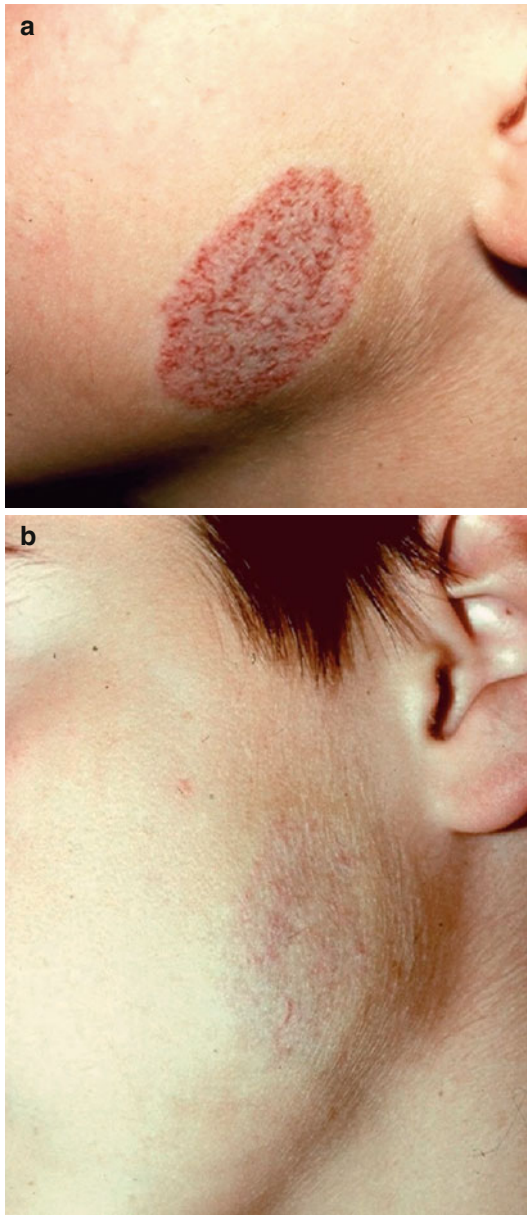

Fig. 2.7 (**a**) Telangiectatic residual strawberry hemangioma. (**b**) After pulsed dye laser treatment

has produced very promising results with some outcomes similar to those seen after sclerotherapy (Table 2.2).

It is important to remember in advance of laser treatment of leg vein telangiectasia to examine the patient carefully to determine whether visible telangiectatic areas are secondary to venous pressure from deeper varicose veins. In the uncomplicated case laser therapy or sclerotherapy can be considered. The majority of leg vein telangiectasia are in the range of 0.1 mm to several millimeters in diameter, much larger than the vessels in a PWS which are 0.1 mm or less. Following the principles of selective photothermolysis, most vessels greater than 0.1 mm will require pulse durations longer than the 0.45 ms short pulsed dye laser used for port wine stains. The larger the vessel, the longer the desired pulse duration. In addition, longer wavelengths of light will be required to penetrate more deeply into these deeper dermal blood vessels.

KTP Laser

The KTP laser produces green light at 532 nm, which is well absorbed by hemoglobin but penetrates relatively superficially. This laser does produce millisecond domain pulses, which should be appropriate for leg vein telangiectasia. However, early results, with this laser, in the treatment of leg veins using small spots and pulse durations of 10 ms or less were disappointing and inferior to those of the long pulsed dye laser (West and Alster 1998). Massey (Massey and Katz 1999) used the KTP laser with a 50 ms pulse and fluences of 18–20 J/cm^2 in the treatment of 46 patients with leg veins. In patients with veins less than 1 mm in diameter, 80 % had greater than 50 % clearing after two treatments. In patients with veins 1–2 mm in diameter, 67 % had greater than 50 % clearing after two treatments. Side effects were minimal and temporary. Crusting or blistering occurred if the chill tip was not kept continuously in contact with the skin. The KTP laser seems most appropriate for superficial red telangiectasia up to 1 mm in diameter. Because there is significant absorption by melanin at 532 nm, patients with darker skin types or tanned skin will have an increased risk of side effects including hypo and hyperpigmentation. Contact cooling does help to reduce this side effect and allow higher fluences.

Long Pulsed Dye Lasers

Based on the theory of selective photothermolysis, the predicted pulse duration ideally suited for thermal destruction of leg veins (0.1 to several millimeters in diameter) is in the 1–50 ms domain

(Dierickx et al. 1995). Long pulsed dye lasers with wavelengths of 585–600 nm with pulse durations of 1.5 ms or longer are now available.

Reichert (1998) treated 80 patients with 250 leg telangiectasias with the long pulsed dye laser using fluences of 16–22 J/cm^2, ice packs were used to cool the skin before treatment. One hundred percent clearance was achieved in vessels with diameters up to 0.5 mm and 80 % fading in vessels between 0.5 and 1.0 mm. There was no incidence of scarring, thrombophlebitis and/or telangiectatic matting. Transient hyperpigmentation occurred in 50 % of cases and hypopigmentation in 50 %.

Long Pulsed Alexandrite Laser

There is a small peak of haemoglobin absorption in the 700–900 nm (Fig. 2.8) range of wavelengths. This has encouraged the use of longer wavelength lasers such as the alexandrite, laser in the treatment of more deeply situated larger caliber leg vein telangiectasia. The long pulsed alexandrite laser emits light in the near infrared spectrum at 755 nm. The laser, when used with pulse durations of 3–20 ms, theoretically penetrates 2–3 mm in depth into the skin.

McDaniel (McDaniel et al. 1999) evaluated the long pulse alexandrite laser in patients with leg vein telangiectasia. By using a variety of different treatment parameters, they concluded that optimal results were achieved with 20 J/cm^2 and double pulses. These parameters produced almost a two third reduction in vessels 0.4–1 mm in diameter after three treatments. Small vessels respond poorly if at all. Others (Kauvar and Lou 2000) treated leg veins measuring 0.3–2 mm in diameter in patients with Fitzpatrick skin types I to III with a 3 ms pulsed alexandrite laser, 8 mm spot, fluences of 6–80 J/cm^2, and associated dynamic epidermal cryogen cooling. Four weeks after a single treatment 48 sites were evaluated, 35 % of the treated sites had cleared by more than 75 %; another 33 % had cleared by more than 50 %. By 12 weeks 65 % of treated areas showed greater than 75 % clearance. Hyperpigmentation was seen in 35 % of treated areas and treatment was noted to be uncomfortable. Ross et al. (2009) found that extending the pulse duration beyond the usual 3 ms (optimal 60 ms) improved results in leg vein telangiectasia could be obtained.

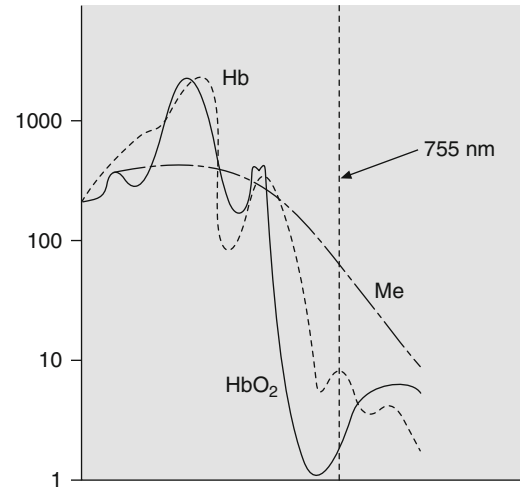

Fig. 2.8 Schematic absorption spectrum of haemoglobin (Hb), oxyhemoglobin (HbO_2) and melanin (Me) to show absorption peak of Hb at 755 nm (Courtesy of Cynosure lasers)

Diode Lasers

Diode lasers were originally introduced in the nineteen eighties with power outputs of only 100 mW. Multiple diode laser arrays have now been developed which can be coupled directly into fiber optic delivery devices. Laser outputs have now increased to 60 W or more. Diode lasers can emit light over a broad range of wavelengths from 600 to 1,020 nm. Most medical research has been with diode lasers such as gallium-arsenide (GaAs) and gallium-aluminum-arsenide (GaAlAs) emitting light in this 795–830 nm range.

These lasers have been used in the treatment of superficial and deep small to medium size leg telangiectasia. Diode lasers emit light that closely matches a tertiary haemoglobin absorption peak at 915 nm. Investigators (Varma and Lanigan 2000) have evaluated an 810 nm diode laser for the treatment of telangiectatic veins on the leg. Vessels measuring 0.5–1.5 mm in diameter were treated using fluences of 12–18 J/cm^2 with a 5 mm spot. Improvements were modest but patient acceptance was high. There were no significant side effects. Others (Passeron et al. 2003)

also investigated a 940 nm diode laser in 60 patients with vessels of varying size. Best results were seen in vessels between 0.8 and 1.44 mm in diameter where 88 % of patients obtained more than 75 % vessel clearance. Vessels smaller than this responded poorly.

It may be possible to improve the results of diode and alexandrite laser treatment by intravenous introduction of an indocyanine green (ICG) dye. This has an enhanced absorption of near infrared light (Shafirstein et al. 2011).

Long Pulsed Nd:YAG Lasers

Several long pulsed Nd:YAG lasers are available with pulse durations in the tens of milliseconds. These pulse widths are more appropriate in targeting large leg veins than the previous Q-switched Nd:YAG nanosecond lasers used in the treatment of tattoos. The 1,064 nm infrared light is deeply penetrating with minimal absorption by melanin. When using long wavelength lasers with deeper penetration but relatively poor absorption, the combination of higher fluences and cooling devices will reduce epidermal injury (Eremia et al. 2002).

In one study (Weiss and Weiss 1999), 50 sites were evaluated with this laser. Number of pulses and fluence was altered based on vessel size. At 3 months follow up a 75 % improvement was noted. There was no epidermal injury with this laser although hyperpigmentation was common. Several studies have now demonstrated the effectiveness of the millisecond pulsed Nd:YAG laser for lower extremity telangiectasia (Rogachefsky et al. 2002; Omura et al. 2003; Mordon et al. 2003). Mordon et al. have focused on methemoglobin production following laser induced heating. This methemoglobin formation leads to an increase in the absorption of the 1,064 nm infrared light, adding to the effect of the Nd:YAG laser.

Despite these developments, sclerotherapy may well remain the treatment of choice for a variety of leg vein telangiectasia. A comparative study of sclerotherapy and long pulsed Nd:YAG laser treatment (Lupton et al. 2002) showed that leg telangiectasia responded best to sclerotherapy, in fewer treatment sessions, as compared to the long pulsed YAG laser. The incidence of adverse sequelae was equal. Bäumler et al. (2006) used a mathematical model to analyze the effectiveness of the selective photothermolysis process in laser treatment of leg veins by Nd:YAG at 1,064 nm. Their model predicts a maximal efficiency of a range of fluences (100–200 J/cm^2) and pulse durations (10–100 ms).

Laser treatment of leg vein telangiectasia appears to be of particular value in patients with telangiectatic matting, needle phobia and for small superficial vessels too small to be treated with a needle.

Facial Telangiectasia

Facial telangiectasias are one of the commonest vascular disorders presenting for treatment. They respond readily to most lasers emitting light absorbed by haemoglobin. The two main groups of lasers used for facial telangiectasia are the pulsed dye and KTP lasers. The PDL has the lowest incidence of scarring but may cause significant bruising after treatment (Fig. 2.9). This may not be cosmetically acceptable to patients with relatively mild disease. In a comparison of the older copper vapor laser and PDL treatment of facial telangiectasia (Waner et al. 1993), similar improvements were seen with both lasers. However, patients preferred the linear crusting produced by the copper vapor laser compared to the purpura induced by the pulsed dye laser. In a comparison study of the argon, dye and pulsed dye lasers (Broska et al. 1994), the pulsed dye laser was shown to produce better results. However, only 6 of 13 patients preferred this laser because of laser induced purpura and post-inflammatory hyperpigmentation. Four different frequency doubled Nd:YAG lasers for the treatment of facial telangiectasia were assessed (Goldberg and Meine 1999), using fluences of between 8 and 24 J/cm^2. The authors demonstrated equal efficacy with all such lasers and no evidence of scarring or pigmentary changes (Figs. 2.10 and 2.11).

With the development of long pulsed dye lasers with epidermal cooling, it may be possible to produce satisfactory improvement in facial telangiectasia while minimizing the purpura seen with the earlier pulsed dye lasers. Some investigators

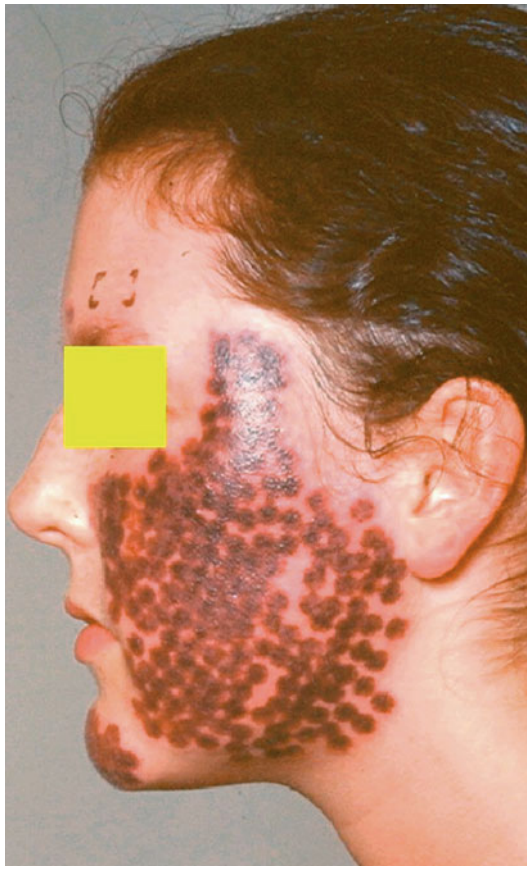

Fig. 2.9 Bruising after pulsed dye laser

(Alam et al. 2003a) have treated patients with facial telangiectasia using with the pulsed dye laser at fluences 1 J/cm^2 below and 0.5 J/cm^2 above the purpura threshold. There was a small reduction in observed telangiectasia with the purpura free treatment. This was seen most commonly with finer telangiectatic vessels. A more significant reduction in telangiectasia was seen in those with laser induced purpura. Similar work has been reported (Tanghetti and Sherr 2003) using a PDL with refrigerated air cooling and extended pulse widths of 40 ms at fluences at or below the purpuric threshold. In all cases, vessel clearance was associated with transient purpura lasting less than seven days. The authors did not feel that it was possible, in a single treatment, to produce vessel clearance without the presence of purpura.

Several authors have published the results of non purpuragenic PDL treatment typical parameters are: 10-mm spot size, fluence 7 J/cm^2, 6–10 ms pulse duration and epidermal cooling (Neuhaus et al. 2009; Hare McCoppin and Goldberg 2010)

A valuable alternative to lasers is Intense Pulsed Light (IPL). These broadband light sources are filtered to produce wavelengths appropriate for absorption by oxyhemoglobin. The relatively large treatment area produces uniform treatment patterns which are helpful in treating diffuse facial redness, and purpura is uncommon (Tanghetti 2011).

Other (Non-vascular) Cutaneous Diseases

Psoriasis

In a psoriatic plaque, the capillaries of the dermal papillae are enlarged, dilated and tortuous. A variety of lasers can be used for the treatment of psoriasis. Since the PDL can be used to treat superficial cutaneous vascular ectasias, it seemed logical to investigate whether this laser had any therapeutic efficacy in the treatment of plaque-type psoriasis. Over a decade ago (Hacker and Rasmussen 1992) there were reports of the potential benefits of the PDL in psoriasis. Subsequent studies (Katugampola et al. 1995; Zelickson et al. 1996; Ross et al. 1996) have confirmed the effectiveness of this treatment. Katugampola et al. treated eight patients with chronic plaque psoriasis using the PDL at 8.5 J/cm^2 with a 5 mm spot, three times, over a 6-week period. Five of their eight patients recorded an improvement of >50 %, with one patient showing complete resolution. Zelickson et al. performed a clinical and histological evaluation of the PDL treatment of psoriasis in 36 patients. There was no difference in response when using either a 450 μs or 1,500 μs pulse duration. Mazer and Fayard (2003b) has looked at psoriatic plaques 1 year after PDL treatment. Of nine areas completely cleared after treatment, six remained clear up to 15 months after therapy.

It appears that PDL treatment can lead to improvement in psoriasis. Multiple treatments are often necessary and this technology may be inappropriate for widespread disease. Some patients with localized resistant plaque psoriasis

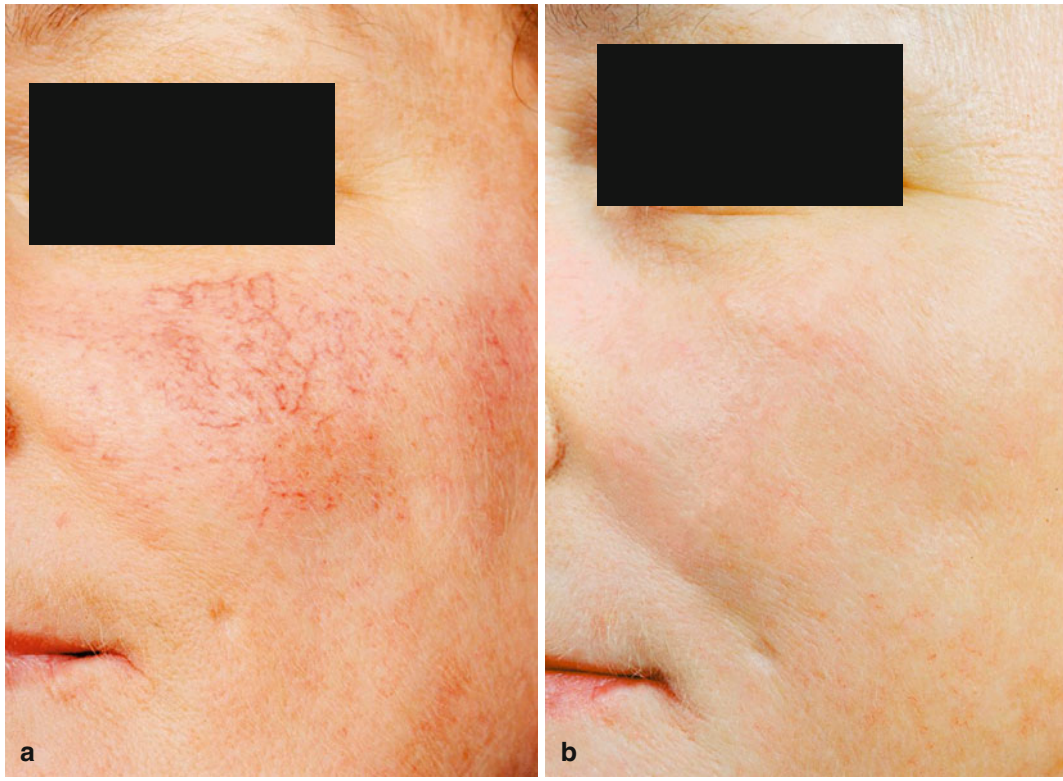

Fig. 2.10 (**a**) Facial telangiectasia pre-treatment. (**b**) Complete clearance after KTP laser treatment (Courtesy of Lasercare Clinics Ltd)

may benefit from this form of therapy. Recent research has explored the possibilities of treating nail psoriasis with this laser (Oram et al. 2010). High-intensity UVB including laser light sources will also improve psoriasis.

Further studies are required to determine the most appropriate use of this laser in the treatment of psoriasis.

Scars

PDL treatment is able to alter argon laser-induced scars, which are often erythematous and hypertrophic. By using optical profilometry measurements Alster's group (Alster and Williams 1995) demonstrated a trend toward more normal skin texture as well as reduction in observed erythema. This work was extended to the treatment of other erythematous and hypertrophic scars using objective measurements. They noted that clinical appearance (color and height), surface texture, skin pliability and pruritus could all be improved.

Alster's work has been confirmed by others (Dierickx et al. 1995; Goldman and Fitzpatrick 1995), who treated 15 patients with erythematous/hypertrophic scars and obtained an average improvement of 77 % after an average of 1.8 treatments. Goldman and Fitzpatrick also treated 48 patients with the PDL. Scars less than 1 year old responded better than those more than 1 year old. Facial scars also showed greater improvement. They noted an 88 % average improvement with total resolution in 20 % of scars after 4.4 treatments.

For persistent scars, combinations of intralesional corticosteroid injections, steroid impregnated tapes and laser therapy may be necessary. Two studies have compared the effects of pulsed dye laser treatment with other treatment modalities, particularly intralesional steroids. Alster (2003) compared pulsed dye laser treatment alone with laser therapy combined with intralesional corticosteroid treatment. Both treatment arms

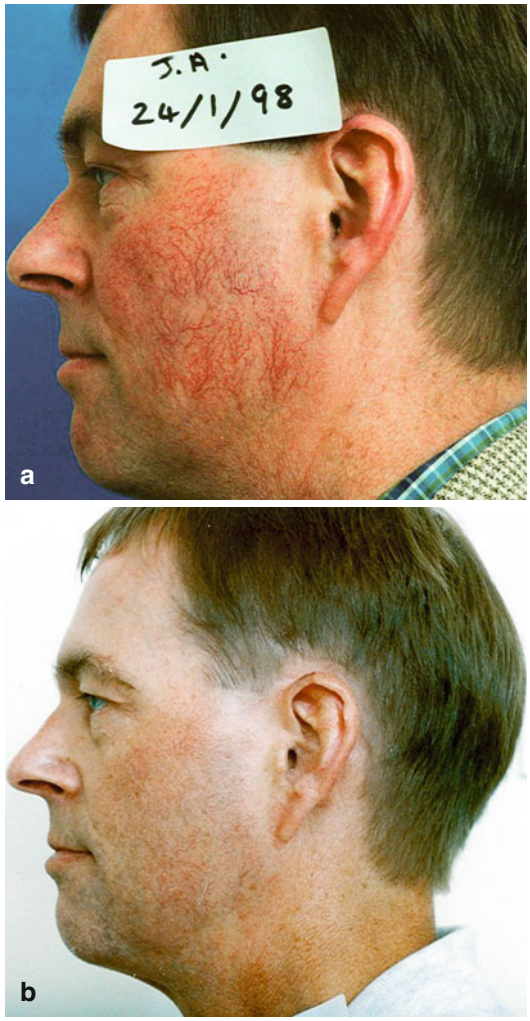

Fig. 2.11 (**a**) Steroid induced facial telangiectasia. (**b**) Post KTP laser treatment (Courtesy of Lasercare Clinics Ltd)

produced improvement in scars; there was no significant difference between the two treatments. Manuskiatti (Manuskiatti and Fitzpatrick 2002) compared scar treatment with intralesional corticosteroids alone, combined steroids and 5-fluorouracil, 5-fluorouracil alone, or pulsed dye laser treatment using fluences of 5 J/cm^2. All treatment areas were improved compared to baseline. The highest risk of adverse sequelae occurred in the corticosteroid intralesional group.

Other studies, however, have failed to demonstrate substantial effects of the pulsed dye laser on scars (Allison et al. 2003; Paquet et al. 2001; Wittenberg et al. 1999). Paquet assessed laser treated scars using remittance spectroscopy. Although a discrete decrease in redness of the scars was reported clinically, this was not confirmed by objective data. Wittenberg et al.., in a prospective single blind randomized controlled study, compared laser treatment with silicon gel sheeting and controls. Although there was an overall reduction in blood volume, flow and scar pruritis over time, there were no differences detected between the treatment and control groups. Allison et al., treating old and new scars with the pulsed dye laser, with fluences of 5–6 J/cm^2 were unable to demonstrate any statistical differences between treatment and control sites by photographic assessments or surface profile measurements. However, they did notice a significant improvement in scar pruritis in the laser treated group as compared to the control group.

There are now multiple studies assessing the effects of the pulsed dye laser in the treatment of scars. Although results are conflicting, particularly when controlled studies are performed, it would appear that in some cases laser therapy can be beneficial in the treatment of such scars. It is likely that vascular-induced erythema and pruritis are the two parameters that are most likely to significantly improve with this treatment.

Other lasers have also been used including scar ablation with Er:YAG and carbon dioxide laser and use of fractionated ablative and non ablative lasers. A systematic review of published research in this field was performed by Vrijman et al. (2011). The authors concluded that most evidence for effectiveness was found for the pulsed dye laser (PDL) 585 nm (eight studies), followed by the PDL 595 nm (two studies), whereas limited evidence (one trial per laser) was available for the fractional nonablative laser 1,540 nm, CO_2 laser 10,600 nm, low-level laser therapy, Nd:YAG laser 532 nm and Erbium:YAG laser 2,940 nm. The PDL 585 nm showed a low efficacy for the treatment of hypertrophic scars. With moderate efficacy, the PDL 595 nm is promising, although more research is necessary. Little evidence was found for the efficacy of other lasers.

Verrucae

Verrucae, although not truly vascular lesions, have been treated with lasers. The pulsed dye laser (PDL) may have potential benefits in the treatment of warts. The laser light can selectively obliterate blood vessels within the verrucae; it may also destroy the most rapidly replicating cells carrying the virus. The ability to focus the energy of the light directly on to the lesional vasculature minimizes injury to healthy skin. The PDL has been reported as successful for the treatment of resistant viral warts (Tan et al. 1993). In this study, 28 of 39 patients experienced resolution of the warts following an average of only 1.68 treatments with fluences of 6.5–7.5 J/cm^2. Warts need to be pared aggressively prior to treatment; higher fluences of 8.5–9.5 J/cm^2 are necessary.

Although the PDL has been reported to be effective in the treatment of plantar warts (Jain and Storwick 1997), these warts appear relatively resistant to the laser treatment. In another study (Huilgol et al. 1996), seven patients (six plantar, one periungual) with recalcitrant verrucae were treated. Although there was a partial response, none of their patients experienced complete resolution of their lesions. Others (Ross et al. 1999) treated 96 warts with only a 48 % complete clearance over an average of 3.4 treatments. A study using the KTP laser at 532 nm (Gooptu and James 1999) showed complete clearing of warts in 12 of 25 patients with resistant verrucae. Sethuraman et al. (2010) assessed the effectiveness of a pulsed dye laser in the treatment of recalcitrant warts in children. This was a retrospective notes review. Sixty-one children with recalcitrant warts were treated with PDL; 75 % of them had total clearance of warts after an average of 3.1 treatments.

Overall success rates were 100 % for both perineal and perianal and face-only warts, 93 % for hands, 69 % for plantar warts, 67 % when both face and extremities were involved, and 60 % when multiple extremities were involved.

There have been very few prospective randomized controlled trials comparing pulsed dye laser therapy with conventional therapy in the treatment of verrucae. In one study (Robson et al. 2000), 40 adult patients were randomized to receive either pulsed dye laser therapy (585 nm) or conventional therapy. Up to four treatments were provided at monthly intervals. One hundred and ninety four warts were evaluated. Complete response was seen in 70 % of the warts treated with conventional therapy and in 66 % of those in the pulsed dye laser group. Thus, there was no significant difference in the treatment responses. A systematic review of local treatments for cutaneous warts (Gibbs et al. 2002) found only limited evidence for the efficacy of the pulsed dye laser.

It should be noted that although pulsed dye laser treatment is widely used in the treatment of viral warts, there are no randomized controlled studies to demonstrate the superiority of this treatment over conventional methods. While undoubtedly effective in selected patients, it is important to note that is a significant spontaneous remission rate in viral warts. More studies with controlled trials are required.

Treatment of Other Cutaneous Vascular Lesions (Table 2.3)

Spider angiomas are easily, and successfully, treated with lasers and treatment with lasers. In addition, both the pulsed dye and KTP lasers have been shown to be safe and efficacious in children. The majority of spider angiomas will clear with one or two treatments without significant complications (Geronemus 1991).

Venous lakes, angiokeratomas, and cherry angiomas have all been reported to respond well to laser therapy. Tumorous outgrowths of vascular tissue such as pyogenic granulomas, nodular hemangiomas and kaposi's sarcoma are likely to have only a partial response owing to the limited depth of penetration of the emitted laser beam. These may respond better to the more deeply penetrating Nd:YAG laser

Areas of persistent erythema, as seen in patients with rosacea and post rhinoplasty, can be treated with the pulsed dye laser (Lowe et al. 1991; Clark et al. 2002) (Fig. 2.12). More treatments are required than for individual telangiectasias. Purpura can be a problem when the PDL is utilized. Purpura can be diminished by using PDL emitting longer pulse durations (Jasim et al. 2004).

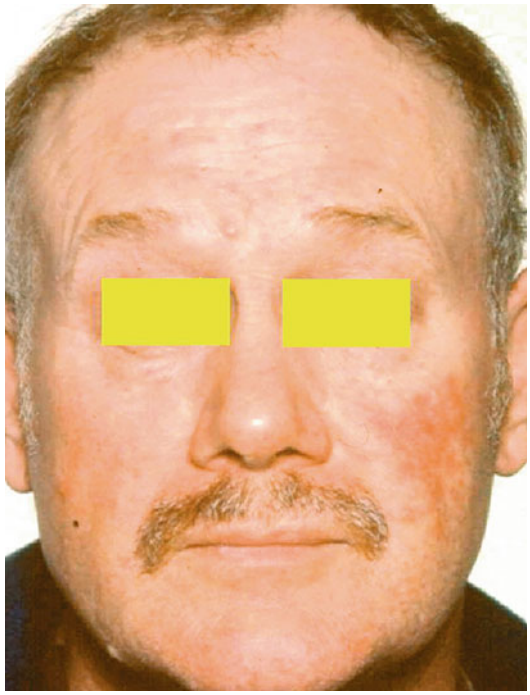

Fig. 2.12 Erythematous telangiectatic rosacea treated with pulsed dye laser (only right cheek treated)

In addition, the first one or two laser treatments often induces a rather spotty lightening on a background erythema, necessitating further treatment.

Matt telangiectasia seen in CREST syndrome can respond well to treatment (Fig. 2.13). Poikiloderma of Civatte, with its combination of pigmentation and telangiectasia seen on the lateral neck, can respond to pulsed dye laser therapy. Low fluences (approximately 4 J/cm^2) should be used because of the high incidence of post treatment hypopigmentation and possible scarring seen in this disorder (Geronemus 1990). Intense Pulsed Light sources can also be utilized. Rusciani et al. (2008) reported 7 years of experience treating this disorder. 175 patients with poikiloderma of Civatte of the neck and chest were treated with IPL at various settings. Clearance of more than 80 % of vascular and pigmented components of was observed. Minimal and transient side effects occurred in 5 % of the patients. No scarring or pigment disturbances were noted after the treatments. Telangiectasia

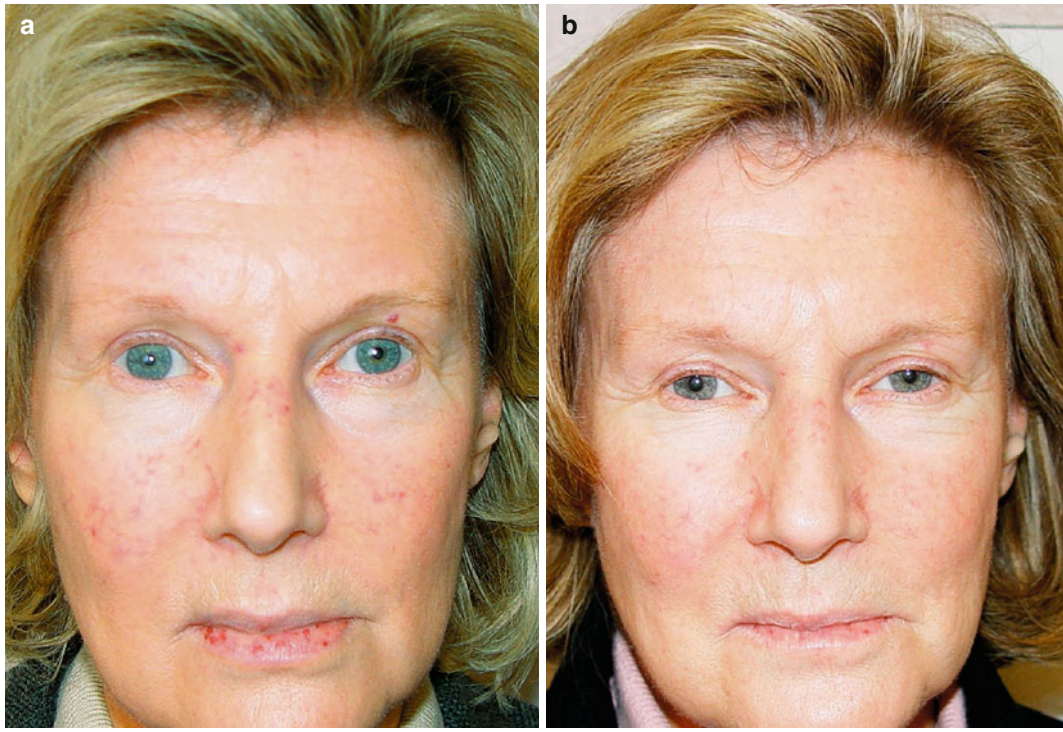

Fig. 2.13 (**a**) Mat telangiectasia in CREST syndrome. (**b**) After course of pulsed dye laser treatment

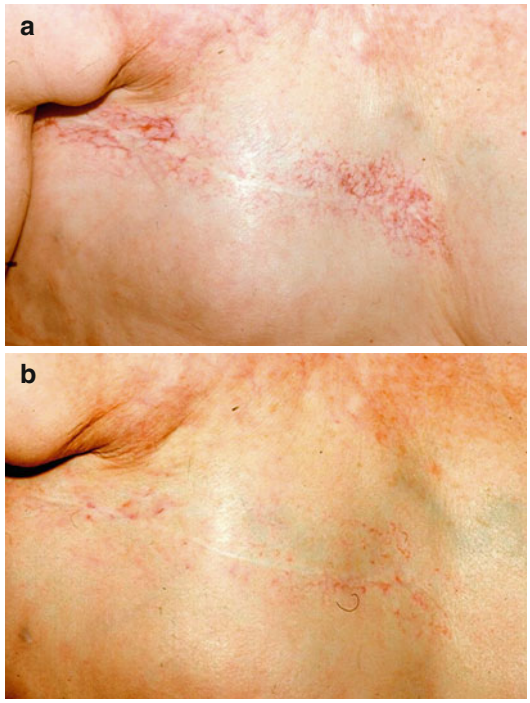

Fig. 2.14 (**a**) Post irradiation telangiectasia on chest wall. (**b**) Near total clearance after one pulsed dye laser treatment (From Lanigan and Joannides 2003)

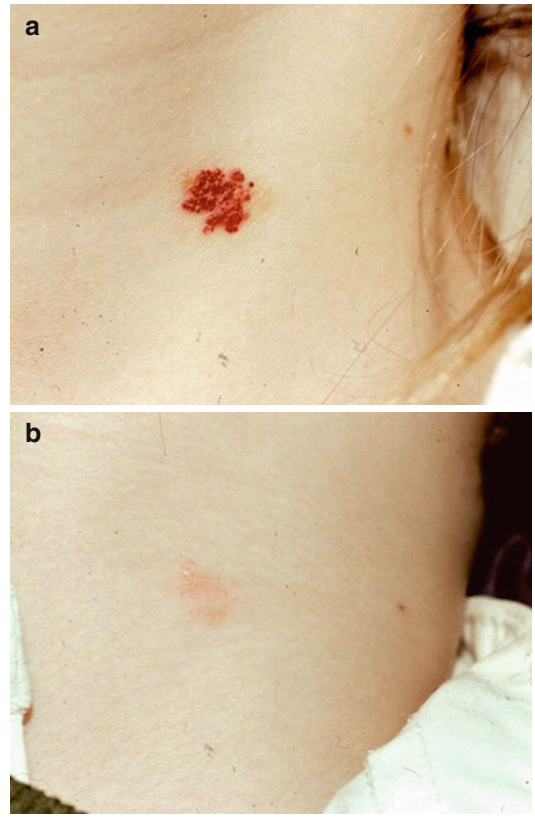

Fig. 2.15 (**a**) Lymphangioma on neck with prominent haemoglobin content. (**b**) Good clearance of redness after pulsed dye laser treatment (From Lanigan 2000b)

after radiotherapy is also easily treated (Lanigan and Joannides 2003) (Fig. 2.14).

Other lesions with a vascular component, such as angio-lymphoid hyperplasia, adenoma sebaceum, lymphangiomas (Fig. 2.15) and granuloma faciale, have all been reported as successfully treated with vascular lasers. The majority of reports of these disorders have been case studies rather than controlled trials. In adenoma sebaceum, if the angio fibromas do not have a prominent vascular component, then CO_2 laser vaporization should be considered.

Contraindications

There are very few, if any absolute contraindications, in the use of vascular specific lasers. There are a number of relative contraindications that the laser clinician should consider before embarking on treatment. The clinician should ascertain that the patient has realistic expectations from the laser treatment. In treating port wine stains only the minority of cases will completely clear, although the majority will substantially lighten. Patients with facial telangiectasia may develop a dysmorphophobia whereby the patient is significantly disturbed by what they perceive as abnormal disfiguring changes – which are not visible to the casual observer. In general, these patients do poorly with laser treatment.

Patients who have had previous treatments to their vascular lesion, including continuous wave lasers, radiation treatment and electro-desiccation, often have some degree of scarring and hypopigmentation. This may not be obvious until the overlying vasculature has been cleared. It is important to document such changes prior to treatment. In general, patients who have had prior treatment, which has resulted in scarring, do not respond as well to subsequent pulsed dye laser therapy.

Patients taking aspirin, nonsteroidal anti-inflammatories and anticoagulants will show more PDL induced purpura. There have been reports of PDL-induced hypertrophic scarring in patients who have recently taken isotretinoin. A true cause and effect relationship has yet to be proven.

Although laser treatment in itself is inherently safe in pregnancy, the treatment does cause pain and can be distressing. It most situations, laser may be best deferred until after delivery.

Consent

An example of a suitable consent form for vascular laser treatment is shown in Fig. 2.16.

Personal Laser Technique

Facial Telangiectasia

It is extremely important when assessing patients for treatment of their facial telangiectasia that they are made fully aware of the available procedures and the likely outcomes and side effects. In general, patients with small fine relatively superficial telangiectasia can be treated with most available lasers. Most patients will prefer the KTP laser because of the reduced associated purpura. Also, when treating extensive areas where there is significant background erythema, the pulsed dye laser is likely to produce a superior result. Generally, I perform a test patch in this group of patients.

When using the pulsed dye laser, although it may be possible to clear the problem without purpura, it is my experience that such an approach generally requires multiple treatments. I attempt to produce vessel damage with fluences as close to the purpura threshold as possible. Most patients do not require local anesthesia for this procedure. A disadvantage of topical anesthetics is the vasoconstriction that occurs, which may make it difficult to see all the vessels. The combination of concurrent epidermal cooling and longer pulse durations will reduce the PDL induced purpura. Patients should avoid traumatizing the area after treatment and use potent sunscreens. Treatments are generally repeated at 4–6 weeks intervals until vessel clearance has occurred. In general, most patients need between two and four treatments.

When using the KTP laser, the object is to heat seal the vessels under direct observation. This treatment requires more skill and training than when using the pulsed dye laser. The target vessel is traced with the laser beam using relatively small spot sizes and repetition rates of 3–8 Hz. This procedure is made easier using illuminated magnification. The aim is to see disappearance of the vessel without obvious epidermal changes particularly white lines. A few small test areas are performed altering the fluence, pulse width or repetition rate to achieve this. Starting parameters could be 6–12 J/cm^2, 3–6 ms with a 1 or 2 mm beam diameter. It may be helpful to use concurrent cooling during the procedure. Immediately afterwards the patients will experience quite marked reactive erythema. This can be reduced with cool dressings and topical aloe vera. The erythema usually clears within 24 h, but some crusting may occur. Large areas of crusting, blistering or erosion suggest that treatment has been too aggressive.

For larger perinasal vessels, the Nd:YAG laser alone or combined with a pulsed dye laser may be preferred. Great care is needed with this laser to avoid excessive thermal damage. Concurrent cooling is essential and shots should not be overlapped.

Port Wine Stains

Pre-treatment assessment of the patient should include a record of previous treatment and its effects. Argon laser treatment in particular can produce frequent pigmentary disturbances especially hypopigmentation which may not be obvious in a partially treated PWS. It will become very obvious after successful PDL therapy. Scarring from previous treatment should be recorded. The patient should be advised not to expose their skin to sunlight, as a tan overlying the PWS will interfere with therapy. Good quality

AGREEMENT/CONSENT FOR VASCULAR LASER TREATMENT

This agreement is between …… Clinics and Doctor/Nurse ……

and (Mr, Mrs, Miss, Ms) ……
(Full name of patient) hereafter known as the patient.

1. Please read this form and the notes very carefully.
2. If there is anything you do not understand about the explanation, or if you want more information, please ask the clinician.
3. Please check that all the information on the form is correct. If it is, and you feel happy with all the explanations given please sign the form.

I the patient understand:

1. The efficacy of the treatment with lasers varies from individual to individual and I understand that a small percentage of patients may fail to respond to treatment and I as an individual may not respond.
2. The treatment that I receive will be appropriate for my specific needs and will be given by an appropriately trained member of the clinic.
3. I understand I must give staff all the relevant medical details prior to treatment.
4. A test patch may be necessary before commencing treatment with lasers.
5. Following treatment the skin will be red, and if the Pulsed Dye laser has been used there will be bruising. Swelling, blistering or crusting can occur and may take several days to resolve, the bruising will take longer (as with any normal bruise).
6. Following treatment you will be given an aftercare sheet, which you should follow. Treated areas should not be picked, scratched or traumatised and should be kept well moisturised.
7. Following treatment there may be hypopigmentation or hyperpigmentation (marked lightening or darkening of the skin). While these reactions are not common there is a possibility that they can occur. However, in time, these will usually fade away, although hypopigmentation may be permanent, I have been advised to use a total sunblock cream. I understand that following my course of treatment I must wear sunblock for a minimum of six weeks to avoid possible post-inflammatory hyperpigmentation.
8. There is a 1-5% risk of scarring with laser treatment of this kind.
9. I understand that photographs will be taken before and during my treatment and that these photographs remain the property of the clinic although I may have access to them at any time.
10. **I understand that it is my responsibility prior to each treatment undertaken that I inform the doctor or nurse of any changes in medical status, including medication or herbal remedies I am taking.**
11. I understand that if I have a suntan I may not be offered treatment; during treatment I have been advised not to use sunbeds.

The patient acknowledges that he/she has read and fully understood this agreement before signing it and has also read and understood any information sheets that they have been given.

I understand and agree to …… terms of business and understand that I can request an additional copy of these terms at any time.

Patient's signature.....

Fig. 2.16 Consent form for vascular laser treatment

standardised color photographs should be taken at baseline and throughout the treatment course. It is useful to show the patients a portfolio of photographs to illustrate the procedure, in particular the bruising that will occur after treatment.

The fluence to be used can be determined by performing a test treatment over a range of fluences and reviewing the patients 6–8 weeks later. The lowest fluence producing lightening of the PWS can be used. As a general rule, with a 10 or 7 mm spot, fluences are in the range of 4.5–8 J/cm^2. The

lower range of fluences should be used in both the pediatric patient and more sensitive anatomic areas. As treatment progresses with lightening of the PWS it is reasonable to cautiously increase the fluence by 0.25–0.5 J/cm^2 to maintain improvement. It has been shown however that not all PWS will clear with PDL treatment. Repeatedly increasing the fluence in the non-responding PWS will unfortunately increase the likelihood of an adverse reaction, such as scarring.

PDL treatment causes discomfort or pain to the patient described as a sharp stinging sensation similar to being flicked with an elastic band. This stinging is replaced immediately by a hot pruritic sensation. Some individuals appear to be able to tolerate large treatments without distress, but this should not be assumed. Two percent of patients surveyed described severe pain after treatment despite attempts at adequate analgesia (Lanigan 1995).

Topical anesthetic agents can assist patients. A eutectic mixture of local anaesthetic (EMLA^R) cream containing lidnocaine 2.5 % and prilocaine 2.5 % has been shown effective in reducing PDL-induced pain (Lanigan and Cotterill 1987). The cream must be applied thickly under occlusion to the PWS for 90 min to 4 h before treatment. It is not indicated for children under 1 year. An alternative to EMLA^R is Ametop^R, a 4 % amethocaine gel which has the advantage of a more rapid onset of action of 30–45 min (Armstrong et al. 1996). It also should be applied under occlusion and is not recommended in infants under 1 month. There are concerns of excessive absorption of Ametop^R from highly vascular surfaces. Large areas should not be treated with this drug. Skin irritation and allergic rashes can occur from these creams. Despite correct techniques, sensitive areas of the face, especially the upper lip and peri-orbital areas, may not be adequately anesthetized with topical creams. Additional infiltrational and nerve block anesthesia can be used to supplement the topical agents; unfortunately this in itself can be traumatic for the patient. The use of vacuum suction at the time of the laser impulse may ameliorate the pain (Lanigan 2009).

In children, these topical anesthetic techniques are often not enough. In my experience the majority will require general anesthesia (Rabinowitz and Esterly 1992). Some authors advocate sedation in combination with other anesthetic techniques without general anesthesia. The procedure can cause anxiety in children as well as discomfort, as their eyes are covered while the laser emits noises as well as light during the treatment. After the test treatment, each further laser procedure involves placement of laser impacts over the whole PWS using the lowest fluence to achieve lightening. This needs to be reduced over the eyelids, upper lip and neck. Each impact of the laser produces a visible purpuric discoloration, which appears either immediately or within minutes. This is a sharply demarcated circle, which allows the operator to place the next spot adjacent to it. For pulsed dye lasers with gaussian beam profiles, spots should be overlapped by approximately 10 %. This will reduce the tendency in some patients to a spotty appearance as the PWS clears. Other PDLs may have different beam profiles and a decision on whether to overlap spots can only be made on the basis of knowledge of the beam energy profile.

After treatment the PWS most patients will note purpura for seven to fourteen days. A minority will have purpura up to 28 days. Small areas may crust or weep, but large areas of blistering suggest reduction of the fluence at the next treatment. The greatest reaction after treatment occurs early in the course of therapy or after increasing the fluence. After each treatment the PWS should be lighter in appearance. Treatments are repeated at an interval of about 8 weeks. Gradually, through a course of treatment the lightening after each treatment gets less until no further progress between visits can be seen. The majority of patients who experienced satisfactory lightening of their PWS do so in their first four to ten treatments. Although improvements can occur beyond 20 treatments, the small benefits should be balanced against the morbidity produced by treatment (Kauvar and Geronemus 1995).

Post-operative Care and Complications

There is minimal post-operative care required after treatment with today's vascular lasers. In most cases, the epidermis will be intact but in a

significant minority there will be some blistering. The first consideration after treatment is to deal with discomfort. This pain can be lessened by cooling the skin either with refrigerated air blowing, cold compresses, spraying with water or aloe vera. With the pulsed dye laser this cooling can be repeated until pain and discomfort has eased. The area can then be kept moisturized with an emollient. If treatment has been performed close to or around the eye, there will be a risk of periocular edema. Patients should be instructed to sleep with an extra pillow to encourage gravitational removal of leaked edema fluid. The area can be washed gently with soap and water. No make-up can be applied until after any crusting has settled.

With the KTP laser and other continuous wave lasers, there may be some blistering and crusting. The operator may consider use of topical antibiotics. There is little evidence to suggest this is required. Patients can also be instructed to take analgesia as needed. All patients should be instructed on the absolute importance of not picking or scratching at treated areas. They will also need to use a total sunblock preparation to lessen post-inflammatory hyperpigmentation. Inability to comply with this will significantly reduce the effectiveness of the procedure.

All persistent side effects are generally due to pigmentary changes and/or scarring. Post inflammatory hyperpigmentation is the commonest side effect and occurs in 10 and 27 %. (Seukeran et al. 1997; Fiskerstrand et al. 1998) of treated patients. Hyperpigmentation is most common in treated port wine stains on the leg and is reversible. Hypopigmentation occurs in up to 2.6 % of patients (Boixeda et al. 1997) and generally occupies only a small area of the treated lesion. Atrophic scarring occurs in 1–5 %; hypertrophic scarring in less than 1 % of pulsed dye laser treated patients. Atrophic textural changes often improve spontaneously over 6–12 months.

Rarer side effects occasionally reported include atrophie blanche – like scarring (Sommer and Sheehan-Dare 1999), dermatitis (Shahidullah and Frieden 1999) and keloid formation during Isotretinoin therapy (Bernestein and Geronemus 1997).

Even when using long pulsed dye lasers, to lessen purpura, significant facial edema can develop. Alam (Alam et al. 2003) reported postoperative edema in 87 % of 15 patients with purpuric free laser parameters. This included 27 % of patients with symptomatic eye swelling.

The KTP laser, which has longer pulse durations and a wavelength which is also absorbed by melanin, has a higher incidence of mild side effects due to epidermal injury. These may be pain, redness, vesiculation and crusting. These side effects are transient and in the treatment of facial telangiectasia are not generally associated with long-term problems. There is a risk of atrophic scarring with this laser. This will occur more commonly when treating para-nasal areas, as these vessels frequently require more aggressive treatment parameters. Concurrent epidermal cooling will significantly reduce the incidence of side effects after treatment with this laser.

Results

Laser treatment of cutaneous vascular disorders is satisfying and rewarding. Treatment of this kind extends back 30 years and there has been a continual improvement in technology and understanding of laser tissue interactions. The majority of patients receiving laser treatment to vascular disorders such as facial telangiectasia, spider naevi and rosacea can expect excellent results with a very low risk of adverse events. For safe, effective treatment, a course of treatments should be planned but it is possible to achieve excellent eradication of the problem. For port wine stains, although the majority of patients will experience significant lightening after a course of treatment, only a minority (around 10 %) can expect complete clearance. There is consensus opinion that a number of other conditions such as viral warts and psoriasis can also improve, the evidence based on randomized double blinded trials is lacking.

The Future

Significant advances have been made in recent years in the technological development of lasers that can target cutaneous vascular disorders by selective photothermolysis. However, results in port wine stains in particular can still be disappointing.

A number of investigators are pursuing a greater understanding of the vascular responses of PWS to lasers through non-invasive imaging and mathematical modeling. The eventual goal is to tailor laser therapy to individual PWS characteristics by altering both laser type and parameter settings. For example, some (Viator et al. 2003) have designed a photoacoustic probe which allows in vivo determination of PWS depth. Others (Sivarajan and and Mackay 2002) have demonstrated that videomicroscopy can be used to assess treatment response in relation to vessel depth. Still other (Nelson et al. 2001) have used optical Doppler tomography to perform real-time imaging of blood flow within PWS. Partial restoration of blood flow occurring immediately or shortly after laser exposure was indicative of reperfusion due to inadequate vessel injury. By using this imaging method, they proposed that PWS could be retreated with higher fluences in a stepwise manner, until a permanent reduction in blood flow occurs. This would be indicative of irreversible vessel damage and expected clinical lightening.

There has been great interest in the healing response after pulsed dye laser treatment of PWS. The repair process includes neovascularisation which will reduce the effectiveness of the treatment. Work from Stuart Nelson's group (Jia et al. 2010; Nelson et al. 2011) has led to promising research combining pulsed dye laser and angiogenesis inhibitors such as rapamycin to enhance treatment response. Shorter treatment intervals may be beneficial for similar reasons (Tomson et al. 2006).

Despite the recent advances made, it remains difficult to fully eradicate PWS with our current armamentarium of lasers and non-coherent light sources. Alternative therapies including photodynamic therapy are being considered (Xiao et al. 2011).

The considerable work in this field reinforces the notion that PWS display considerable clinical and histological heterogeneity. This is likely to mean that a number of approaches will be needed to optimize treatment of PWS. There is a clear need for further trials, particularly to establish the role of non-coherent light sources and lasers, other than the PDL. To ensure comparability of future studies, common objective clinical outcome measures need to be employed, together with, where possible, non-invasive imaging techniques which can increase our understanding of laser–port wine stain interactions. However, we should also recognize the importance of incorporating measures of patient satisfaction into study design, since after all it is patients' own assessments which ultimately reflect treatment outcomes (Currie and Monk 2000; Lanigan 2000a).

In recent years, one of the most innovative devices to be developed was the fractionated laser. A wide choice of these devices are now available with both ablative and non ablative wavelengths. These devices are used mainly to treat wrinkles, rhytides, furrows, fine lines, textural irregularities such as acne scarring and pigmented lesions. The role of these lasers in treating vascular dyschromias is still being explored but shows some promise (Bogdan Allemann and Kaufman 2010).

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Laser Treatment of Pigmented Lesions

3

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Core Messages

- Accurate diagnosis of pigmented lesions is mandatory before laser treatment. For some pigmented lesions, laser treatment may even be the only treatment option.
- Tattoos respond well to Q-switched lasers.
- Amateur and traumatic tattoos respond more readily to treatment than do professional tattoos.
- Cosmetic tattoos should be approached with caution.
- Treatment of melanocytic nevi remains controversial, but worth pursuing.

History

Selective Photothermolysis

The idea of treating cutaneous pigmented lesions with lasers was first tested in the early 1960s by Goldman, who used a normal mode ruby laser (Goldberg and Stampien 1995). His research indicated that the target was the melanosome. Unfortunately, due to laboratory difficulties, further research was halted.

In the past 15 years, selective photothermolysis has largely transformed dermatologic laser surgery. The term *selective photothermolysis* describes site-specific, thermally mediated injury of microscopic tissue targets by selectively absorbed pulses of radiation. Three basic elements are necessary to achieve selective photothermolysis: (1) a wavelength that reaches and is preferentially absorbed by the desired target structures; (2) an exposure duration less than or equal to the time necessary for cooling of the target structures; and (3) sufficient fluence to reach a damaging temperature in the targets. When these criteria are met, selective injury occurs in thousands of microscopic targets, without the need to aim the laser at each one.

At wavelengths that are preferentially absorbed by chromophoric structures such as melanin-containing cells or tattoo-ink particles, heat is created in these targets. As soon as heat is created, however, it begins to dissipate by conduction. The most selective target heating is achieved when the energy is deposited at a rate faster than the rate for cooling of the target structures. In contrast to diffuse coagulation injury, selective photothermolysis can achieve high temperatures at structures or individual cells with little risk of scarring because gross dermal heating is minimized.

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Pigmented Lesion Removal by Selective Photothermolysis

Because melanin absorbs light at a wide range of wavelengths – from 250 to 1,200 nm, several lasers or intense pulsed light sources can effectively treat pigmented lesions. For tattoos, light absorption depends on the ink color, but the predominant color (blue-black) also absorbs well throughout the 532–1,064 nm range. Almost any laser with sufficient power can be used to remove benign pigmented lesions of the epidermis. The selective rupture of skin melanosomes was first noted by electron microscopy in 1983, after 351 nm, sub-microsecond excimer laser pulses of only about 1 J/cm^2. At fluences damaging melanocytes and pigmented keratinocytes, epidermal Langerhans cells apparently escape injury.

With regard to wavelength, absorption by melanin extends from the deep UV through visible and well into the near-IR spectrum. Across this broad spectrum, optical penetration into skin increases from several micrometers to several millimeters. One would therefore expect melanosomes and the pigmented cells containing them to be affected at different depths across this broad spectrum.

A variety of thermally mediated damage mechanisms are possible in selective photothermolysis, including thermal denaturation, mechanical damage from rapid thermal expansion or phase changes (cavitation), and pyrolysis (changes in primary chemical structure). Mechanical damage plays an important role in selective photothermolysis with high-energy, submicrosecond lasers for tattoo and pigmented lesion removal. The rate of local heating and rapid material expansion can be so severe that structures are torn apart by shock waves, cavitation, or rapid thermal expansion.

Grossly, the immediate effect of submicrosecond near-UV, visible, or near-IR laser pulses in pigmented skin is immediate whitening. This response correlates very well with the melanosome rupture seen by electron microscopy and is therefore presumably a direct consequence of melanosome rupture. A nearly identical but deeper whitening occurs with Q-switched laser exposure of tattoos, which like melanosomes consist of insoluble, submicrometer intracellular pigments. Although the exact cause of immediate whitening is unknown, it is almost certainly related to the formation of gas bubbles that intensely scatter light. Over several to tens of minutes, these bubbles dissolve, causing the skin color to return to normal or nearly normal. In addition, pyrolysis may occur at the extreme temperatures reached within melanosomes or tattoo ink particles, directly releasing gases locally. Regardless of its cause, immediate whitening offers a clinically useful immediate endpoint that apparently relates directly to melanosome or tattoo ink rupture (Fig. 3.1).

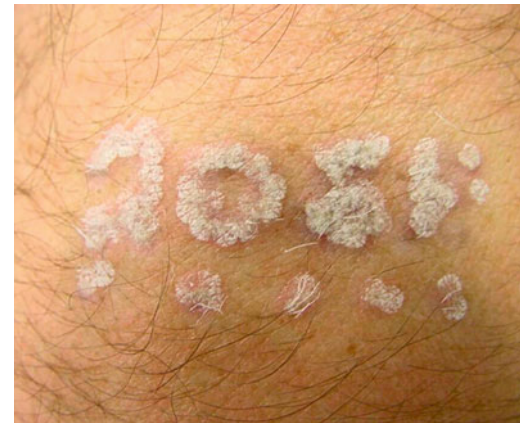

Fig. 3.1 Immediate whitening after laser treatment

Melanin in both the epidermis (as in cafe-au-lait macules and lentigines) and the dermis (as in nevus of Ota), as well as dermal tattoo particles, is an important target chromophore for laser selective photothermolysis. Clinically, selective photothermolysis is highly useful for epidermal and dermal lesions in which cellular pigmentation itself is a cause. These include lentigines, cafe-au-lait macules (which display a high rate of recurrence), Nevus spilus, Becker nevi, blue nevi, and nevus of Ota. However, selective thermolysis has only been variably effective for dermal melasma, postinflammatory hyperpigmentation, or drug-induced hyperpigmentation.

Currently Available Technology

Lasers and Intense Pulsed Light Sources Used to Treat Pigmented Lesions and Tattoos (Tables 3.1, 3.2, and 3.3)

Continuous-Wave Lasers (CW Lasers)

Although Q-switched lasers are now the modality of choice for most pigmented lesions, continuous-wave and quasi-continuous lasers, when used properly, can also be effective. The lasers include the CW argon laser (488 and 514 nm), a CW dye laser (577 and 585 nm), a CW krypton (521–530 nm), a quasi-CW copper vapor laser (510 and 578 nm), an erbium (2,940 nm), and CO_2 (10,600 nm) laser.

The CW and quasi-CW visible light lasers can be used to selectively remove pigmented lesions. However, because of the shorter wavelengths of these lasers, they penetrate only superficially. Thus, they are effective only for epidermal pigmented lesions. Furthermore, in the absence of reproducible spatial thermal injury confinement, the risk of scarring and pigmentary changes is significant in the hands of inexperienced operators.

The pigment non-selective erbium and CO_2 lasers can be used to remove epidermal pigment effectively because of the ability to target H_2O in the epidermis. The non-specific thermal damage leads to destruction of the lesion with denuding of the epidermis. Pigment is thus damaged as a secondary event. This destruction is followed by healing that may have some erythema and possible pigmentary and textural changes.

Q-Switched Lasers

The fundamental principle behind laser treatment of cutaneous pigment and tattoos is selective destruction of undesired pigment with minimal collateral damage. This destruction is achieved by the delivery of energy at the absorptive wavelength of the selected chromophore. The exposure time must also be limited so that the heat generated by the laser–tissue interaction is confined to the target.

The target chromophore of pigmented lesions is the melanosome and that of tattoos is the insoluble, submicrometer intracellular pigments. Q-switched lasers produce pulses in the nanosecond range. These high peak power lasers deliver light with a pulse width shorter than the approximately 1-μs thermal relaxation time of the melanosomes or the tattoo ink particles. Various Q-switched lasers (532 nm frequency-doubled Q-switched Nd-YAG laser, 694 nm ruby, 755 nm Alexandrite, 1,064 nm Nd-YAG) are therefore used for the treatment of various epidermal, dermal, mixed epidermal and dermal pigmented lesions and tattoos (Table 3.2).

To date, Q-switched lasers have been shown to treat both epidermal and dermal pigmented lesions effectively in a safe, reproducible fashion. Q-switched lasers used for the treatment of superficial pigmented lesions include the 532 nm frequency-doubled Q-switched Nd-YAG laser, the 694 nm ruby and the 755 nm alexandrite lasers. Strong absorption of light at these wavelengths by melanin make these lasers an excellent treatment modality for superficial pigmented lesions. The Q-switched 694 nm ruby, 755 nm Alexandrite lasers and 1,064 nm Nd-YAG lasers are useful for treating deeper pigmented lesions such as nevus of Ota and tattoos. The Q-switched 1,064 nm should be used when treating patients with darker skin, because it reduces the risk of epidermal injury and pigmentary alteration.

Pulsed-Dye Laser

The short wavelength (510 nm) and 300 ns pigment lesion dye laser (PLDL) is highly effective in the treatment of superficial pigmented lesions and red tattoos, but is no longer commercially available.

Long-Pulsed Lasers

To target large, pigmented lesions, such are hair follicles or nevocellular nevi, lasers with longer (millisecond-range) pulse durations are more suitable (Table 3.1). These include the long-pulsed 694 nm ruby, 755 nm alexandrite, 810 nm diode and 1,064 nm Nd-YAG lasers. The millisecond pulse width more closely matches the thermal relaxation time of the hair follicles or the nested melanocytes. Collateral thermal damage provides an injury to the stem cells

Table 3.1 Long pulse lasers for treatment of pigmented lesions

Light source	Wavelength (nm)	System name	Pulse duration (ms)	Fluence (J/cm^2)	Spot size (mm)	Repetition rate (Hz)	Other features
Long pulse ruby	694	E2000 (Palomar)	3, 100	10–40	10, 20	1	Cooling handpiece 0–10 °C Fiber delivery Photon recycling
		Epitouch Ruby (Sharplan)	1.2	10–40	3–6	1.2	Triple pulse technology
		Ruby Star (Aesclepion-Meditec)	4	Up to 35	Up to 14	1	Dual mode: may also be Q-switched
		Sinon (Wavelight)	4	Up to 30	5, 7, 9	0.5–2	Cold air unit May also be Q-switched
Long pulse Alexandrite	755	Apogee (Cynosure)	0.5–300	25–50	5, 10, 12, 15	3	Cold air or integrated cooling
		Gentlelase (Candela)	3	10–100	6, 8, 10, 12, 15, 18	Up to 1.5	Dynamic cooling device
		Epitouch ALEX (Sharplan)*	2–40	Up to 50	5, 7, 10	1	Scanner option
		Ultrawave II/III (Adept Medical)	5–50	5–55	8, 10, 12	1–2	Available with 532 nm and/or 1,064 nm Nd:YAG
		Epicare (Light Age)	3–300	25–40	7, 9, 12, 15	1–3	
		Arion (WaveLight)	1–50	Up to 40	6, 8, 10, 12, 14	Up to 5	Cold air unit
Diode laser	800	LightSheer (Lumenis)	5–400	10–100	9X9, 12x12	Up to 2	Cooling handpiece
		Apex-800 (Iridex)	5–100	5–60 (600 W)	7, 9, 11	Up to 4	Cooling handpiece
		SLP1000™ (Palomar)	5–1,000	Up to 575 J	12	Up to 3	SheerCool™ triple contact cooling, photon recycling
		MedioStar (Aesclepion-Meditec)	50	Up to 64	10, 12, 14	Up to 4	
		F1 Diode Laser (Opusmed)	15–40	10–40 J	5, 7	4	

Long-pulsed Nd:YAG	1,064	CoolGlide (Cutera)	0.1–300	Up to 300	3, 5, 7, 10	Up to 2	Contact pre-cooling
		Lyra (Laserscope)	20–100	5–900	10		Contact cooling Photonrecycling
		Ultrawave I/II/III (Adept Medical)	5–100	5–500	2, 4, 6, 8, 10, 12	1–2	Available with 532 nm Nd:YAG and/or 755 nm Alexandrite
		Gentle Yag (Candela)	0.25–300	Up to 600	1.5, 3, 6, 8, 10, 12, 15, 18	Up to 10	Cryogen spray optional
		VARIA (CoolTouch)	300–500	Up to 500	3–10		Pulsed cryogen cooling with thermal quenching
		Acclaim 7000 (Cynosure)	0.4–300	300	3, 5, 7, 10, 12	5	Cold air or integrated cooling
		Smartepil II (Cynosure)	Up to 100	16–200	2.5, 4, 5, 7, 10	6	Smart cool Scanner
		Dualis (Fotona)	5–200	Up to 600	2–10		
		Vasculight Elite (Lumenis)	2–16	70–150 J	6	0.33	Combined with IPL
		Profile (Sciton)	0.1–200	Up to 400			
		Mydon (WaveLight)	5–90	10–450	1.5, 3, 5, 7, 10	1–10	Contact or air cooling

Table 3.2 Q-switched lasers for treatment of pigmented lesions and tattoos

Light source	Wavelength (nm)	System name	Pulse duration (ns)	Fluence (J/cm^2)	Spot size (mm)	Repetition rate (Hz)	Other features
Q-Switched ruby	694	Sinon (Wavelight)	20	Up to 15	3, 4, 5	0.5–2	Cold air unit (optional) Also long pulse
		Spectrum RD-1200 (Palomar)	28	3–10 J	5, 6, 5	0.8	
		Ruby Star (Aesclepion-Meditec)	30	Up to 10	Up to 5	1	Dual mode: may also be Q-switched
Q-Switched Alexandrite	755	Accolade (Cynosure)	60	7–30 J	2.4, 3, 5	Up to 5	
		Ta2 Eraser (Light Age)	60	7.5 J	4	8–10	
		Alexlazr (Candela)	50	Up to 12	2, 3, 4	Up to 5	
Q-Switched Nd:YAG	532/1,064	Softlight (Thermolase)	12–18	2.5–3	7	Up to 10	Only 1,064 nm
		MedLite C6 (HOYA/ConBio)	<20	Up to 12	3, 4, 6, 8	Up to 10	532 and 1,064 nm
		Q-Clear (Light Age)		2–12	2, 3, 4	1–6	532 and 1,064 nm
		Q-YAG 5™ (Palomar)	3	Up to 12.5	2, 4, 6	Up to 10	532 and 1,064 nm

Table 3.3 Intense pulsed light sources treatment of pigmented lesions

Light source	System name	Spectrum (nm)	Optical filter for pigment (nm)	Pulse duration (ms)	Pulse delay (ms)	Fluence (J/cm^2)	Spot size (mm)	Special features
IPL	Ellipse Flex (DDD, Horsholm, Denmark)	400–950	555–950	2×2.5	10	8–10	10×48	Dual mode filtering technique
IPL	Quantum SR (Lumenis)	560–1,200		6–26	5–60	15–45	8×34	
IPL	Prolite (Alderm, Irvine, CA)	550–900	550–900	2	2	10–50	10×20 20×25	FLP (Fluorescent Pulsed Light
IPL	PhotoLight (Cynosure Chelmsford, MA)	400–1,200	550–1,200	5–50		3–16	46×18	Xenon pulsed lamp
IPL	Quadra Q4 (Derma Med USA)	510–1,200		48		10–20	33×15	Quad Pulsed Light System
IPL	SkinStation (Radiancy, Orangeburg, NY)	400–1,200		35		4–7	35×12	Light Heat Energy (LHE)
IPL	SpectraPulse (Primary Technology, Tampa, FL)	510–1,200		3×12	4 and 5 Resp	10–20	15×33	Light Energy Recycling (LER)
IPL+Nd-YAG	VascuLight Elite (Lumenis)	515–1,200		0.5–25		3–90	35×8	Contact cooling/ combined with 1,064
IPL+Nd-YAG	StarLux (Palomar)	400–1,200	LUX-G: 500–670 and 870–1,200 LUX-Y: 525–1,200 LuxR: 650–1,200 LuxRs: 650–1,200	LuxG: 0.5–500 LuxY: 1–500 LuxR: 5–500 LuxRs: 5 –500		LuxG: Up to 50 LuxY: Up to 35 LuxR: Up to 30 LuxRs:Up to 50	LuxG:12×12 LuxY:16×46 LuxR:16×46 LuxR:12×28	Lux 1,064
IPL+Nd-YAG	Xeo (Cutera)	600–850	600–850			5–20		
IPL+BIPOLAR RF	Aurora SR (Yokneam Illit, Syneron)	580–980	580–980			Light energy, 10–30 RF energy, 5–20	12×25	

located in the outer rooth sheeth or the melanocytes adjacent to the target area that may actually not contain melanin. However, it is unlikely that every nevus cell is destroyed. Cautious follow-up of nevi treated with laser light is necessary.

Intense Pulsed Light Sources

Intense pulsed light (IPL) systems are high-intensity light sources, which emit polychromatic light (Table 3.3). Unlike lasers, these flashlamps work with non-coherent light over a broad wavelength spectrum of 515–1,200 nm. Because of the wide spectrum of potential combinations of wavelengths, pulse durations, pulse intervals and fluences, IPLs have proven to very efficiently treat photodamaged pigmented lesions like solar lentignes and generalized dyschromia.

Indications

There are many types of pigmented lesions. Each varies in the amount, depth and density of melanin or tattoo ink distribution. The approach to the treatment of cutaneous pigmentation depends on the location of the pigment (epidermal, dermal or mixed), the way it is packaged (intracellular, extracellular) and the nature of the pigment (melanin or tattoo particles). Among the benign pigmented lesions which do respond well to laser treatment are lentignes, ephelides (freckles), nevus of Ota, nevus of Ito, and "blue" nevus. Varying results are obtained in café au lait-maculae, nevus spilus and nevus of Becker. Treatment of congenital and acquired nevi is still controversial because of the risk of incomplete destruction of deeper situated nevus cells. Hyperpigmentation, like melasma and post-inflammatory hyperpigmentation, only shows a moderate response. Finally, laser treatment in itself can result in post-inflammatory hyperpigmentation.

Epidermal Pigmented Lesions

In general, epidermal pigment is easier to eradicate than dermal pigment because of its proximity to the skin's surface. Several lasers can effectively treat epidermal lesions. These include the Q-switched laser systems, pulsed visible light lasers and flashlamps, CW lasers and CO_2 or erbium lasers. The goal is to remove unwanted epidermal pigmentation and as long as the injury is above the dermal-epidermal junction, it will heal without scarring.

Lentigo Simplex, Solar Lentigo

Lentigines are benign macular epidermal lesions caused by ultraviolet that contain melanin within keratinocytes and melanocytes. The superficial nature of lentigines allows the use of several lasers, including, frequency- doubled Q-switched Nd-YAG, Q-switched ruby, alexandrite, Nd-YAG, pulsed 510 nm, CW argon, CO_2 or erbium and other pulsed visible-light lasers. Labial melanocytic macules are similar lesions found on the mucosal surface and respond well to treatment with Q-switched lasers (Fig. 3.2).

Lentigines frequently clear with 1–3 treatments. The argon laser (488, 514 nm), the 510 pigment laser and the 532 nm green light lasers treat lentigines with superior efficacy, especially lightly pigmented lesions in which less chromophore is present. These shorter wavelength lasers are better absorbed by melanin but have less penetration.

Fractional photothermolysis (FP) has recently been used successfully to treat lentigines and overall dyschromia. A novel 1,927 nm thulium fiber laser was introduced as an addition to the 1,550 nm erbium-doped fiber laser (Wanner et al. 2007). This wavelength has a ten times greater absorption coefficient for water, conferring greater ability to target epidermal processes. Fractional ablative devices have also been used to improve photodamage (Sherling et al. 2010). Studies have shown greater improvement with microfractionl CO_2 when compared to microfractional Er:YAG.

Correct diagnosis is a main concern when treating lentigines. Lentigo maligna should not be treated with laser. Although initially one can obtain excellent cosmetic results, recurrences are frequently seen. Lentigo maligna frequently has

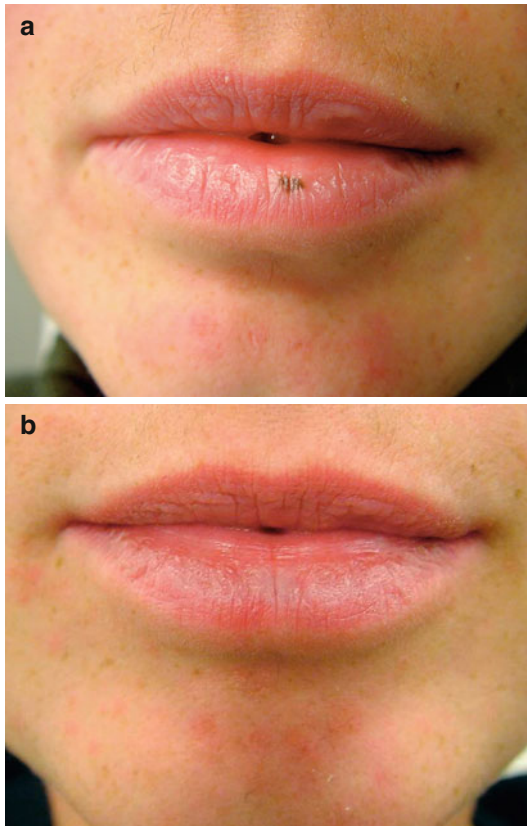

Fig. 3.2 (**a**) Labial lentigo before treatment. (**b**) Complete clearance of labial lentigo after single treatment with a Q-switched alexandrite laser

an amelanotic portion, which is not susceptible to laser treatment and will allow for recurrence. These cases emphasize the importance of careful clinical assessment before any laser surgery and the need to advise patients to return for evaluation if pigmentation does return.

Seborrheic Keratosis

Seborrheic keratoses are benign epidermal lesions that have melanin distribution similar to lentignes and a thickened, hyperkeratotic epidermis. Liquid nitrogen cryotherapy and other surgical methods like CO_2 or erbium laser are useful in treating these lesions, but are not practical modalities to tolerate in patients who have large numbers of lesions. Using pulsed green or Q-switched lasers offer the possibility to quickly and efficiently destroy hundreds of flat pigment seborrheic keratoses.

Ephelides

Ephelides or freckles are responsive to Q-switched laser treatment. Patients who tend to freckle are likely to refreckle with any sun exposure. At a follow-up of 24 months after laser treatment, 40 % patients showed partial recurrence. However, all the patients maintained >50 % improvement. The use of a broad band sunscreen is therefore indicated.

Café au Lait Macules

Café au lait macules are light to dark brown flat hypermelanotic lesions and may be a solitary benign finding or associated with certain genodermatoses (e.g., neurofibromatosis). Histologically, hypermelanosis is present within the epidermis and giant melanosomes may be present in both basal melanocytes and keratinocytes. Although café au lait macules are thin, superficial lesions, they are notoriously difficult to treat and multiple treatments are required for even the possibility of complete eradication. There is probably a cellular influence in the dermis that triggers the pigmentation in the more superficial cells. This underlying biology may also explain why pigment recurrences are often observed. Lesions may remain clear for up to a year with spontaneous or UV-induced recurrences in more than 50 % of cases. Patient education is important so that the possibility of recurrence is understood. However, given the significant disfigurement associated with many of these larger facial lesions, laser treatment is an excellent treatment option. Q-switched lasers with wavelengths of 532 nm and 694 nm, or the pulsed 510 nm (Alster 1995) laser can adequately treat the café au lait macules (Fig. 3.3). Erbium laser superficial abrasion of the epidermis of a "Q-switched laser-resistant" cafe-au-lait macule has also been reported to be successful treatment modality.

Nevus Spilus

When darker-pigmented macules or papules (junctional or compound melanocytic nevi) lie within the café au lait macule, the lesion is called nevus spilus. The lasers used for café au lait macules have also been used for nevus spilus

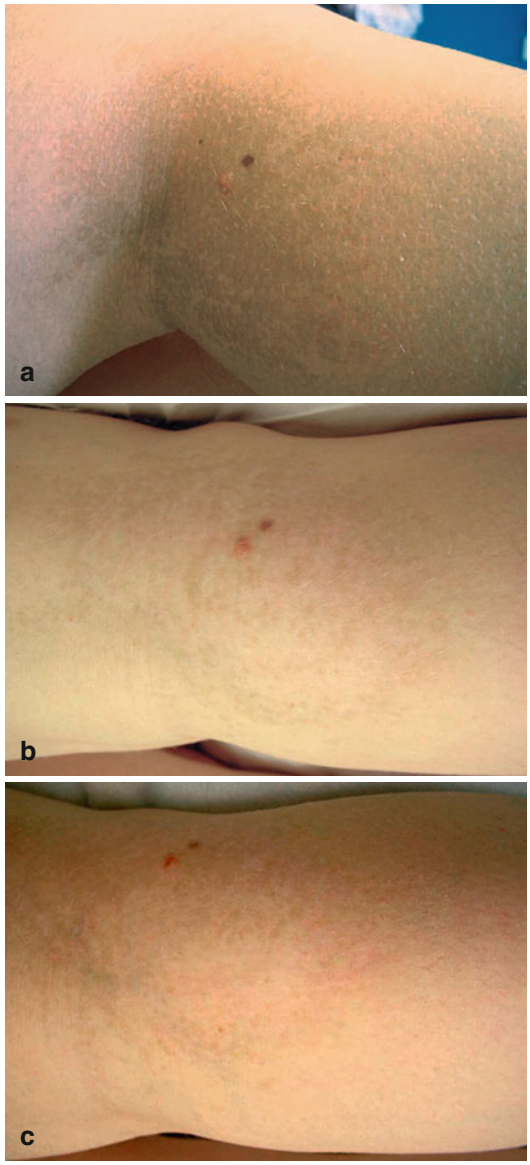

Fig. 3.3 Café au lait macule. Complete clearing after 4 treatments

(Carpo et al. 1999). The darker lesions tend to respond better than the lighter café au lait macule. There can be complete removal of the junctional or compound nevus portion but no improvement in the cafe-au-lait portion. Cases of nevus spilus transformation into melanoma have been reported in the literature. These cases emphasize the need for careful clinical assessment before any laser surgery and continued evaluation after laser treatment.

Dermal–Epidermal Pigmented Lesions

Becker's Nevus

Becker's nevus is an uncommon pigmented hamartomas that develops during adolescence and occurs primarily in young men. The nevus is characterized by hypertrichosis and hyperpigmentation and is usually located unilaterally over the shoulder, upper arm, scapula or trunk. These lesions often require the use of millisecond pigment-specific lasers for treatment of the hair, but the pigment lightening is variable. Test sites with a variety a pigment-specific Q-switched and millisecond lasers or flashlamps is recommended to determine which one (or combination) will be the best treatment option (Fig. 3.4). More recently, ablation of the epidermis and superficial dermis with an erbium laser has been shown to result in occasional complete pigment clearance with a single treatment.

Post-inflammatory Hyperpigmentation

Treatment of post-inflammatory hyperpigmentation with laser is unpredictable and often unsatisfactory. Furthermore, patients with hyperpigmentation following trauma are likely to respond to laser irradiation with an exacerbation of their pigment. The use of test sites is therefore recommended before an entire area is treated.

Post-sclerotherapy Hyperpigmentation

Cutaneous pigmentation commonly occurs following sclerotherapy of varicose veins. Pigmentation most likely reflects hemosiderin deposition, which is secondary to extravasation of red blood cells through the damaged endothelium (Goldman et al. 1987). Hemosiderin has an absorption spectrum that peaks at 410–415 nm followed by a gradually sloping curve throughout the remainder of the visible spectrum. Several Q-switched or pulsed lasers have therefore been reported to result in significant resolution of hemosiderin pigmentation (Sanchez et al. 1981).

Melasma

Melasma is an acquired, usually symmetric light to dark brown facial hypermelanosis. It is associated with multiple etiologic factors (pregnancy,

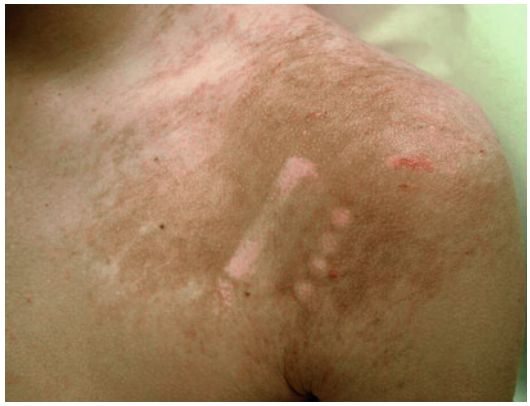

Fig. 3.4 Beckers nevus. Good clearing in testspot with long-pulsed Alexandrite laser (*round spots*) and in testspot with IPL (*rectangles*)

racial, and endocrine) and one of the primary causes of its exacerbation appears to be exposure to sunlight. Although the results after Q-switched laser treatment are usually initially encouraging, repigmentation frequently occurs.

Destruction of the abnormal melanocytes with erbium:YAG or CO_2 laser resurfacing has been attempted. It effectively improves melasma, however, there is almost universal appearance of transient post-inflammatory hyperpigmentation which necessitates prompt and persistent intervention. Combination of pulsed CO_2 laser followed by Q-switched alexandrite laser (QSAL) treatment to selectively eliminating the dermal melanin with the alexandrite laser has also been examined. Combined pulsed CO_2 laser and QSAL showed a better result than CO_2 or QSAL alone but was associated with more frequent adverse effects. Long-term follow-up, and a larger number of cases, are required to determine its efficacy and safety for refractory melasma.

Nevocellular Nevi

Although laser treatment of many pigmented lesions is accepted, treatment of nevocellular nevi is an evolving field with much controversy. It has yet to be determined if laser treatment increases the risk of malignant transformation by irritating melanocytes or decreases it by decreasing the melanocytic load. For this reason, laser treatment of nevi should be undertaken cautiously.

Congenital Melanocytic Nevi

The management of giant congenital melanocytic nevi (GCMN) remains difficult. It has been well proved that there is an increased risk of malignant changes among patients with these lesions, although the amount of increased risk for each individual patient is not clear. There is also a balance to be achieved between limiting the risk of malignant change and minimizing the disfiguring appearance of these lesions.

Sometimes GCMN are too large to be removed by multiple surgical excisions or use of osmotic tissue expanders. Removal of superficial nevus cells is possible by dermabrasion, curettage, shave excision or laser. High energy CO_2 laser therapy is less traumatic and can produce acceptable cosmetic results. Erbium laser treatment can also be used because it causes less thermal damage and faster wound healing. These techniques, although improving the cosmetic appearance, do not remove all nevus cell nests. Therefore they do not completely eliminate the risk of malignant transformation.

Treatment of giant, congenital nevi with a long-pulsed ruby laser has been reported. These systems show promise with follow-up for at least 8 years after laser treatment. There has been no evidence of malignant change in the treated areas. However the longer laser emitted pulsewidths can lead to thermal damage of surrounding collagen with resultant scar formation. This is especially true with darker, thicker lesions with a deep dermal component, which are often the ones whose removal is most desired. Combination therapy is therefore under investigation where Q-switched or resurfacing lasers may be used first to reduce the superficial component, followed by one of the millisecond pigment specific lasers.

Congenital and Acquired Small Melanocytic Nevi

The Q-switched ruby, alexandrite and Nd-YAG lasers have been studied for treatment of melanocytic nevi (Goldberg and Stampien 1995). Although clearing rates as high as 80 % have been reported, short-pulsed lasers are not recommended for nevi, because of the high post laser treatment recurrence rates.

Melanocytic nevi often have nested melanocytes with significant amounts of melanin and therefore may act more as a larger body than as individual melanosomes. It has therefore been suggested that longer pulsed ruby, alexandrite or diode lasers or Q-switched lasers in combination with longer-pulsed lasers may provide a more effective treatment with fewer recurrences. All laser systems have been partially beneficial. No lesions have had complete histologic removal of all nevomelanocytes (Duke et al. 1999).

Dermal Pigmented Lesions

The development of Q-switched lasers has revolutionized the treatment of dermal melanocytoses. The dendritic cells found deep in the dermis are particularly sensitive to short pulsed laser light, frequently resulting in complete lesional clearing without unwanted textural changes.

Nevus of Ota, Nevus of Ito

Nevus of Ota is a form of dermal melanocytic hamartoma that appears as a bluish discoloration in the trigeminal region. Histologic examination shows long, dermal melanocytes scattered largely the upper half of the dermis. Nevus of Ito is a persistent grayish blue discoloration with the same histologic characteristics of nevus of Ota, but is generally present on the shoulder or upper arm, in the area innervated by the posterior supraclavicular and lateral brachial cutaneous nerves.

The dermal melanocytes found within these lesions contain melanin and are highly amenable to treatment with Q-switched ruby (Goldberg and Nychay 1992), alexandrite (Alster 1995) or Nd-YAG lasers. Four to eight treatment sessions are typically required to treat these lesions. Possible side effects like post-inflammatory hyperpigmentation, hypopigmentation or scarring and recurrences are infrequent. Although there have been no reports on successful treatment of nevus of Ito, treatment with Q-switched lasers should be efficacious.

Blue Nevi

Blue nevi are benign melanocytic lesions that arise spontaneously in children or young adults. The melanocytes are deep within the dermis and the blue-black color results from the Tyndall light scattering effect of the overlying tissues. Although extremely rare, malignant blue nevi have been reported. Because of their benign nature, blue nevi are usually removed for cosmetic reasons. The deep dermal melanocytes respond well to Q-switched laser treatment, as long as the lesion does not extend in the deep subcutaneous tissue.

Acquired Bilateral Nevus of Ota-Like Macules (ABNOMs)

Acquired bilateral nevus of Ota-like macules (ABNOM), also called nevus fuscoceruleus zygomaticus or nevus of Hori, is a common Asian condition that is characterized by bluish hyperpigmentation in the bilateral malar regions. Unlike nevus of Ota, ABNOM is an acquired condition that often develops after 20 years of age, involves both sides of the face, and has no mucosal involvement. Histologically, actively melanin synthesizing dermal melanocytes are dispersed in the papillary and middle portions of the dermis. Since these lesions are histologically a form of dermal melanocytosis like nevus of Ota, melanin-targeting lasers should be effective in the treatment. Although promising results in the treatment of Hori's nevus with Q-switched ruby CO_2 with Q-switched ruby alexandrite and Nd-YAG lasers have been reported, the treatment responses have been noted to be less effective than that of nevus of Ota. Multiple laser sessions are necessary to obtain cosmetically desired improvement. A higher rate of postinflammatory hyperpigmentation is often present after laser treatments.

Tattoos

The popularity of tattoos is burgeoning with 20–30 million tattooed individuals in the Western World. Requests for removal can be expected to rise concurrently with increased applications. Despite their relatively easy acquisition, the removal of tattoos has long been a real problem. Laser removal of tattoos is potentially a more cosmetically acceptable method of removing tattoos than surgical excision or dermabrasion.

Tattoo Pigments

Tattoos, a form of exogenous pigment, are usually composed of multiple colors and various

dyes. In contrast to drugs and cosmetics, tattoo pigments have never been controlled or regulated in any way, and the exact composition of a given tattoo pigment is often kept a "trade secret" by the manufacturer. In most cases, neither the tattoo artist nor the tattooed patients have any idea of the composition of the tattoo pigment.

Until recently, most coloring agents in tattoo pigment were inorganic heavy metal salts and oxides, like aluminum, titanium, cadmium, chromium, cobalt, copper, iron, lead, and mercury. There has been a shift in recent years away from these agents toward organic pigments, especially azo- and polycyclic compounds. These pigments are considered safer and well tolerated by the skin, although allergic reactions and phototoxicity occur.

Laser Removal of Tattoos

For Q-switched laser tattoo treatment to be effective, the absorption peak of the pigment must match the wavelength of the laser energy. Similar colors may contain different pigments, with different responses to a given laser wavelength, and not all pigments absorb the wavelengths of currently available medical lasers.

Tattoos absorb maximally in the following ranges: red tattoos, from 505 to 560 nm (green spectrum); green tattoos, from 630 to 730 nm (red spectrum); and a blue-green tattoo, in two ranges from 400 to 450 nm and from 505 to 560 nm (blue-purple and green spectrums, respectively). Yellow tattoos absorbed maximally from 450 to 510 nm (blue-green spectrum), purple tattoos-absorbed maximally from 550 to 640 nm (green-yellow-orange-red spectrum), blue tattoos absorbed maximally from 620 to 730 nm (red spectrum), and orange tattoos absorbed maximally from 500 to 525 nm (green spectrum). Black and gray absorbed broadly in the visible spectrum, but these colors most effectively absorb 600–800 nm laser irradiation.

Three types of lasers are currently used for tattoo removal: Q-switched ruby laser (694 nm), Q-switched Nd:YAG laser (532 nm, 1,064 nm), and Q-switched alexandrite (755 nm) (Adrian and Griffin 2000; Kilmer 2002). The Q-switched ruby and alexandrite lasers are useful for removing black, blue and green pigment (Alster 1995). The Q-switched 532 nm Nd:YAG laser can be used to remove red pigments and the 1,064 nm Nd:YAG laser is used for removal of black and blue pigments (Kilmer et al. 1993). Since many wavelengths are needed to treat multicolored tattoos, not one laser system can be used alone to remove all the available inks (Levine and Geronemus 1995).

There is still much to be learned about removing tattoo pigment. Once ink is implanted into the dermis, the particles are found predominantly within fibroblasts, macrophages and occasionally as membrane-bound pigment granules.

Exposure to Q-switched lasers produces selective fragmentation of these pigment-containing cells. The pigment particles are reduced in size and found extracellularly. A brisk inflammatory response occurs within 24 h. Two weeks later, the laser altered tattoo ink particles are found repackaged in the same type of dermal cells.

It is not yet clear how the liberated ink particles are cleared from the skin after laser treatment. Possible mechanisms for tattoo lightening include: (1) systemic elimination by phagocytosis and transport of ink particles by inflammatory cells, (2) external elimination via a scale-crust that is shed or (3) alteration of the optical properties of the tattoo to make it less apparent. The first of these appears clinically and histologically to be the dominant mechanism.

There are five types of tattoos: professional, amateur, traumatic, cosmetic and medicinal. In general, amateur tattoos require less treatment sessions than professional multi-colored tattoos. Densely pigmented or decorative professional tattoos are composed of a variety of colored pigments and may be particularly difficult to remove, requiring ten or more treatment sessions in some cases (Fig. 3.5). A 100 % clearing rate is not always obtained and, in some instances, tattoos can be resistant to further treatment. Amateur tattoos are typically less dense, and are often made up of carbon-based ink that responds more readily to Q-switched laser treatment (Fig. 3.6). Traumatic tattoos usually have minimal pigment deposited superficially and often clear with a few treatments (Fig. 3.7). Caution should be used when treating gunpowder or firework tattoos, because

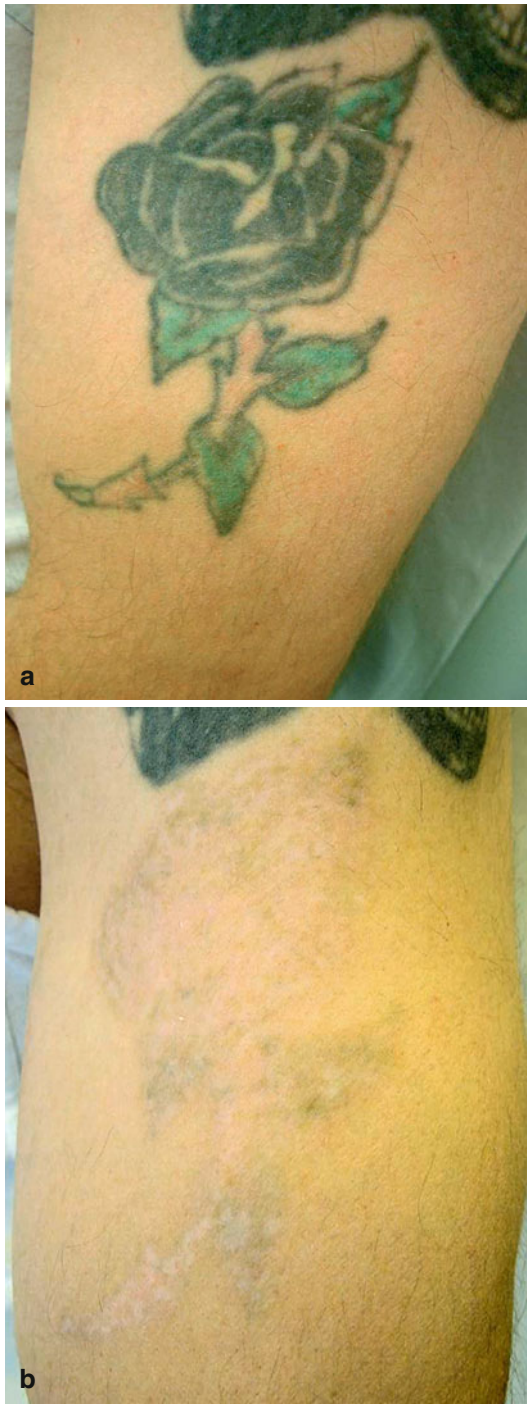

Fig. 3.5 Professional tattoo. Partial clearing after 4 treatments

the implanted material has the potential to ignite and cause pox-like scars.

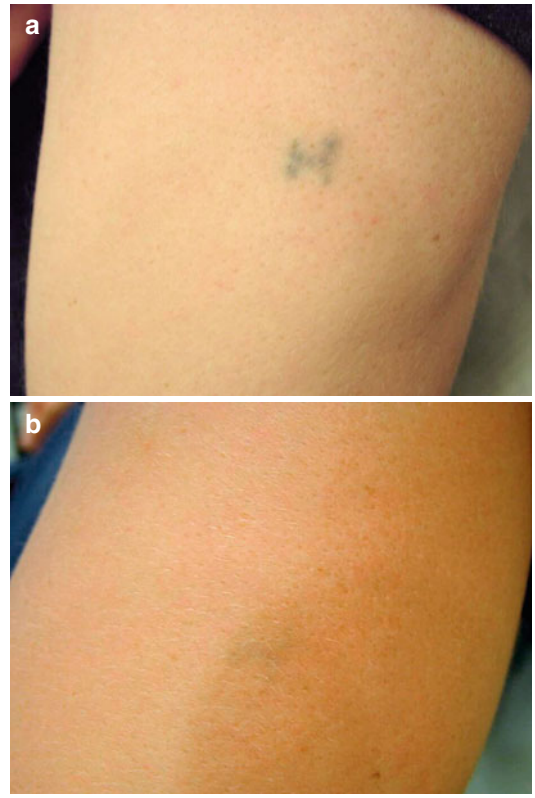

Fig. 3.6 Amateur tattoo. Complete clearing after 2 treatments

Consent

After obtaining informed consent (Fig. 3.8), the following options are considered.

Personal Laser Technique

The approach to treatment will vary with the chosen laser and the whether the pigmented lesion to be treated is epidermal, dermal or mixed. Tattoos may show a different response (Tables 3.4, 3.5, and 3.6).

Q-Switched Ruby Laser (694 nm)

The first Q-switched laser developed was a ruby laser. Current models employ a mirrored articulated arm with a variable spotsize of 5 or 6.5 mm, a pulsewidth of 28–40 ns and a maximum fluence

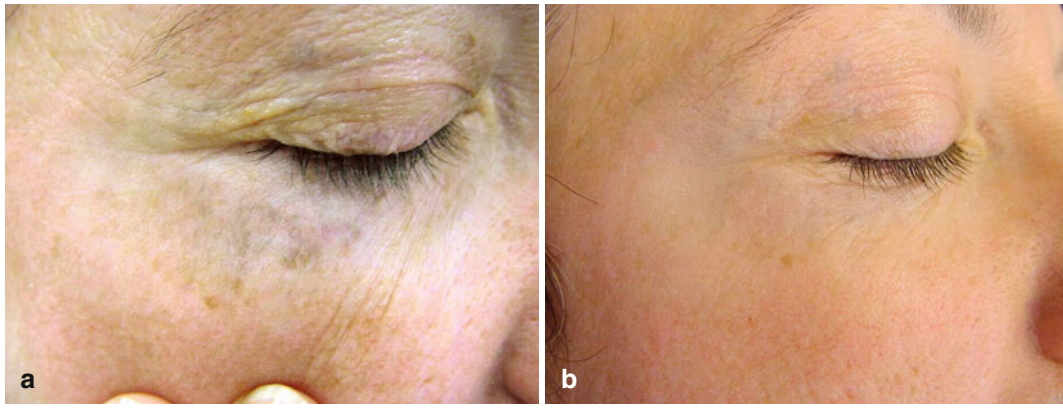

Fig. 3.7 Traumatic tattoo. Clearing after 3 treatments

Table 3.4 Suggested treatment parameters for pigmented lesions

Indication	Laser	Spotsize	Fluence (J/cm^2)
Lentigines	510 nm PLPD	3	2.5
	QS 532 nm Nd-YAG	4	3
	QS 694 nm ruby	6.5	3–5
	QS 755 nm alexandrite	4	3.4
Café au lait macules	510 nm PLPD	5	2–3.5
	QS 532 nm Nd-YAG	3	1–1.5
	QS 694 nm ruby	6.5	3–4.5
	QS 755 nm alexandrite	3	4–5
Becker's nevus	QS 532 nm Nd-YAG	3	1.5–2
	QS 694 nm ruby	6.5	4.5
	QS 755 nm alexandrite	3	6
	QS 1,064 nm Nd-YAG	3	4–5
Nevus Spilus	QS 532 nm Nd-YAG	3	1.5–2
	QS 694 nm ruby	6.5	4.5
	QS 755 nm alexandrite	3	6
	QS 1,064 nm Nd-YAG	3	4–5
Tattoo	510 nm PLPD	5	2–3.5
	QS 532 nm Nd-YAG	3	2–3.5
	QS 694 nm ruby	6.5	5–8
	QS 755 nm alexandrite	3	6–6.5
	QS 1,064 nm Nd-YAG	3	5–8
Nevus of Ota	QS 694 nm ruby	6.5	5–6
	QS 755 nm alexandrite	3	6.5
	QS 1,064 nm Nd-YAG	3	5.0

of up to 10 J/cm^2. The 694 nm wavelength is most well absorbed by melanin. Because hemoglobin absorbs 694 nm light poorly, ruby laser treats pigmented lesions very efficiently.

Most lentigines and ephelides clear after 1–3 treatments with the Q-switched ruby laser (QSRL). Café au lait macules, nevus spilus, Becker's nevus respond moderately well. Recurrences are frequent with these lesions, especially when incomplete clearing is obtained. The QSRL has become the treatment of choice for dermal pigmented lesions like nevus of Ota or Ito. The long wavelength, the big spot size and the high delivered energy per pulse generates a high fluence deep in

CONSENT FORM FOR TREATMENT BY PIGMENT LASER

The undersigned:

Patient: . . . . . .

Born on: . . . . . / . . . . . / . . . .

Resident of . . . . . .

Physician: . . . . . .

1. INTRODUCTION

The contents of this form give a brief overview of the information exchanged and explained during the preceding oral conversations between both parties.

The patient is considered to be well informed before consenting to receiving pigment laser treatment.

It is obvious that the treating physician is prepared to answer all your possible questions regarding this operation.

2. NATURE AND COURSE OF THE TREATMENT

The pigment laser is a device producing highly energetic light. During the treatment, a laser beam is pointed at the skin. The laser beam selectively destroys the melanin pigment or tattoo particles in the skin, while the surrounding tissues are left untouched. In general, local anesthesia is not needed. In case it should be necessary for one or another reason, the treating physician will discuss the modalities thereof in detail. During laser treatment, the patient, the physician and the personnel are to wear special glasses to protect the eyes against the laser light.

3. AIM OF THE TREATMENT

The aim of the treatment is to clear up a lesion caused by melanin pigment or tattoo particles. The number of treatments depends on the extent, the nature, the age and the intensity of the pigmentation of the skin lesion. A complete disappearance of the treated lesion is aimed at, but can never be guaranteed in advance.

The physician thus agrees with the patient to operate according to the rules of art, but cannot promise any well-defined result (= commitment to make every possible effort).

4. RISKS

Potential complications of the treatment are:

- Wound infection: occurs very rarely and heals when treated appropriately.
- Formation of scar tissue: highly exceptional.
- Increased or decreased pigmentation:

In some cases, the wound heals with increased pigmentation (hyperpigmentation). This usually happens among patients with darker skin tones or as a result of sun exposure. Other patients are predestined to have this kind of reaction and may have experienced this before, during the healing of other wounds. In order to minimize the risk of hyperpigmentation, post-operational protection of the skin against sun exposure is of the utmost importance. Among some patients, this hyperpigmentation can even occur despite good sun protection. Hyperpigmentation is usually only temporary, but needs a few months to clear. Seldom does the hyperpigmentation persist nevertheless.

Among some patients, the treated area may show decreased pigmentation (hypopigmentation) and thus obtain a lighter color than the surrounding skin tissue. This is usually only a temporary reaction, after which the skin will gradually pigment again. In some cases, however, the depigmentation may be permanent.

The physician has informed the patient how to take care of the treated skin area. Not following these postoperative instructions may cause complications.

Fig. 3.8 Consent form

5. EFFECTS
Immediately after being treated, the skin will turn whitish gray. Exceptionally, erosion (superficial wound) and/or pinpoint bleeding may occur. A bluish red discoloration as a consequence of bleeding may also appear and may last up to 2 weeks before disappearing.

6. ALTERNATIVE TREATMENTS
Cryotherapy, excisional surgery and dermabrasion are possible alternatives.

7. PHOTOGRAPHS
In order to have a better view on the results of the operation, and for educational and scientific purposes, such as presentations and scientific publications, photographs may possibly be taken. The patient will be turned unrecognizable on these pictures. The patient is well informed about this and agrees to it.

8. REVOCATION OF CONSENT
The patient deliberately consents to the treatment and can at any moment decide to stop further treatment.

9. OBSERVATIONS
Observations of the physician:
....
....
....

Observations of the patient:
....
....
....
....

10. Each of the consenting parties declares to have received a copy of this consent form. The signature is preceded by the self-written formula 'read and approved'.
The patient declares that all his/her questions have been answered.

Date: ....

....
Patient's signature Physician's signature

Fig. 3.8 (continued)

Table 3.5 Most effective Q-switched lasers for different tattoo ink colors

Tattoo ink color	Laser
Blue/black	Q-Switched ruby, Q-Switched alexandrite, Q-Switched 1,064 nm Nd-YAG
Green	Q-Switched ruby, Q-Switched alexandrite
Red/orange/purple	Q-Switched frequency-doubled 532 nm Nd-YAG laser, 510 nm pigment lesion pulsed dye laser

the tissue. This all leads to efficient targeting of deep melanocytes. As effective as other Q-switched lasers are for removing black tattoo ink, the QSRL is one of the better lasers for removing dark blue or green ink. Removal of red tattoo ink is problematic given that the QSRL is a red light source and is not well absorbed by the red ink particles. Yellow ink does not respond to QSRL treatment because the absorption of yellow inks is very low in this laser's red to near-infrared spectrum of delivered light.

Table 3.6 Response of pigmented lesions and tattoos to various lasers and light sources

	Pigmented lesions			Tattoos	
	Epidermal	Mixed	Dermal	Amateur	Professional
510 nm pigment lesion pulsed dye laser	+++	+	+	++	+++ (red colors)
532 nm Q-switched Nd-YAG laser	+++	+	+	++	+++ (red colors)
694 nm Q-switched ruby laser	+++	+	+++	+++	+++ (green colors)
755 nm Q-switched Alexandrite laser	+++	+	++	+++	+++ (green colors)
1,064 nm Q-switched Nd-YAG laser	++	+	+++	+++	+++
Intense pulsed light source	+++	+	+		

+++, excellent; ++, good; +, fair

When selecting the energy level for treatment with the QSRL, immediate tissue whitening with no or minimal tissue bleeding should be observed. The required energy level is determined by the degree of pigmentation or the amount and color of the tattoo ink. The 6.5 mm spot is recommended for most lesions, with an initial fluence of 3–5 J/cm^2. The excellent QSRL melanin absorption frequently leads to transient hypopigmentation, that may take months to resolve. Rarely (in 1–5 % of cases) one sees permanent depigmentation.

Q-Switched Nd:YAG Laser (532–1,064 nm)

The Q-switched Nd:YAG laser (QSNd:YL) emits 2 wavelengths, 532 and 1,064 nm, with a pulse duration of 5–10 ns, delivered through a mirrored, articulated arm. Current models have spot sizes of 2–8 mm and can operate at up to 10 Hz.

The long QSNd:YL 1,064 nm wavelength has the least absorption by melanin and the deepest penetration. It is therefore potentially effective for both epidermal and dermal pigmented lesions. Use of a frequency-doubling crystal, allows emission of a 532 nm wavelength (green). This wavelength is well absorbed by both melanin and hemoglobin. Because of the superficial penetration, this 532 nm laser is limited to treat epidermal pigmented lesions.

Epidermal lesions such as lentigines or ephelides treated with the QSNd:YL respond as well to treatment as they do after QSRL treatment. Café au lait macules, nevus spilus, Becker's nevus do not respond as well to QSNd:YL treatment. The Q-switched 1,064 nm laser is highly effective for removing deep dermal pigment such as nevus of Ota and Ito. Because this wavelength is less absorbed by melanin, higher energy is required than with the QSRL. Newly available Q-switched Nd:YAG lasers which generate high fluences at large spotsizes, have optimized treatment results. In an effort to treat tattoos without interference of melanin absorption, the 1,064 nm Q- switched Nd-YAG laser was developed. It is most effective for treating black ink tattoos, especially in darker skin types. The 532 nm wavelength is the treatment of choice for red tattoo pigment.

When treating epidermal pigmented lesions with the 532 nm wavelength, non-specific vascular injury will occur, leading to purpura, which takes 5–10 days to resolve. Because of the ultrashort pulse duration, the Q-switched Nd-YAG produces the greatest amount of epidermal debris. This can be minimized by the use of larger spot sizes. Recent studies have shown that larger spot sizes and lower fluences are as effective in removing tattoo pigment as smaller spot sizes at higher fluences, and have fewer side effects. Therefore when using the 1,064 nm wavelength, treatment should therefore begin with a 4–8 mm spot size at 3–6 J/cm^2.

Q-Switched Alexandrite Laser (755 nm)

The alexandrite laser has a wavelength of 755 nm, a pulse duration of 50–100 ns, a spot size of 2–4 mm and is delivered by a fiberoptic arm. Fiberoptic delivery allows a more even beam profile with fewer hot spots.

The wavelength of the Q-switched alexandrite laser (QSAL) is similar enough to that of the

QSRL to obtain comparable results for the treatment of epidermal and dermal pigmented lesions, perhaps with the added advantage of a slightly deeper penetration. Similar to the QSRL, this laser is effective at removing black, blue and most green tattoo inks, and less proficient at removing red or orange inks.

Depending on the spot size, a starting fluence of 5–6 J/cm^2 is usually employed. Immediately after treatment, gray-whitening of the skin occurs, followed by erythema and edema. There is a lower risk of tissue splatter because of the longer pulse duration and the more even beam profile. There is also a lower risk of transient hypopigmentation because of slightly less QSAL melanin absorption as compared to the QSRL.

Pulsed Dye Laser (510 nm)

The short wavelength of the pulsed dye laser (PDL) makes it optimal for treatment of superficial pigmented lesions. Epidermal lesions such as lentigines, ephelides and flat pigmented seborrheic keratoses respond extremely well to the 510 nm pulsed dye laser. Its shallow depth of penetration into the skin, makes it less than ideal for treating dermal pigmented lesions. However, like the frequency doubled 532 nm Nd-YAG laser, the 510 nm PDL laser effectively removes bright tattoo colors like red, purple and orange.

Continuous Wave (CW) Lasers

The CW argon (488 and 514 nm), CW dye (577 and 585 nm), CW krypton (521–530 nm), and the pulse train quasi-CW copper vapor lasers (510 and 578 nm) all have been used to treat pigmented lesions. However, when these lasers are used in freehand mode, reproducibility is lacking and the thermal damage is somewhat unpredictable. The risk of scarring and pigmentary changes is therefore significant in the hands of inexperienced operators. In general, these CW lasers, when used by skilled operators, are effective in the treatment of epidermal pigmented lesions.

CO2 and Erbium Lasers

The CO_2 and erbium lasers are sources that emit infrared (IR) light at a wavelength of 10,600 and 2,940 nm respectively. These wavelengths are well absorbed by water. The lasers destroy the superficial skin layers non-selectively and can be used to remove superficial epidermal pigment, especially seborrheic keratoses. Superficial erbium laser epidermal abrasion of a "Q-switched laser-resistant" cafe-au-lait macule has also been reported. Theses ablative lasers can also be helpful in treating resistant tattoos by removing epidermis immediately before Q-switched laser treatment. This will lead to facilitated transepidermal tattoo particle elimination.

Intense Pulsed Light (IPL) Sources

Melanin pigmentation, as part of photoaging, can be epidermal or dermal. It often is a combination of both. In early solar damage, melasma is a regular constituent; often with both dermal and epidermal pigment deposition. In later stages of solar degeneration the solar lentigo, which is mainly located in the epidermis, is a prominent feature. Recently, intense pulsed light sources (IPL) have shown to be highly effective in the treatment of photodamaged pigmented lesions like solar lentigines, and generalized dyschromia (Fig. 3.9). Unfortunately light spectra, pulse duration, number of pulses as well as delivered fluence and the use of skin cooling vary considerably among the published investigations, making direct comparisons of IPL devices quite difficult.

Further Treatment Pearls

When treating pigmented lesions and tattoos, the laser handpiece should be held perpendicular over the area to be treated. Pulses should be delivered with 0–10 % overlap until the entire lesion is treated.

The desired laser tissue interaction produces immediate whitening of the treated area with

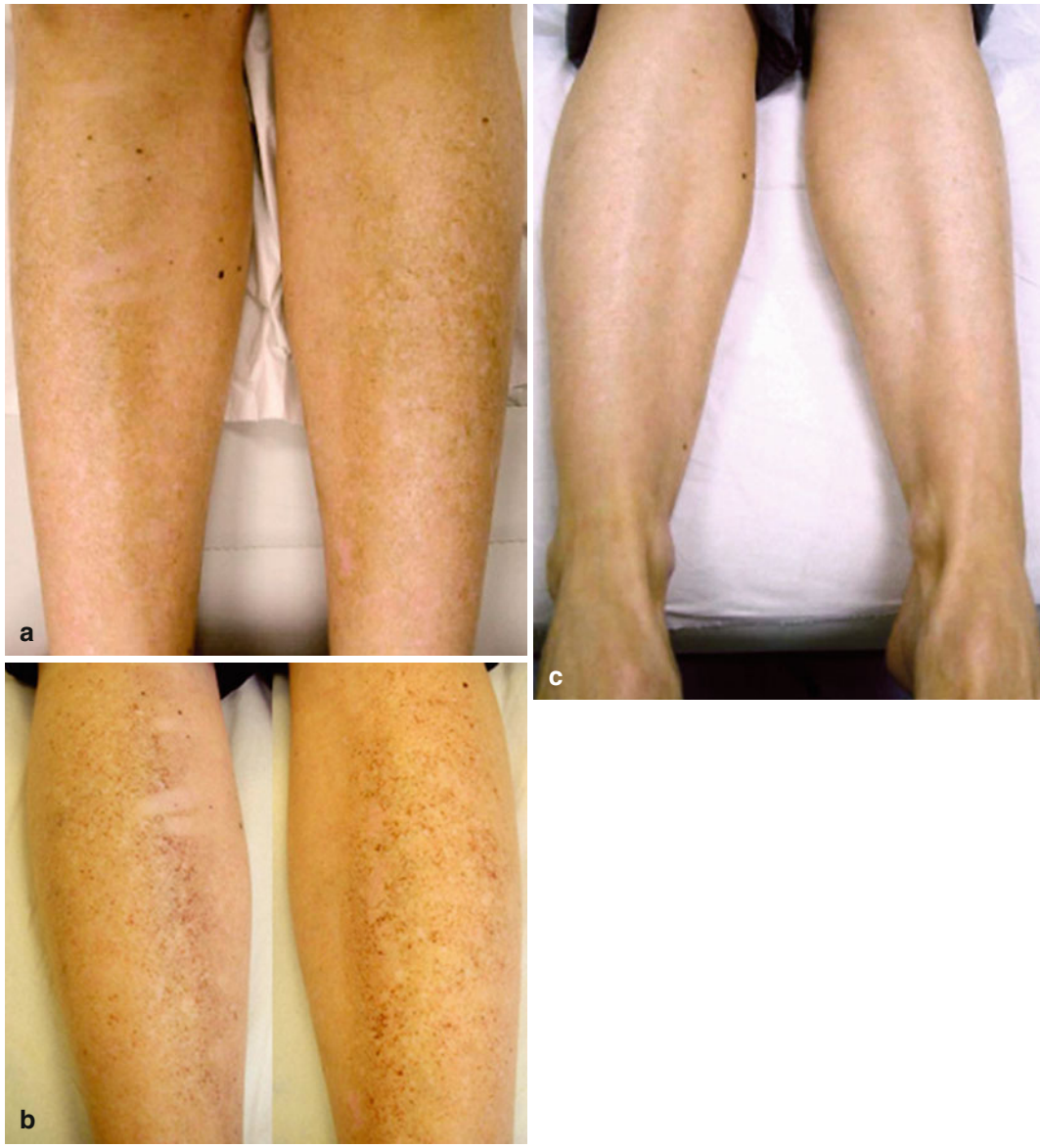

Fig. 3.9 Actinic bronzing. Sloughing of pigment 2 days after treatment. Complete clearance 1 month after treatment 1

minimal or no epidermal damage or pinpoint bleeding. It is best to use the largest spot size to minimize epidermal damage. If epidermal debris is significant, the fluence should be lowered. Higher fluences may be needed with subsequent treatments when less pigment or tattoo ink particles are still present in the skin.

IPL treatment or Q-switched laser treatment of epidermal pigmented lesions rarely requires anesthesia. When needed, a topical anesthetic cream can be applied 1–2 h before the procedure to reduce the discomfort. For more complete anesthesia, local anesthetic infiltration or regional nerve block can be used.

Treatment parameters are determined by the type of lesion and the patient's skin type. As discussed above, the ideal response is immediate whitening of the skin with little or no epidermal disruption. If the fluence is too low, the whitening will be minimal, whereas if the fluence is too

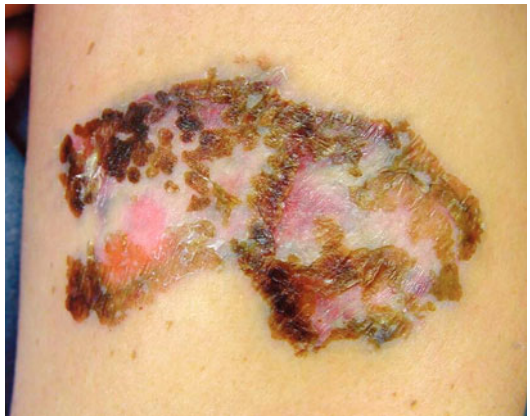

Fig. 3.10 Crusting 1 week after laser treatment of tattoo

high, the epidermis is ruptured and bleeding might occur. Following treatment with a 510 PDL or a QS 532 nm laser, pinpoint bleeding usually appears and lasts for 7–10 days. This occurs because of vessel rupture after haemoglobin absorption.

The whitening of the treated area lasts about 15 min and an urticarial reaction appears around the treated area. In the following days, the treated area usually becomes darker and develops a crust that falls of in 7–10 days (Fig. 3.10). The postoperative care consists of application of a healing ointment, and avoidance of sun exposure, in an effort to reduce the risk of post-inflammatory hyperpigmentation.

Patients with darker skin types should be treated at lower fluences. Their threshold response will occur at lower fluences than is seen with patients with lighter skin types. Treatment of suntanned individuals should be avoided because of the high risk of laser-induced hypopigmentation.

While one to three treatments are sufficient to treat most lentigines, multiple treatments will be necessary for pigmented birthmarks like café au lait macules.

Anesthesia is rarely required for dermal pigmented lesions. When treating larger areas topical or intralesional anesthesia may be necessary. When treating nevus of Ota, regional nerve blocks usually provide adequate anesthesia.

Treatment parameters are again determined by the type of lesion and the patient's skin type. In general, higher fluences are necessary than those required for the treatment of epidermal lesions. The threshold response should be immediate whitening of the skin with little or no epidermal disruption. The same postoperative aftercare and precautions apply as for epidermal pigmented lesions. Dermal melanocytoses require multiple treatment sessions, usually performed at 6 weeks intervals or longer. Lesions as nevus of Ota continue to lighten for several months after each treatment.

Anesthesia is usually not required for small tattoos. For certain individuals or for larger tattoos, topical or intralesional anesthesia might be necessary.

If adequate fluences are available, it is best to use the largest laser spot size. This will reduce backward scattering and therefore minimize epidermal rupture. Following treatment, wound care is required to help healing and prevent infection. An antibiotic ointment should be applied. A dressing should be worn for several days until healing has been completed.

Tattoo treatment usually requires multiple treatments to obtain adequate clearing. Amateur tattoos respond more quickly than do multi-colored professional tattoos. Complete clearing of tattoos is not always possible. During the initial consultation, the patient should be informed about this. However, dramatic lightening can be expected.

Cosmetic tattoos should be approached with caution. When treating tattoos with colors that may darken (white, light pink, tan or some brown colors), a single test spot should be placed to assess immediate darkening (Figs. 3.11 and 3.12). If darkening occurs, the same test site should be retreated to be sure the ink can be lightened before proceeding further. Although the darkened pigment may clear easily, it can sometimes be very recalcitrant to treatment. In this case, CO_2 or erbium vaporization can be used, as an adjunctive treatment modality, by removing the epidermis immediately before Q-switched laser treatment and/or by facilitating transepidermal tattoo particle elimination.

Treatment sessions are performed at interval of 6 weeks or greater. Waiting longer between treatment sessions might be even more beneficial as tattoos may continue to clear for several months following each treatment.

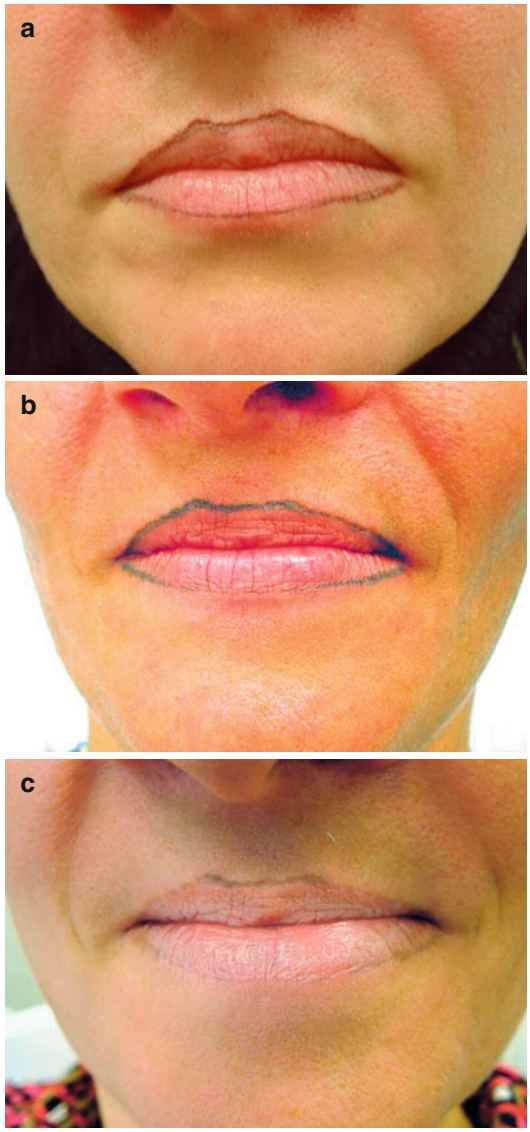

Fig. 3.11 Cosmetic tattoo. Darkening of pigment after first treatment. Partial clearing after 6 treatments with Q-switched Alexandrite laser

Complications

Unlike previous treatment modalities for pigmented lesions, Q-switched lasers induce minimal side effects. These include pigmentary changes, partial removal, infection, bleeding, textural changes and tattoo ink darkening.

Pigmentary changes following laser treatment of pigmented lesions are not uncommon.

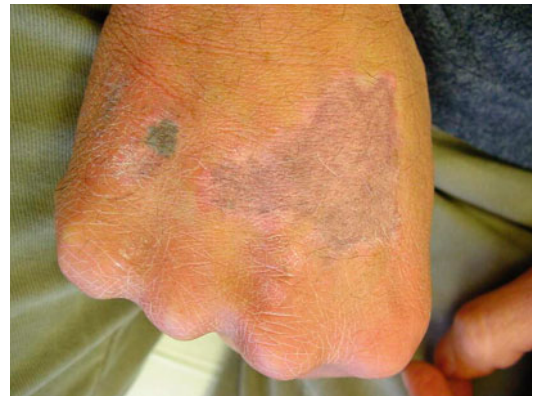

Fig. 3.12 Color shift to green after laser test with Q-switched Alexandrite laser

Transient hypopigmentation is most common after treatment with the 694 or 755 nm wavelengths because absorption by melanin is so strong. Permanent hypopigmentation can be seen with repetitive treatment sessions, particularly at higher fluences. The 1,064 nm wavelength is the least injurious to melanocytes and is therefore the treatment of choice for dark-skinned individuals undergoing laser tattoo treatment. Transient hyperpigmentation, which has been reported in up to 15 % of cases is more common in darker skin types or following sun exposure (Kilmer et al. 1993). The incidence of scarring is less than 5 %. It is associated with the use of excessive fluences. It is also more common when certain areas like the chest and ankle are treated. This complication has also been observed in areas with dense deposition of ink, such as in double tattoos. Larger laser spot sizes tend to minimize epidermal damage and are associated with fewer textural changes.

Pigment darkening of cosmetic skin color tattoos can occur after exposure to any Q-switched laser. The darkening occurs immediately and is most often seen with the red, white or flesh-toned ink colors that are frequently used in cosmetic tattoos. These colors often contain ferric oxide and titanium dioxide that can change to a blue-black color after Q-switched laser treatment. The mechanism probably involves, at least for some tattoos, reduction of ferric oxide (Fe_2O_3, "rust") to ferrous oxide (FeO, jet black). Recently,

multiple color changes following laser therapy of cosmetic tattoos has been reported (Fig. 3.11). Performing small test areas before complete treatment and using several laser wavelengths throughout the course of therapy are essential to the successful treatment of cosmetic tattoos.

Localized allergic reactions can occur with almost any treated tattoo color (Ashinoff et al. 1995). It can result in an immediate hypersensitivity reaction such as urticaria. In the alternative a delayed hypersensitivity reaction such as granuloma formation may occur. The most serious complication reported after Q-switched laser tattoo removal was a systemic allergic reaction. The Q-switched target intracellular tattoo pigment, causing rapid thermal expansion that fragments pigment-containing cells and causes the pigment to become extracellular. This extracellular pigment may then be recognized by the immune system as foreign, potentially triggering an allergic reaction. Therefore, if a patient exhibits a local immediate hypersensitivity reaction, prophylaxis before subsequent laser treatments with systemic antihistamines and steroids should be considered Pulsed CO_2 and erbium lasers do not seem to trigger this reaction, since the particle size does not change. These lasers may be used to enhance transepidermal elimination of ink.

Future Developments

Non-invasive, real-time optical diagnostic tools (like Optical Coherence Tomography, confocal microscopy, multispectral digital imaging, polarized multispectral imaging) are being studied for their role in the accurate pre-laser diagnosis of pigmented lesions as well as a tool for determining efficacy and safety following treatment.

Current tattoo laser research is focused on newer picosecond lasers. The systems may be more successful than the Q-switched lasers in the removal of tattoo inks. Such lasers, because they emit picosecond pulse widths cause optimal photomechanical disruption of the tattoo ink particles. Another tattoo approach would the development of laser-responsive inks. In this case tattoo removal might be feasible with only one or two treatment sessions.

It is also possible that a laser that emits trains of low-fluence, submicrosecond pulses might cause even more selective injury to pigmented cells by limiting mechanical damage modes. The use of pulse trains, specifically designed to selectively affect pigmented cells in skin, has not yet been tested.

Since the clearing of tattoo pigment following laser surgery is influenced by the presence of macrophages at the site of treatment, it has also been suggested that the adjuvant use of cytokines like macrophage colony-stimulating factor other chemotactic factors such as topical leucotrienes or the use of a topical immunomodulators like imiquimod might recruit additional macrophages to the treatment site. This could expedite the removal of tattoo pigment following laser surgery.

The extraction of magnetite ink tattoos by a magnetic field has been investigated after Q-switched laser treatment. When epidermal injury was present, a magnetic field, applied immediately after Q-switched ruby laser treatment, did extract some ink. Magnetically-extractable tattoos may therefore become feasible one day. Delivery of intradermally focused small energy nanosecond laser pulses might become another approach for more efficient and safer tattoo removal. Finally optical clearing of skin with hyperosmotic chemical agents is currently under investigation. This approach reduces optical scattering in the skin, thereby enhancing the effective light dose that reaches the tattoo particles.

In 2009, a new tattoo ink was made available in the United States. Infinitink (Freedom Inc., Cherry Hill, NJ), created to be easily removed using laser treatment, uses bioresorbable dyes encapsulated in polymethylmethacrylate beads (Choudhary et al. 2010). These beads also contain additional pigments specially designed to allow targeting by specific laser wavelengths. Tattoos created with Infinitink can be removed in far fewer laser treatments than those with traditional pigments. It is the hope that the adoption of these types of pigments by the tattoo industry and consumers will make owning, and if desired removing, a tattoo safer.

QS laser treatment may effectively remove various kinds of unwanted tattoos. The laser surgeon must be educated in the nuances of laser tattoo removal to ensure safe and effective treatment. Tattoo removal was revolutionized with the invention of the laser, and the continued refinement of this technology has led to better and more-predictable outcomes, but further research is needed regarding the safety of tattoo pigments and the breakdown products formed with exposure to laser light. Current investigation in the field is focused on faster lasers and more-efficient targeting of tattoo pigment particles. In the future, these new technologies will offer safer and more-effective laser tattoo removal.

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Laser Treatment of Unwanted Hair

4

Jeremy Man and David J. Goldberg

Core Messages

- A wide variety of lasers can now induce permanent changes in unwanted hair
- Hair removal lasers are distinguished not only by their emitted wavelengths, but also by their delivered pulse durations, peak fluences, spot size delivery systems and associated cooling
- Nd:YAG lasers with effective cooling represent the safest approach for the treatment of darker skin
- Complications from laser hair removal are more common in darker skin types
- Pain during laser hair removal is generally a heat related phenomenon and is multifactoral
- Laser treatment of non-pigmented hairs remains a challenge

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History

Human hair, its amount and distribution, plays an important role in defining appearance in contemporary society. Hair also functions in many mammals as a sensory organ, reduces friction in certain anatomic sites, protects against the environment by providing thermal insulation and thermoregulation, aids in pheromone dissemination and plays both social and sexual roles (Wheeland 1997).

Laser hair removal is third most commonly done non-surgical procedure done in cosmetic practices (Hovenic and DeSpain 2011). Individuals seeking consultation for the removal of unwanted body hair may have increased hair in undesirable locations secondary to genetics or medical conditions. These individuals may be classified as having hirsutism or hypertichosis (Azziz 2003). More commonly those seeking hair removal have hair that would be considered normal in distribution and density. However, these individuals for emotional, social, cultural, cosmetic, or other reasons want the hair to be removed (Littler 1999).

There has always been the need for an ideal method of hair removal that is both practical and effective. Traditional hair removal techniques have included shaving, waxing, tweezing, chemical depilation and electrolysis. The use of topically eflornithine 13.9 % has also been used most recently as well.

In the early twentieth century, radiograph machines were widely used for removal of facial

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hair in women. Unfortunately these treatments were associated with a high risk of complications and the potential for subsequent treatment-induced carcinogenesis (Ort and Anderson 1999).

Maiman, using a ruby crystal in 1960, developed stimulated laser emission of a 694 nm red-light. This was the first working laser, and it is from this prototype that today's lasers are derived. Since 1960, research and technical advances have led to modern day lasers. Leon Goldman, the father of laser surgery, published preliminary results on the effects of a ruby laser for the treatment of skin diseases (Goldman et al. 1963). Ohshiro et al. noted hair loss from nevi after treatment with a ruby laser (Ohshiro and Maruyama 1983).

Early reports described the use of a CO_2 laser to eliminate unwanted hair on flaps used for pharyngoesophageal procedures (Kuriloff et al. 1988). A continuous-wave Nd:YAG laser has also been shown to remove hair in urethral grafts (Finkelstein and Blatestein 1990). All of this early work described lasers using ablative techniques with the effect of non-specific vaporization of skin cells. These methods are not commonly used for hair removal today because of their limited effectiveness as well as their commonly induced permanent pigmentary changes and scarring.

The first United States Food and Drug Administration approved laser for hair removal was the Nd:Yag laser in 1995. Subsequently, a plethora of lasers have been developed for laser hair removal (Hovenic and DeSpain 2011).

Selective Photothermolysis

A detailed understanding of laser-tissue interaction emerged in 1983 as the theory of selective photothermolysis was conceived for the laser treatment of pediatric port wine stains (Anderson and Parrish 1983; Moclli et al. 1986).

The theory of selective photothermolysis led to the concept of a laser-induced injury confined to microscopic sites of selective light absorption in the skin, such as blood vessels, pigmented cells, and unwanted hair with minimal damage to the adjacent tissues. To achieve this selective effect, lasers would need to fulfill three requirements:

1. They should emit a wavelength that is highly absorbed by the targeted structure.
2. They should produce sufficiently high energies to inflict thermal damage to the target.
3. The time of tissue exposure to the laser should be short enough to limit the damage to the target without heat diffusion to the surrounding tissues. This is known as the thermal relaxation time (TRT).

These concepts revolutionized cutaneous laser treatment and led to the development of successful laser and light based hair removal devices.

Extended Theory of Selective Photothermolysis

The concept of selective photothermolysis (Anderson and Parrish 1983) emphasizes both the selective damage and minimum light energy requirements seen with current laser technology. However, the use of such a short pulse width laser system may become inapplicable when the target absorption is non-uniform over a treatment area. This may be seen when the actual target exhibits weak or no absorption, yet other surrounding portions of the target exhibit significant absorption. If this is the case, the weakly absorbing part of the target chromophore has to be damaged by heat diffusion from the highly pigmented/strongly absorbing portion of the chromophore (the heater or absorber). Such non-specific thermal damage evokes the concept of thermal damage time (TDT). The TDT of a target is the time required for irreversible target damage with sparing of the surrounding tissue. For a non-uniformly absorbing target structure, the TDT is the time it takes for the outermost part of the target to reach a target damage temperature through heat diffusion from the heated chromophore.

According to the concept of extended selective photothermolysis, target damage can still be selective even though the TDT is many times as long as the thermal relaxation time (TRT) of the actual target.

This new extended theory of selective thermal damage of non-uniformly pigmented structures in biological tissue (Altshuler et al. 2001) postulates that the target is destroyed by heat diffusion from the absorbing chromophore to the target but not by direct heating from laser irradiation as is seen with selective photothermolysis. This theory has now been applied to the treatment of unwanted hair. Ultimately, the use of hair removal lasers expanded rapidly with the subsequent development of appropriate cooling devices that minimized epidermal injury (Ronda and Roland 1999).

Physical Basis of Laser Hair Removal

Successful treatment of unwanted hair is dependent on an understanding of the optical properties of the skin. It is these properties that determine the behavior of light within the hair shaft and bulb, including the relative amount of absorption of incoming photons (Polla et al. 1987).

Different physical factors including delivered fluence, wavelength, pulse duration, and spot size diameter, play an important role in maximizing the efficacy and safety of laser assisted hair removal.

For optimal laser hair removal, one needs to use an optimal set of laser parameters based on anatomic and physical principles. This is determined by a time-temperature combination with the ultimate effect being transfollicular denaturation.

Pulse Duration

Laser pulse width seems to play an important role in laser assisted hair removal (Van Gemert and Welch 1989). Thermal conduction during the laser pulse heats a region around each microscopic site of optical energy absorption. The spatial scale of thermal confinement and resultant thermal or thermomechanical damage is therefore strongly related to the laser pulse width. Q-switched laser nanosecond pulses effectively damage individual pigment cells within a hair follicle by confinement of heat at the spatial level of melanosomes (Zenzie et al. 2000). They can induce leukotrichia and cause a temporary hair growth delay, but do not inactivate the follicle itself (Dover et al. 1989).

On the other hand, lasers with longer pulse durations, not only allow gentle heating of the melanosomes, but also target the entire follicular epithelium by allowing thermal conduction from the pigmented hair shaft and pigmented epithelial cells to the entire follicular structure including the hair bulge.

Therefore, lasers emitting longer pulse durations can achieve two goals: (1) Epidermal melanosomes are preserved. This then helps to preserve the epidermis. (2) Adequate heat diffusion occurs to the surrounding follicle and hair bulge from the light absorbing melanized bulb and shaft.

Terminal hair follicles with a bulb of 300 μm have a thermal relaxation time of 100 ms. Permanent removal requires that follicular stem cells within the bulge be damaged. Insufficient heating will lead to transient loss of hair via induction of catagen phase (Wheeland 1997).

Epidermal melanocytes have a thermal relaxation time between 3 and 10 ms and hair bulbs have a thermal relaxation time between 40 and 100 ms. For optimal effect, it is postulated that a treatment time between 10 and 50 ms may be best.

The use of a longer laser emitted pulse width may necessitate the use of higher fluences because the longer pulse now heats a larger volume of tissue. This may be of some benefit in allowing higher fluences to be used on dark skin types with both less risk of epidermal injury and increased chances of transfollicular damage.

Spot Size

Large diameter laser exposure spots (e.g., >10 mm) are associated with substantially less loss of energy intensity with depth of dermal penetration as compared to small-diameter exposure spots. This is because optical scattering by dermal collagen causes light to diffuse as it penetrates into the dermis. The larger the spot the less is the associated scattering.

Fluence

In general, higher delivered laser fluences lead to better laser hair removal results. However, the higher the utilized fluence, the greater the

discomfort and risk of complications. The effective fluence for any one area of hair is determined mainly by hair color, whereas the tolerated fluence is determined mainly by skin color.

The tolerance fluence can be increased substantially by various means, such as cooling the skin surface before, during, and/or after the optical pulse.

Factors Affecting Efficacy/Results

Hair Color

Hair color is genetically determined, and is a result of both the type and amount of melanin within the hair shaft. Melanin production occurs only during the anagen phase, by melanocytes in the bulb that transfer melanin granules to hair keratinocytes. Distinct types of melanosomes exist in hair of different color. Dark hair contains large numbers of eumelanin granules, whereas, light hair contains mostly pheomelanin. Red hair contains erythromelanin granules that are rich in pheomelanin. In gray hair, melanocytes show degenerative changes such as vacuoles and poorly melanized melanosomes, whereas, in white hair melanocytes are greatly reduced in number or are absent (Hertzberg and Gusck 1970).

Most individuals demonstrate greater melanin density in their hair as compared to their skin epidermis such that the absorption coefficient of the hair shaft and bulb is roughly 2–6 times that of the epidermis. Thus, hair will generally absorb more of the melanin absorbing wavelengths emitted from today's laser and light source hair removal systems.

Thus, color contrast between the epidermis and the hair shaft are paramount in determining the optimal wavelengths and pulse duration for successful treatment. For high contrast (dark hair and light skin) high fluences, shorter wavelengths, and relatively short pulse durations can be used without risking epidermal injury. Conversely low contrast areas (dark hair and dark skin) require lower fluences, longer wavelengths, and longer pulse durations for safe treatment.

Treatment of fair haired individuals is difficult. Exogenous pigments have been tried including dyes and carbon particles, as well as photosensitizers. A recent article on the use of eyeliner or hair dye combined with IPL showed promising results with the majority of patients seeing some improvement (Alijanpoor et al. 2011). Both PDT as well as topical ALA followed by radiofrequency and IPL have been used with some success (Grossman et al. 1995; Goldberg et al. 2005). More recently, melanin encapsulated liposomes have been utilized with disappointing results (Sand et al. 2007).

Growth Centers of Hairs

The hair follicle is a self-regenerating structure and contains a population of stem cells capable of reproducing themselves. It has been noted, at least in animal models, that a complete hair follicle can be regenerated even after the matrix containing hair follicle is surgically removed (Kim and Choi 1995). Although the dermal papilla is not technically part of the actual hair, it remains a very important site for future hair induction, and melanin production in terminal hairs.

Long term hair removal has been traditionally thought to require that a laser or light source impact on one or more growth centers of hair. The major growth centers have always been thought to be in the hair matrix. However, research evaluating growth of new hair has revealed that the matrix is not the only growth center. New hairs may evolve from the dermal papilla, follicular matrix, or the 'bulge' (Oliver 1966a). These stem cells are usually found in a well-protected, highly vascularized and innervated area, often in close proximity to a population of rapidly proliferating cells. They always remain intact and, in fact, are left behind after hair plucking. Stem cells are relatively undifferentiated both ultrastructurally and biochemically (Oliver 1966b). They have a large proliferative potential, and are responsible for the long-term maintenance and regeneration of the hair generating tissue. They can be stimulated to proliferate in response to wounding and certain growth stimuli.

Hair Cycle

All human hairs show various stages of hair growth (Seago and Ebling 1985). It was Dry (1926) who first divided the hair cycle into three

stages; anagen, the period of activity or growth phase; catagen, the period of regression or regression phase; and telogen, the period of quiescence or resting phase.

Anagen growth phase varies greatly (and can last up to 6 years) depending on age, season, anatomic region, sex, hormonal levels, and certain genetic predispositions. It is these variations that have led to the tremendous disparity in hair cycles reported by various investigators (Seago and Ebling 1985; Cotsarelis et al. 1990).

The catagen stage is relatively constant and is generally of 3 weeks duration, whereas the telogen phase usually lasts approximately 3 months.

The overall length of the hair is determined primarily by the duration of the anagen phase. Human hair appears to grow continuously, because the growth cycles of different hair follicles are in dysynchrony with each other.

The histologic appearance of a hair follicle also differs dramatically with the stages of growth (Kligman 1959). The anagen follicle penetrates deepest in the skin, typically to the level of subcutaneous fat. Catagen is characterized by pyknotic changes in the nuclei of the kerotinocytes, followed by apoptosis of the transient portion of the follicle. The entire transient portion (which begins at the level of the insertion of arrector pili muscle and extends to the deepest portion) is absorbed, except for the basement membrane. As the new anagen progresses, the secondary hair germ descends, enlarges, and begin to produce a hair shaft.

Although reports of anagen duration, telogen duration, and the percentage of telogen hairs represent an inexact science, most discussions of laser hair removal take into account different anatomic areas in terms of anagen and telogen cycles.

It is the sensitivity of the anagen hair to a variety of destructive processes including laser and light source damage that leads to a metabolic disturbance of the mitotically active anagen matrix cells. The response pattern is dependent both on the duration and intensity of the insult.

Lin et al. (1998) and Richard and Meharg (1995) postulate that follicles treated in the telogen phase show only a growth delay for weeks, whereas, when those follicles treated in the anagen phase may be susceptible to lethal damage, may have a growth delay, or may simply switch into telogen phase. This could partly explain the growth dynamics of the hair cycle. Repeated treatments could lead to a synchronization of the anagen phase by induction and/or shortening of the telogen phase, which could increase the effectiveness of hair removal with each consecutive treatment. Another explanation might be that the follicle is not destroyed immediately, but shows a growth arrest after only one (shortened) anagen cycle. has questioned the assumption that effective laser hair removal is determined solely by treating hairs in the anagen cycle. She suggests that melanin within a hair follicle may be more important than the actual time of treatment.

Cooling

Laser hair removal associated epidermal cooling can be achieved by various means, including ice (Gilchrest et al. 1982), a cooled gel layer, a cooled glass chamber (Chess and Chess 1993), a cooled sapphire or copper window (Altshuler et al. 1999), a pulsed cryogen spray (Nelson et al. 1995), or solid air flow.

Epidermal melanin and melanized hairs present competing sites for absorption of light energy. Selective cooling is essential to effectively minimize photothermal-induced epidermal adverse effects. In addition, epidermal cooling also permits higher fluences to be delivered to the treated follicular structures. Ideally, the epidermal temperature should be significantly but harmlessly decreased by the cooling procedure, while the target follicular temperature should remain unchanged or changed insignificantly. If this condition is not met, the laser fluences must be increased to compensate for the lower target temperature (Dierickx et al. 1998).

Age

In an isolated study (Schroeter et al. 2003) a significant negative correlation was noted between successful hair removal and the age of the patients, suggesting that hair removal was more effective in younger patients. However, other studies on hair removal have not found age to be a factor in determining efficacy.

Hormones

A number of hormones affect hair growth, with thyroid and growth hormones producing a generalized increased growth in hair (Randall 1994; Deplewski and Rosenfield 2000). Estrogens have only minimal effects on hair growth. Androgens are the most important determinant of the type of hair distributed throughout the body (Uno 1986; Randall 1994; Pans and Cotsarelis 1999). The principal circulating androgen, testosterone, is converted in the hair follicle by 5-alpha reductase to dihydrotestosterone (DHT), which stimulate the dermal papilla to produce a terminal melanized hair. The effect of androgens on hair growth is skin area-specific, due to local variations in androgen receptor and 5-alpha reductase content (Randall 1994; Azziz et al. 2000). While the effect of androgens on hairs (i.e. terminalization of vellus hairs) will be more readily apparent in skin areas with a greater numbers of hair follicles, hair follicle density does not correlate with follicular sensitivity to androgens. Some areas of the body, termed non-sexual skin (e.g., that of the eyelashes, eyebrows, and lateral and occipital aspects of the scalp), are relatively independent of the effect of androgens.

Other areas are quite sensitive to androgens. In these locations hair follicles are terminalized even in the presence of relatively low levels of androgens. Such areas include the pubic area and the axilla, which begin to develop terminal hair even in early puberty when only minimally increased amounts of androgens are observed. Finally, some areas of skin respond only to high levels of androgens. These sites include the chest, abdomen, back, thighs, upper arms and face. The presence of terminal hairs in these areas is characteristically masculine, and if present in women is considered pathological, i.e., hirsutism.

Hirsutism is defined as the presence in women of terminal hairs in a male-like pattern. This affects between 5 and 10 % of surveyed women (Lumachi and Basso 2010; Knochenhauer et al. 1998; Paparodis and Dunaif 2011). Hirsutism above all else, should be principally considered a sign of an underlying endocrine or metabolic disorder, and these patients should undergo a thorough evaluation. The hormonal therapy of hirsutism consists of medications that either suppress androgen production, or block androgen action.

The main purpose of hormonal therapy is to stop new hairs from growing and potentially slow the growth of terminal hairs already present. Although hormonal therapy alone will sometimes produce a thinning and loss of pigmentation of terminal hairs, it generally will not reverse the terminalization of hairs.

Currently Available Lasers and Light Sources Used for Hair Removal

In the US, the Food and Drug Administration (FDA) has traditionally used electrolysis results as a benchmark to evaluate laser treatment efficacy, despite the near lack of significant scientific data about electrolysis. In the initially submitted studies, all hair removal devices were required to show a 30 % decrease in hair growth at 3 months after a single treatment (Tope and Hordinsky 1998).

This criterion clearly does not equate with permanent hair loss, as a delay in hair growth, which usually lasts for 1–3 months is simply consistent with the induction of the telogen stage. Permanent hair reduction results should be based on the cyclic growth phases for hair follicles, and should refer to a significant reduction in the number of terminal hairs after a given treatment. There must be a reduction that is stable for a period of time longer than the complete growth cycle of hair follicles at any given body site (Dierickx et al. 1998).

Multiple laser systems are currently available and approved by the United States Food and Drug Administration (FDA) for hair removal. The lists below includes the more popular systems. It is not meant to be all inclusive.

Ruby Lasers

Ruby lasers (694 nm) are rarely used and no systems are currently being marketed.

The mechanism of ruby laser induction of follicular injury is likely to be thermal, the

precise contributions of photomechanical damage or thermal denaturation to follicular injury are unknown. It is possible that after absorption of radiant energy, the large temperature differences between the absorbing melanosomes and their surroundings produces a localized rapid volume expansion. This would then lead to microvaporiztion or "shock waves", which cause structural damage to the hairs (Anderson and Parrish 1983). On the other hand, thermal denaturation leading to melanosomal damage is also possible. Histologic evaluation of laser treated mouse skin has revealed evidence of thermal coagulation and asymmetric focal rupture of the follicular epithelium (Lin et al. 1998). Secondary damage to adjacent organelles could theoretically result either from thermal diffusion or from propagation of shock waves.

Because of its comparatively short ruby laser wavelength, this hair removal system is best suited for the treatment of dark hair in light skin. It also may be more efficacious than longer wavelength devices for the treatment of light hair or red to red-brown hair (Ross et al. 1999; Campos et al. 1999). Because of the high melanin absorption coefficient at 694 nm, the ruby laser must be used with caution in darkly pigmented or tan patients.

A number of reports have documented the efficacy of ruby laser hair removal invarying types of skin using different laser parameters. The published hair reduction rates have ranged from a 37–72 % reduction 3 months after one to three treatments to a 38–49 % hair reduction 1 year after three treatment sessions (Williams et al. 1998; Sommer et al. 1999; Wimmershoff et al. 2000). As would be expected, multiple treatments at 3–5 weeks intervals produce a greater degree of hair reduction than is seen after a single session (Sommer et al. 1999). In general, higher delivered fluences do lead to better hair removal success, although complications also increase (Dierickx et al. 1998; Campos et al. 2000a).

The use of ruby lasers has fallen out of favor with the advent of newer and more effective technologies for laser hair removal.

Alexandrite Lasers

Several long-pulsed alexandrite lasers (755 nm) are being used for hair removal, including:

Apogee series (Cynosure, Chelmsford, MA)
Arion (Quantel Derma, Erlangen, Germany)
Clearscan ALX (Sciton, Palo Alto, CA)
Elite (Cyanosure, Westford, MA))EpiCare LP/LPX (Light Age, Somerset, NJ)
GentleLase (Candela, Wayland, MA)
GentleMax (Candela, Wayland, MA)
Prowave (Cutera, San Francisco, CA)

The Apogee system (Cynosure) provides pulse durations between 5 and 300 ms, spot size between 5 and 15 mm and fluences up to 50 J/cm^2. A cooling handpiece (SmartCool) blows a continuous flow of chilled air into the treatment area. The scanner option (SmartScan) enables treatment of large areas with an unobstructed view, speedy treatment, and ease of use with minimal operator fatigue.

The Arion (Quantel Derma) can deliver a 5–140 ms pulse duration with spot sizes from 8 to 12 mm and fluences up to 40 J/cm^2. Cooling is via a cold air unit.

The Clearscan ALX (Sciton) can deliver up to a 200 ms pulse duration with spot sizes ranging from 3 mm, 6 mm and scanned pattern of 30 × 30 mm. Fluences can go up to 140 J/cm^2 and the system uses contact cooling.

The Elite (Cynosure) is a two in one alexandrite and Nd:YAG laser. The alexandrite part of the machine provides a 5–15 mm spot size with pulse widths of 0.5–300 ms and fluences of 25–50 J/cm^2. Skin cooling is via cold air.

The Epicare LP/LPX (Light Age) provide a 3–300 ms pulse duration with variable spot size ranging from 3 to 15 mm and 3 to 18 mm respectively. Maximum fluence ranges up to 500–700 J/cm^2 respectively. Cooling is via cold air.

The GentleLase (Candela) delivers a 3 ms pulse duration, spot sizes of 6–18 mm, and fluences ranging from 10 to 100 J/cm^2. It employs a dynamic cooling device (DCD) to protect the epidermis. The DCD cooling method uses short (5–100 ms) cryogen spurts, delivered to the skin surface through an electronically controlled solenoid valve; the quantity of cryogen delivered is proportional to the spurt duration.

The GentleMax (Candela) is similar to the GentleLase (Candela) however also has an Nd:YAG built in. Pulse duration is adjustable from 0.25 to 300 ms with spot sizes 1.5–18 mm and fluences up to 600 J/cm^2. The device uses a dynamic cooling device similar to the GentleLase.

The Prowave (Cutera) is a 770–1,100 nm wavelength machine and provides a variable pulse duration depending on program chosen, however it ranges from 0.1 to 100 ms. The machine has a set spot size of 10×30 mm and can deliver fluences ranging from 5 to 35 J/cm^2.

There are a number of advantages in using long-pulsed alexandrite laser for hair removal. Some of the long-pulsed alexandrite laser systems are compact and can be used in small rooms if adequate ventilation is available. Their flexible fiberoptic arm is easy to manipulate and provides access to hard-to-reach body areas. The large spot sizes and frequency (1–5 Hz) improves the possibility of rapidly treating large body areas.

The alexandrite laser wave length of 755 nm is absorbed about 20 % less strongly by melanin compared with the ruby laser wavelength of 694 nm. Its absorption by the competing chromophore, oxyhemoglobin, is substantially increased as compared to the 694 nm wavelength. However, the longer wavelength of 755 nm penetrates more deeply into the dermis and is less absorbed by epidermal melanin. This theoretically decreases the risk of epidermal damage, especially in individuals with darker skin types.

Because dermal scattering decreases with increasingly longer wavelengths, 755 nm light penetrates deeper into tissue than does shorter wavelengths. In theory, the use of longer wavelengths should increase the ratio of energy deposited in the dermis relative to the epidermis. This would result in relatively increased bulb heating while at the same time promoting epidermal sparing (Ross et al. 1999).

The reported hair removal success rate using an alexandrite laser has ranged from 40 to 80 % at 6 months after several treatments (Boss et al. 1999; McDaniel et al. 1999; Garcia et al. 2000; Gorgu et al. 2000; Lloyd and Mirkov 2000). In a controlled randomized study using a single 20 J/cm^2, 5–20 ms alexandrite laser on various anatomic sites, investigators reported a 40 % reduction in hair growth 6 months after treatment (McDaniel et al. 1999). This increased to >50 % (on the upper lip), if a second treatment was performed after 8 weeks. In another study one treatment with a variable pulsed alexandrite laser produced maximum hair growth reduction at 6 months of 40–56 % for the lip, leg, and back (McDaniel et al. 1999). Finally one study noted a mean 74 % bikini hair reduction 1 year after five alexandrite laser treatments (Lloyd and Mirkov 2000).

Diode Lasers

Diode lasers (800 nm) used for hair removal include:

F1 Diode (Opusmed, Montreal, Canada)
Leda (Quantel Derma, Erlangen, Germany)
MeDioStar XT (Aesclepion, Jena, Germany)
LightSheer Duet (Lumenis, Santa Clara, CA)
Soprano XL (Alma Lasers, Buffalo Grove, IL)

The F1 Diode (Opusmed) has a spot size of 5 or 7 mm and uses pulse durations of 15–40 ms and fluences of up to 40 J/cm^2. Cooling is via a chiller tip.

The Leda (Quantel Derma) has a 50×12 mm or 10×12 mm spot size and uses pulse durations of 6–60 ms and fluences of up to 60 J/cm^2. Cooling is via contact cooling.

The MeDioStar XT (Aesclepion) has a 4×3, 8×6 or 14×10 mm spot size and uses pulse durations of 5–500 ms. Fluences vary depending on spot size, but maximum energy is 210 J/cm^2. The device uses an integrated cold air cooling device.

The Lightsheer Duet is a dual device with both the old Lightsheer chill tip device along with a vacuum assisted larger handpiece. The spot size is either 9×9 or 22×35 mm and fluences can range from 10 to 100 J/cm^2 for the small spot size to 4.5–12 J/cm^2 for the large non cooled vacuum assisted handpiece. Pulse width ranges from 5 to 400 ms. The smaller tip uses contact cooling.

The Soprano XL (Alma Lasers) has a spot size of 12×10 mm and pulse widths of 10–1,350 ms. Fluences can range up to 120 J/cm^2. Cooling is via contact cooling.

Although the myriad diode lasers vary in their delivered energies, spot sizes, pulse duration and associated cooling devices, they all set a popular standard for efficiency, reliability, and portability.

Because of reduced scattering at the longer 810 nm diode wavelengths, light from the diode laser penetrates more deeply into the skin. At 800 nm, 24 % of incident fluence reaches a depth of 3 mm, whereas only 5 % reaches the same depth with 700 nm light (Ross et al. 1999). Also 800 nm energy is 30 % less absorbed by melanin than that of the ruby laser, yet the 800 nm wavelength leads to better optical penetration (Campos et al. 2000b).

In general, the diode laser system has been found to be better tolerated by patients with darker skin types (V-VI) as compared to the ruby laser (Adrian and Shay 2000). This is likely due to its longer wavelength, longer pulse width, and associated active cooling.

In a prospective controlled trial, the 810 nm diode laser demonstrated a significant reduction in hair growth (Lou et al. 2000). Overall, clinical studies with the diode laser system have reported variable success rates ranging from 65 to 75 % hair reduction at 3 months after one to two treatments with fluences of 10–40 J/cm^2. This was increased to >75 % hair reduction in 91 % of subjects 8 months after three to four treatments at 40 J/cm^2 (Williams et al. 1999). As expected, repeated treatments, generally at 4 weeks interval, appears to improve results (Lou et al. 2000).

Nd:YAG Lasers

Millisecond Nd:YAG lasers (1,064 nm) used for hair removal include:

Acclaim (Cynosure, Chelmsford, MA)
ClearScan Yag (Sciton, Palo Alto, CA)
CoolGlide CV/XEO/Excel/Vantage (Cutera, San Francisco, CA)
Cynergy (Cynosure, Chelmsford, MA))
Dualis XP, XP Plus and XS Max (Fotona, Concord, NC)
GentleYAG (Candela, Wayland, MA)
Gemini (Iridex, Mountain View, CA)
LightPod Neo (Aerolase, Tarrytown, NY)
Lyra (Iridex, Mountain View, CA)
MultiFlex (Ellipse, Atlanta, GA)
Mydon (Quantel Derma, Erlangen, Germany)
NaturaLase 1064/LP (Focus Medical, Bethel, CT)
Profile (Sciton, Palo Alto, CA)
SmartEpil (Deka, Florence, Italy)
SP Plus (Fotona, Willmar, MN)
Synchro_FT (Deka, Florence, Italy)
Varia (CoolTouch, Roseville, CA)

The longer Nd:YAG laser wavelength provides deeper penetration, a necessary factor in the attempt to achieve optimal laser hair removal results. In addition, the 1,064 nm wavelength is relatively less absorbed by epidermal melanin than are the 694–810 nm wavelengths. It is this decreased melanin absorption that leads to the greater pigmented epidermal safety seen with these systems.

Although the 1,064 nm wavelength is less well absorbed by melanin than shorter wavelengths, the absorption appears to be enough to achieve the selective photothermolysis of the pigmented hair follicle (Lin et al. 1998). The use of appropriate fluences and effective epidermal cooling devices leads to an effective hair removal device with little risk of complications when such lasers are used correctly. Although the relatively low melanin absorption would appear to be a disadvantage in the treatment of pigmented hair, the Nd:YAG laser's advantage is its ability to reduce the thermal damage of the laser treated melanin containing epidermis. Thus, side effects are decreased in darker skinned patients (Bencini et al. 1999; Russ et al. 2000).

Although Nd:YAG laser treatment usually leads to less dramatic results when compared to other laser systems available for hair reduction, its 1,064 nm wavelength decreased absorption by melanin may also cause a lesser incidence of epidermal side effects, including blistering and abnormal pigmentation (Nanni and Alster 1999). Short-term hair reduction in the range of 20–60 % has been obtained with the long pulsed Nd:YAG lasers (Bencini et al. 1999; Goldberg and Samady 2000).

Early clinical studies have demonstrated less hair reduction/laser session with Nd:YAG lasers

as compared to the published results with either ruby or alexandrite lasers (Goldberg et al. 1997; Bencini et al. 1999; Goldberg and Samady 2000). However, one study showed a 70–90 % hair reduction 12 months after completion of the final treatment in the axilla (Alster et al. 2001).

Q-Switched Nd:YAG Laser

Q-switched Nd:YAG lasers have been used to target topically applied carbon particles that have previously been applied to the hair follicle. This method was one of the first available laser hair removal techniques. This short-term hair removal technique has also been used without the prior application of carbon.

Immediately after Q-switched 1,064 nm laser irradiation of carbon coated hairs, the carbon is heated to its vaporization temperature of about 3,700 °C. Vaporization leads to a huge volume expansion with resultant supersonic proliferation of high pressure waves. These shock waves, in turn, produce mechanical damage, as well as the development of heat. It is not clear how much mechanical and/or heat energy produced by this mechanism is required for destruction of a hair follicle. However, histologic evidence of follicular damage is seen after such a laser exposure. This results in a clinical delay of hair growth.

Depending on the position and amount of the topically applied chromophore, as well as the energy administered, it may be possible to occasionally irreversibly damage a hair follicle even with a Q-switched laser.

Histologic studies have documented the presence of carbon in the follicle after low fluence Nd:YAG lasing. This carbon appears to penetrate superficially in a large number of follicles with and without a hair shaft in place; deep follicular penetration is rare. The disadvantages of this technique, therefore, appear to relate to the fact that that the carbon granules may not consistently reach the requisite hair bulge or bulb.

Different studies have compared the effectiveness of Q-switched Nd:YAG laser hair removal with ruby and alexandrite laser treatments. Millisecond pulse ruby and alexandrite lasers showed greater hair reduction than was seen with Q-switched Nd:YAG lasers. Relatively weak absorption by the innate target chromophore melanin of Q-switched Nd:YAG laser energy translates into less energy available to damage the follicle. Therefore, a lesser hair removal effect is seen.

Several studies have examined the 1,064 nm Q-switched Nd:YAG laser with and without a topically applied chromophore. However, in one controlled study (Nanni and Alster 1997), using a single Q-switched Nd:YAG laser treatment, 100 % hair regrowth was observed at 6 months irrespective of the treatment. Although capable of inducing delayed regrowth, Q-switched Nd:YAG laser treatment appears to be ineffective at producing long-term hair removal.

Intense Pulsed Light Systems (IPL)

Intense pulsed light (IPL) systems are high intensity pulsed light sources which emit polychromatic light in a broad wavelength spectrum of 515–1,200 nm (Lask et al. 1997a). The emitted wavelengths determine not only the absorption pattern of the emitted light but also the penetration depth of the light (Lask et al. 1997b). With the aid of different cut-off filters (515–755 nm), which only allow a defined wavelength emission spectrum, the optimal wavelength spectrum can be filtered to correspond to the depth of the target structure (i.e., hair follicles) (Goldman 1998; Raulin and Greev 2001). Similarly the emitted wavelengths can be adopted to the patient's individual skin type. Higher cutoff filters reduce the emission of melanin absorbing wavelengths; thus being safer for darker skin types (Raulin and Greev 2001).

The pulse duration of IPL systems can be set to a wide range of parameters. The use of single pulses is possible. In the alternative high fluences can be divided into multiple pulses. The intervals between individual pulses can be set at values between 1 and 300 ms. This delay, in theory, allows the epidermis and smaller vessels to cool down between pulses while the heat is retained in the larger target (hair follicles). This results in

selective thermal damage. The extent of maximum delivered fluences and the spot size vary, depending on utilized IPL.

When an IPL is used, a transparent refrigerated gel is placed on the skin to cool the epidermis and to improve light delivery to the skin during treatment. The large rectangular spot sizes associated with most IPL handpieces allows a large number of hairs to be treated simultaneously.

The IPL delivery of a broad range of wavelengths has some advantages. The presence of longer wavelengths provides better penetration depth into the dermis, while shorter wavelengths can be filtered out to protect the epidermis in darker skinned individuals. Shorter emitted wavelengths may also be useful to treat red-brown hair (Ross et al. 1999).

One of the greatest technical advantages of IPL systems is the large exposure area that is used. This improves the resultant damage of deep follicles. A disadvantage is that the rectangular spot size prevents treatment of hair bearing areas on marked convexities or concavities (Ross et al. 1999).

Several studies have demonstrated the long-term efficacy of IPL hair removal devices (Gold et al. 1997; Weiss et al. 1999; Sadick et al. 1999). In one study of 67 subjects of Fitzpatrick skin phototypes I–IV, mean hair loss was 48 % at 6 months or more after a single treatment (Sadick et al. 1999). In another study, after a single treatment, hair reduction ranging from 33 to 60 % was observed at 6 months after treatment (Goldberg et al. 1997; Weiss et al. 1999). Further studies of 14 subjects treated with this technology, followed for >12 months after their last treatment, showed a mean of 83 % hair reduction was obtained after two to six treatments (Sadick et al. 2000). As would be expected, repeated treatments appear to improve outcome (Schroeter et al. 1999). Despite this, some have suggested that more than three IPL treatments do not appear to increase the success rate (Sadick et al. 2000). Not all would agree with this. Finally treatment with IPL, with and without bipolar radiofrequency, has been said to be useful for the treatment of light colored hair (Gold et al. 1999, Schroeter et al. 1999, Sadick et al. 2000). Generally more treatments are required and the results are not expected to be as good as those seen when treating darker colored hairs.

Home Use Devices

In recent years, a number of at home use devices have been developed for purposes ranging from photorejuvenation to laser hair removal. The FDA has cleared a number of devices for at home use for hair removal. A recent article examined the available data and found that the majority of studies done on such devices have been uncontrolled trials with only one randomized controlled study. Efficacy ranged from 6 to 72 % with 3–6 month followup with the majority of side effects being erythema but with blistering, crusting, edema and pigment changes reported (Thaysen-Petersen et al. 2012). Further evaluation is necessary.

Electro-Optical Synergy Device (ELOS)

ELOS devices are relatively new concepts in the treatment of excessive hair. The devices combine both conducted electricity (radiofrequency) with optical devices (laser/light) in order to treat a variety of skin types. The idea is to use the light energy to heat the hair follicle which is then thought to concentrate the bipolar radiofrequency energy in the area resulting in the destruction of the hair follicle. Average clearance was 75 % at 18 months (Waldman and Kreindle 2003).

Advantages

Laser-assisted hair removal is now an accepted successful treatment for the permanent removal of unwanted hair. It has been proven to be more effective than electrolysis and clearly represents the best method for removing large areas of hair in a relatively short period of time.

Previous methods of removing hair including depilatories, plucking, waxing and shaving can lead to irritation of sites. Furthermore, none of these have a long-lasting result.

Disadvantages

The theoretical explanations behind laser assisted hair removal seem logical. However, questions do remain. It is very difficult to predict the ideal patient and ideal treatment parameters for each patient. Even the same patient may respond differently to the same parameters on two different treatment sessions.

It is impossible to estimate the exact amount of energy absorbed by each hair follicle after laser irradiation owing to skin non-homogeneity, multilayering, and anisotrophic physical properties of hair growing at different angles in relation to the laser impact. In addition because growing hair depths vary between 2 and 7 mm depending on the body location, laser absorption characteristics will vary depending on the anatomic site. Finally, the percentage of anagen and telogen hairs varies from site to site, from person to person and from season to season. It is not even clear whether the treatment of anagen as compared to catagen or telogen hairs even matters.

Many studies now show the hair follicle to be an incredibly resilient structure, regrowing after a seemingly lethal injury (Oliver 1967; Reynolds and Jahoda 1991). It is the delivery of adequate fluences, optimizing wavelengths and pulse durations, while reducing unwanted epidermal injuries that leads to the optimal treatments of pigmented hair. Unfortunately the treatment of unwanted light or white hairs remains a challenge.

Indications

Individuals may seek laser hair removal because of excess hair induced by genetics or associated medical conditions such as hypertrichosis, hirsutism or polycystic ovarian syndrome. More commonly laser hair removal patients simply have unwanted hair that would be considered normal in distribution and density. Yet, these individuals for emotional, social, cultural, cosmetic, or other reasons want the hair to be removed. Also, individuals with psuedofolliculitis barbae, a relatively common disorder seen with coarse, curly hairs that occurs in glabrous skin, often seek laser hair removal.

The ideal candidate for laser hair removal is dark haired, fair skinned individual with little melanin within the overlying epidermis. Such patients tolerate the use of more effective higher fluences and relatively shorter wavelengths. In darker skinned individuals it may be preferable to utilize a longer wavelength laser device. Epidermal protection is also afforded by utilizing longer pulse durations and active cooling.

Contraindications

There are a number of relative contraindications that the laser physician should consider before treatment. The physician should ascertain that the patient has realistic expectations from the laser treatment. Patients with a history of hypertrophic or keloidal scarring should be treated more conservatively, using test spots and lower fluences. Likewise, patients with a history of recent isotretinoin use should be treated less aggressively.

Any patient with a history of herpes simplex infections should be given prophylactic antiviral therapy prior to any laser treatment at that anatomic site. Patients who regularly takes aspirin or anticoagulant therapy should discontinue taking these medications at least 10 days prior to treatment, if possible. If these medications are not discontinued, patients may have more bruising, as these medications can predispose to vessel extravasation after treatment. It is recommended that patients having a history of persistent post-inflammatory hyperpigmentation, darkly tanned skin, or skin types greater than Fitzparick phototype III, not be treated with lasers having shorter wavelengths, as such individuals are at a greater risk of post-inflammatory hyperpigmentation.

Patients having photosensitivity disorders, or using systemic medications known to be photosensitizing, should be carefully screened.

Although laser treatment in itself is inherently safe in pregnancy, the treatment does cause pain and can be distressing and is best deferred in some patients until after delivery.

Previous or current use of gold salts can lead to permanent dyschromias upon laser use.

All patients should be instructed to postoperatively avoid sun exposure and wear a broad spectrum sunscreen of SPF 30 or higher on treated exposed areas.

Consent

Informed consent is mandatory and should include treatment options, potential reasonable risks and benefits. One should avoid any guarantees. Figure 4.1 is a suggested consent for laser/light source hair removal

Personal Laser Approach

Alexandrite Laser

Most individuals are no longer using ruby lasers. However, the same general approach to alexandrite laser treatments would apply of the ruby laser was used for hair removal in lighter skin types. We have found the alexandrite lasers to be very helpful in treating Fitzpatrick I-III skin phenotypes (Figs. 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 4.10, 4.11, 4.12, 4.13, and 4.14). Although it has been suggested that alexandrite lasers, with their longer 755 nm wavelength, are safer in treating darker complexions than are ruby lasers, we have not consistently found this to be the case. It would appear that the ability to treat darker complexions with alexandrite lasers may be more related to the longer pulse durations emitted by some of these systems. It should be noted that unless appropriate cooling is utilized, some Fitzpatrick skin phenotype III and even suntanned type II complexioned individuals tend to have postinflammatory pigmentary changes after laser treatment.

Diode Laser

We have found the 810 nm diode lasers very useful in treating Fitzpatrick I–IV skin phenotypes (Figs. 4.15, 4.16, 4.17, and 4.18). The laser should always be used with a cooling device. When used with the longer emitted 30 ms pulse durations, some darker Fitzpatrick skin phenotypes can be treated with a lessening of postinflammatory pigmentary changes. Diode systems are small, portable and very user-friendly.

As a general rule, somewhat lower fluences are required for effective hair removal than are required with the ruby lasers. This may be related to the deeper penetration of the 800 nm wavelength.

Nd:YAG Laser

We have found the nanosecond Q-switched Nd:YAG lasers to be highly effective in inducing temporary short-term hair removal. Skin cooling is not required when a nanosecond laser is used. This contrasts with the requisite need for some form of epidermal cooling with virtually all millisecond hair removal lasers.

When the Q-switched Nd:YAG laser technique is utilized with a topical carbon suspension, there is often a greenish hue to the area being treated when visualized through goggles. This is presumably due to the interaction between the 1,064 nm wavelength and the carbon chromophore. When the 1,064 nm Q-switched Nd:YAG laser is used without topical carbon chromophore, dark terminal hairs often turn white on laser impact. Usually no post-treatment crusting is noted. Erythema may vary from non-existent to significant in its extent. It is quite safe to treat individuals who have darker complexions with nanosecond Q-switched Nd:YAG laser.

Millisecond Nd:YAG laser systems are the safest laser hair removal systems for Fitzpatrick skin types V–VI (Figs. 4.19 and 4.20). Although they can also be used for lighter skin types, we have not found the same degree of success when these lasers are compared to the shorter wavelength systems. Although postinflammatory pigmentary changes from this laser are rare, such changes can be occasionally expected in some individuals with dark complexions.

OPERATIVE CONSENT: LASER/LIGHT SOURCE HAIR REMOVAL

Patient _____ Date_____

I am aware that laser/light source hair removal is a relatively new procedure. My doctor has explained to me that much of what has been written about these methods in newspapers, magazines, television, etc. has been sensationalized. I understand the nature, goals, limitations, and possible complications of this procedure, and I have discussed alternative forms of treatment. I have had the opportunity to ask questions about the procedure, its limitations and possible complications (see below).

I clearly understand and accept the following:

1. The goal of these surgeries, as in any cosmetic procedure, is improvement, not perfection.
2. The final result may not be apparent for months postoperatively.
3. In order to achieve the best possible result, more than one procedure will be required. There will be a charge for any further operations performed.
4. Strict adherence to the postoperative regimen (i.e. appropriate wound care and sun avoidance) is necessary in order to achieve the best possible result.
5. The surgical fee is paid for the operation itself and subsequent postoperative office visits. There is no guarantee that the expected or anticipated results will be achieved.

Although complications following laser/light source hair removal are infrequent, I understand that the following may occur:

1. Bleeding which in rare instances could require hospitalization.
2. Infection is rare but should it occur, treatment with antibiotics may be required.
3. Objectionable scarring is rare, but various kinds of scars are possible.
4. Alterations of skin pigmentation may occur in the areas of laser surgery. These are usually temporary, but rarely can be permanent.
5. A paradoxical increased hair growth may occur at or near treated sites. This generally responds to further treatments.

.

This authorization is given for the purpose of facilitating my care and shall supersede all previous authorizations and/or agreements executed by me. My signature certifies that I understand the goals, limitations and possible complications of laser surgery, and that I wish to proceed with the operation.

_____
Patient

_____ _____
Witness Date

Fig. 4.1 Consent form

IPL

We have found intense pulsed light sources to be useful in treating Fitzpatrick I and IV skin phenotypes. (Figs. 4.21, 4.22, 4.23, and 4.24) Although some IPL sources are FDA cleared in the USA for Fitzpatrick skin phenotypes V, we have found that the incidence of postinflammatory changes may be too high for practical use in some of these individuals. In choosing emitted

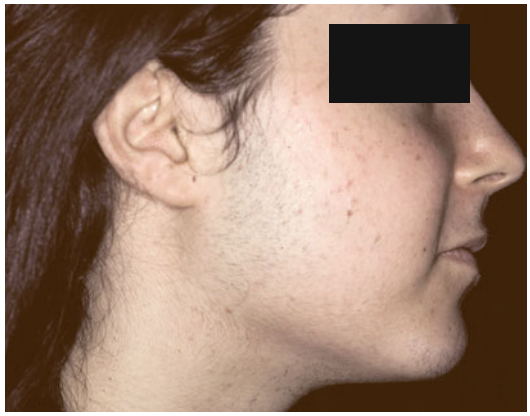

Fig. 4.2 Before alexandrite laser hair removal

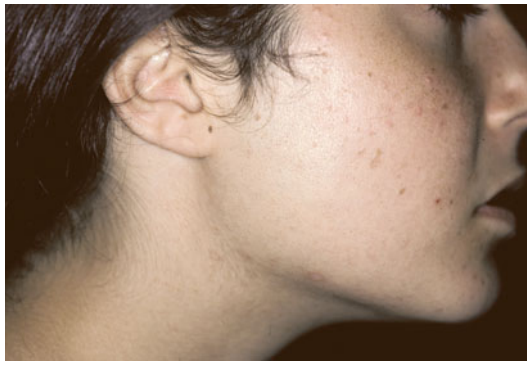

Fig. 4.3 6 months after 5 alexandrite hair removal sessions

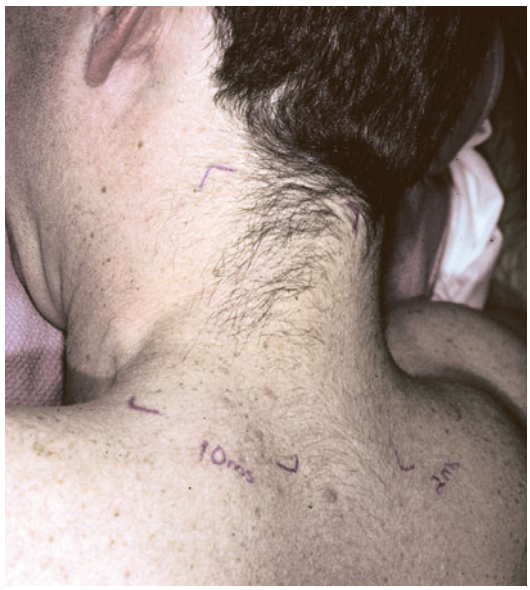

Fig. 4.4 Before alexandrite laser hair removal

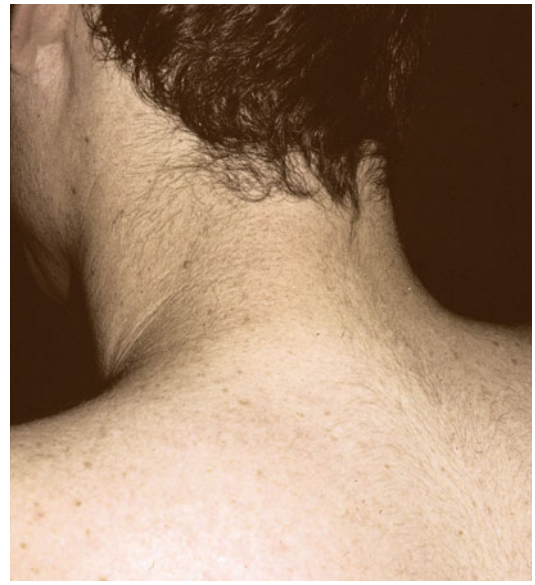

Fig. 4.5 6 months after 5 alexandrite hair removal sessions

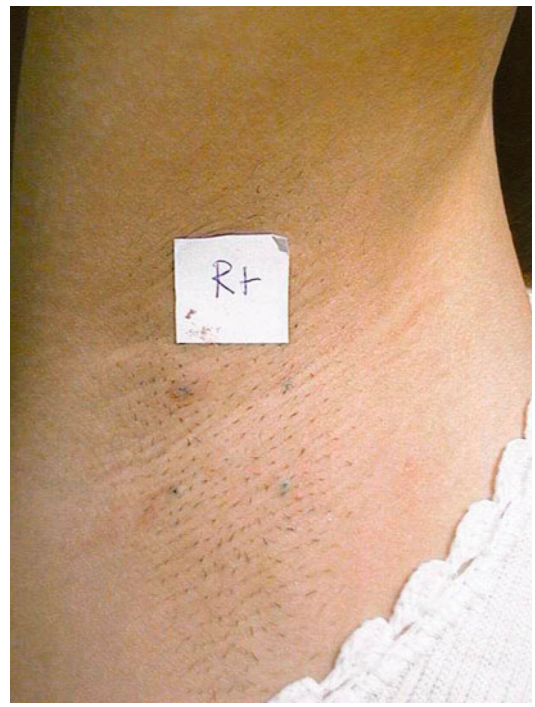

Fig. 4.6 Before alexandrite laser hair removal

pulse durations, we have noted that shorter pulse durations are more helpful for finer hairs, while longer pulse durations appear to have greater

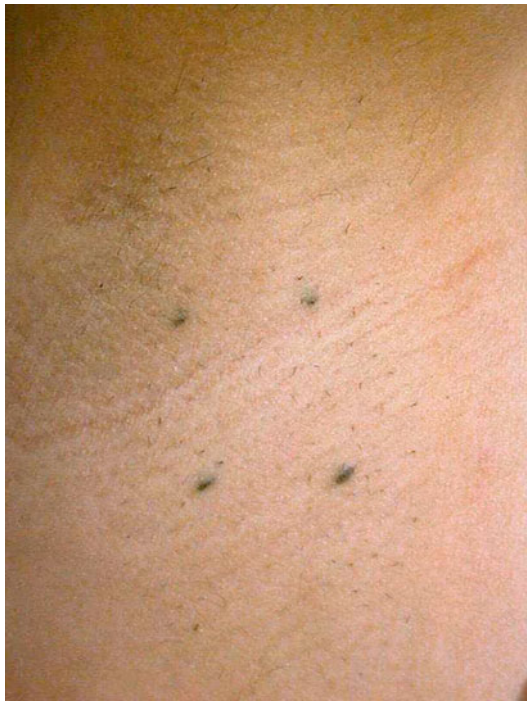

Fig. 4.7 6 months after 3 alexandrite hair removal sessions

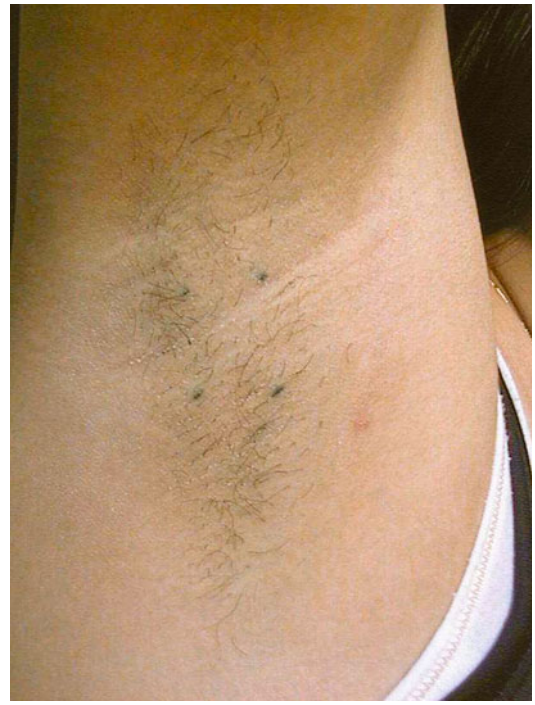

Fig. 4.9 Before alexandrite laser hair removal

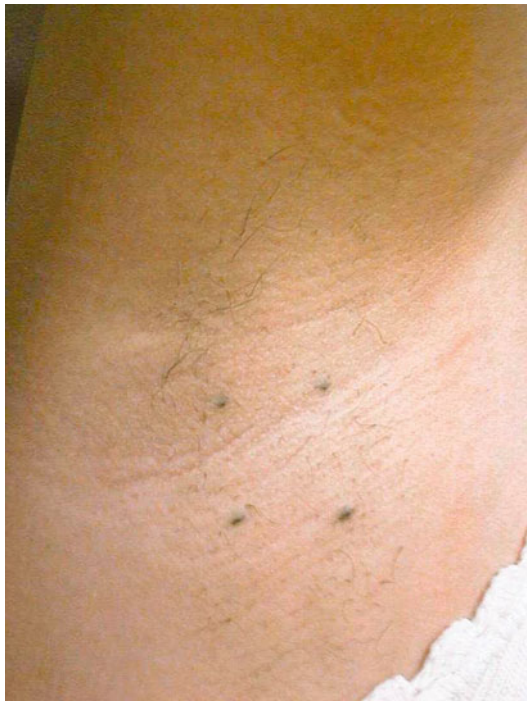

Fig. 4.8 9 months after 3 alexandrite hair removal sessions

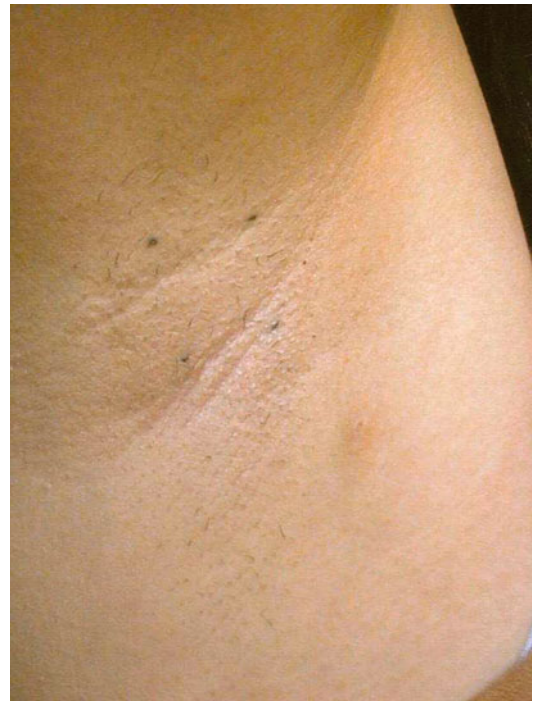

Fig. 4.10 6 months after 3 alexandrite hair removal sessions

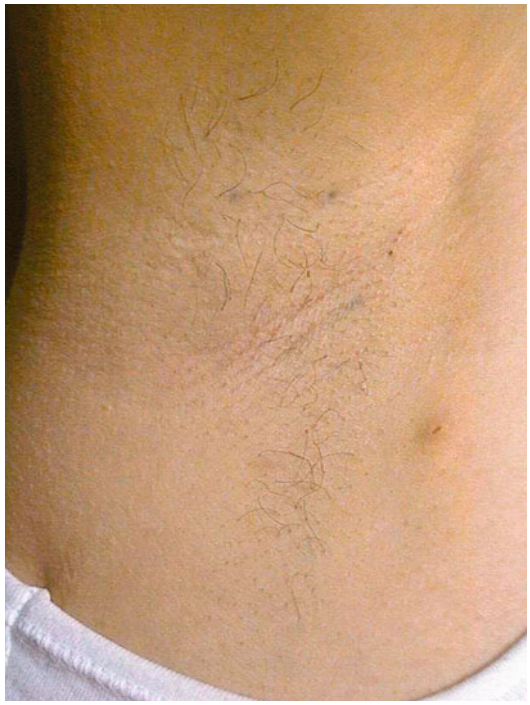

Fig. 4.11 9 months after 3 alexandrite hair removal sessions

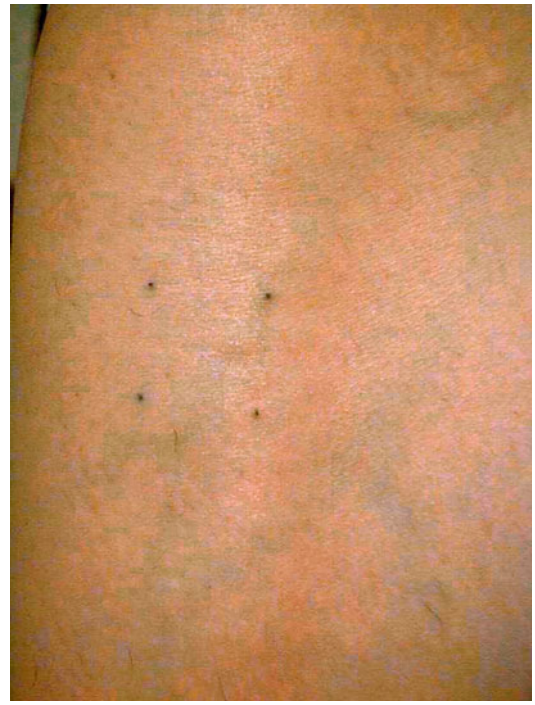

Fig. 4.13 6 months after 3 alexandrite hair removal sessions

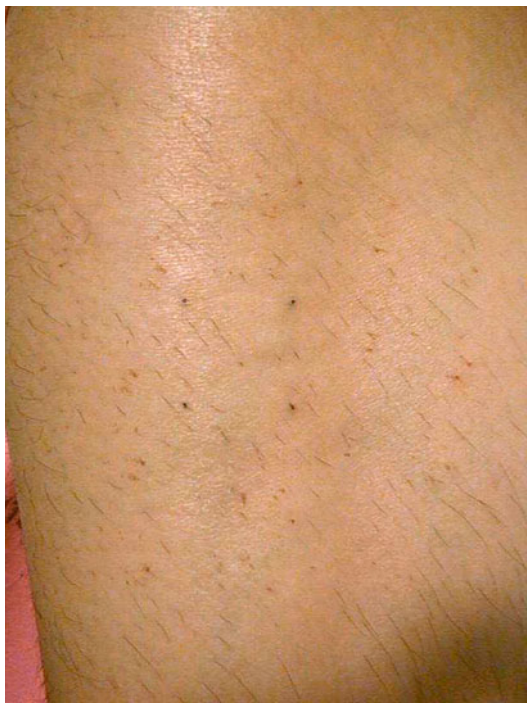

Fig. 4.12 Before alexandrite laser hair removal

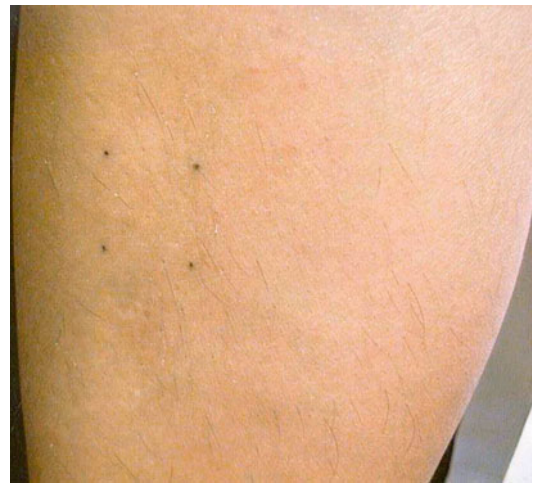

Fig. 4.14 9 months after 3 alexandrite hair removal sessions

efficacy in treating thicker hairs. In addition, longer pulse durations, because of their epidermal pigment sparing capacity, are chosen for darker skin phenotypes. The choice of pulsing mode and interpulse times are also dictated by

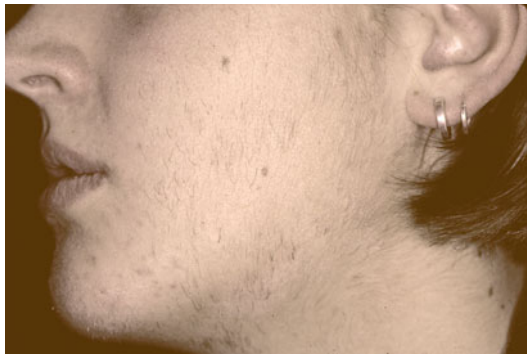

Fig. 4.15 Before diode laser hair removal

Fig. 4.16 6 months after 2 diode hair removal sessions

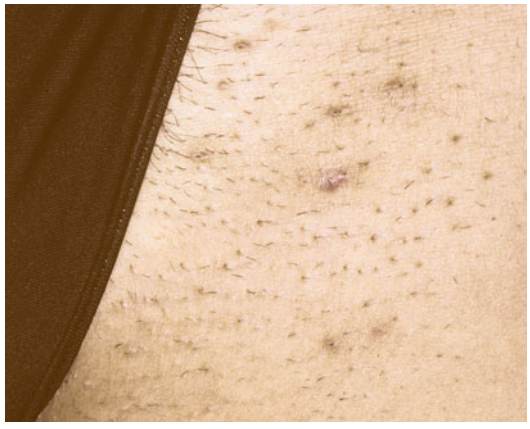

Fig. 4.17 Before diode laser hair removal

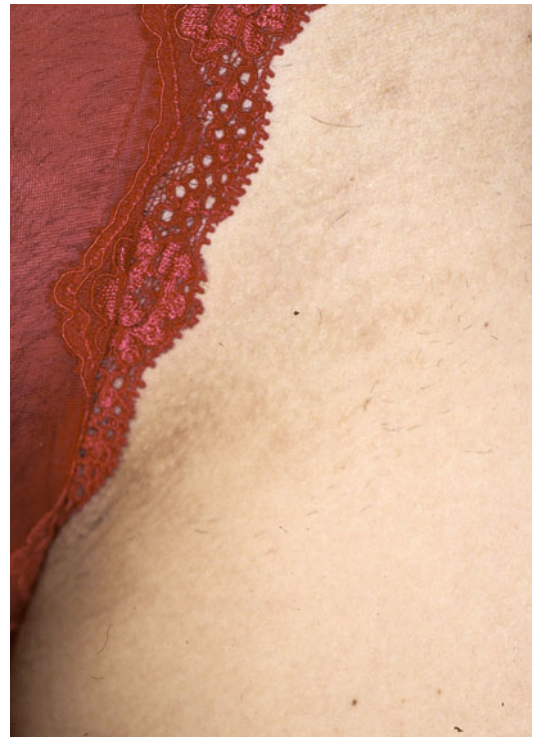

Fig. 4.18 6 months after 5 diode hair removal sessions

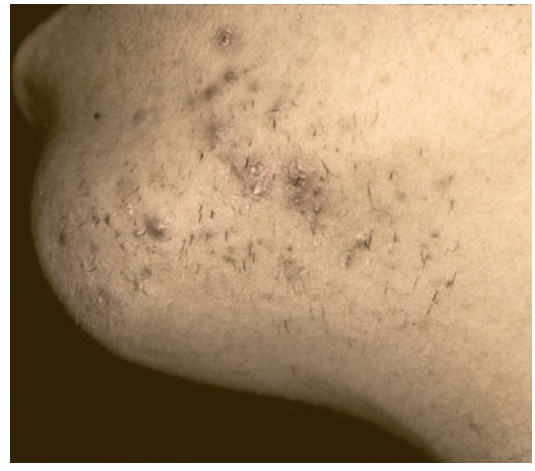

Fig. 4.19 Before Nd:YAG laser hair removal

complexion. Darker complexions are usually treated with a double/triple pulse and longer interpulse times, in comparison with the parameters chosen with lighter skin complexions. As is true for all lasers used for hair removal, the higher the fluences, the better the results. The fluence chosen should be as high as can be tolerated without creating an epidermal blister.

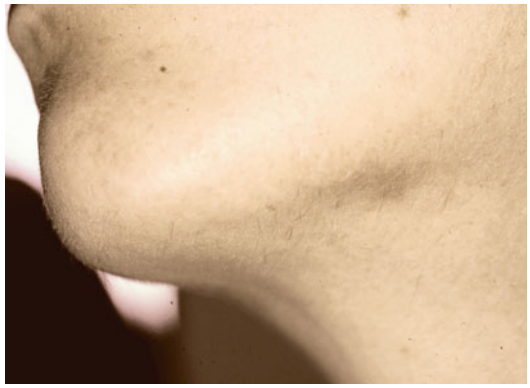

Fig. 4.20 6 months after 5 Nd:YAG hair removal sessions. Note not only decreased hair but also improvement in pseudofolliculitis barbae

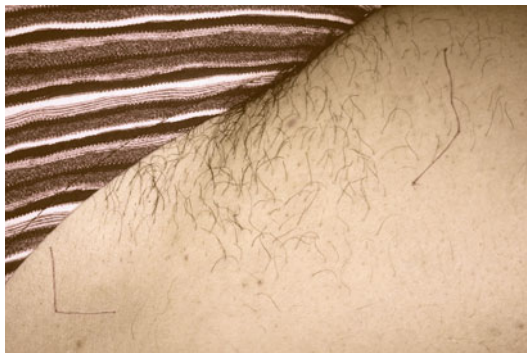

Fig. 4.21 Before IPL hair removal

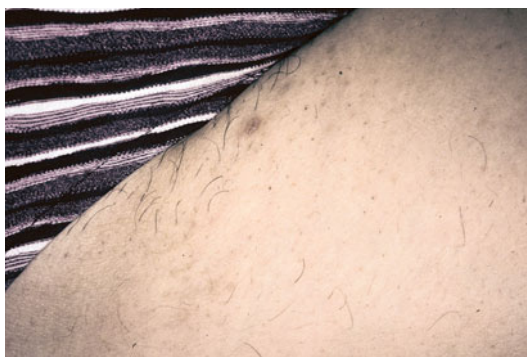

Fig. 4.22 6 months after 3 IPL hair removal sessions

Intense pulsed light sources have shown the greatest safety when used with optimal skin cooling.

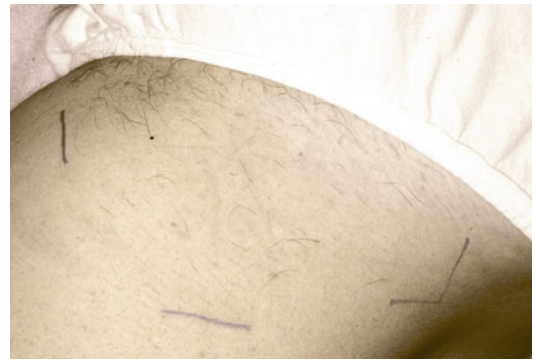

Fig. 4.23 Before IPL hair removal

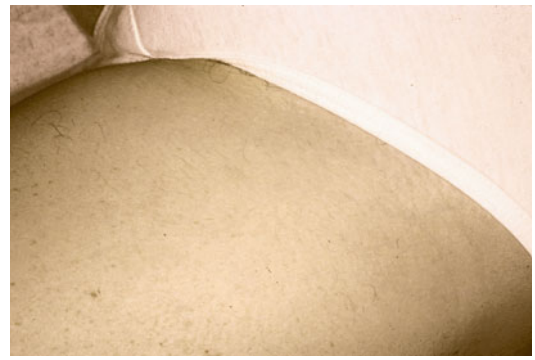

Fig. 4.24 6 months after 3 IPL hair removal sessions

Treatment Approach

The hair removal treatment technique with all lasers and intense pulsed light sources commences with pre-operative shaving of the treatment site. This reduces treatment-induced odor, prevents long pigmented hairs that lie on the skin surface from conducting thermal energy to the adjacent epidermis, and promotes transmission of laser energy down the hair follicle. A small amount of post-treatment crusting and erythema is to be expected. In darkly pigmented or heavily tanned individuals, it may be beneficial to use topical hydroquinones and meticulous sunscreen protection for several weeks prior to treatment in order to reduce inadvertent injury to epidermal pigment. Individuals with recent suntans should not be treated until pretreatment hydroquinones have been used for at least 1 month. Postinflammatory

pigmentary changes still are to be expected in individuals who have darker complexions.

All of the lasers and intense pulsed light sources described in this chapter, when used with almost all fluences, can lead to temporary hair loss at all treated areas. However, choosing appropriate anatomic locations and using higher fluences will increase the likelihood of permanent hair reduction after multiple treatments. Even though permanent hair loss is not to be expected in all individuals, lessening of hair density and thickness is an expected finding.

The ideal treatment parameters must be individualized for each patient, based on clinical experience and professional judgment. For individuals who have darker complexions, the novice might consider delivering the laser energy in several individual test pulses at an inconspicuous site with lower energy fluences. The delivered energies are then slowly increased. Undesirable epidermal changes such a whitening and blistering are to be avoided.

Prolonged and permanent hair loss may occur following the use of all the aforementioned described millisecond systems. However, great variation in treatment results is often seen. Most patients with brown or black hair obtain a 2–6 months growing delay after a single treatment. There is usually only mild discomfort at the time of treatment. Pain may be diminished by the use of topical or injected anesthetics.

Transient erythema and edema are also occasionally seen and irregular pigmentation of 1–3 months duration is often noted. These changes are far less common after treatment with an Nd:YAG laser. Permanent skin changes, depigmentation, or scarring is rare.

Finally, it is true for all hair removal lasers that the higher the delivered fluences, the better the results. The fluence chosen should be as high as can be tolerated without creating an epidermal blister.

Post-operative Considerations

The use of ice packs may reduce postoperative pain and minimize swelling. Analgesics are usually not required unless extensive areas are treated. Prophylactic courses of antiviral agents should be considered in patients with a history of herpes simplex infections in the to be treated area. Topical antibiotic ointment applied twice daily is indicated if post-treatment epidermal injury occurred. Mild topical steroid creams may be prescribed to reduce swelling and erythema. Any trauma, such as picking or scratching of the area, should be avoided. During the first week of healing, sun exposure should be avoided or sunblocks used. Make-up may be applied on the next day unless blistering or crusts developed. The damaged hair is often shed during or after the first week of the treatment. Patients should be reassured that this not a sign of hair regrowth.

Complications

The incidence of cutaneous adverse effects, after laser hair removal, is both patient and laser parameter related. Patients with darker colored skin, especially skin type V and VI, are more likely to experience cutaneous adverse effects, related to the abundance of melanin in their epidermis. However, such complications are not limited to patients with genetically determined dark skin. This may also be seen in patients with darker skin due to other reasons, such as suntanning and lentiginous photoaging. The incidence of adverse effects will be modified by utilized wavelength, fluence, pulse duration and associated cooling.

Pigmentary Changes

There is a remarkable variation in the reported incidence of post-operative pigmentary changes after laser hair removal. Unfortunately most studies have not been carried out under standardized conditions. In different studies, varied laser parameters have been used, follow up periods have varied from 90 days to 2 years, and the preoperative skin characteristics were not standardized (hair color, skin pigmentation, anatomical region). Finally, the majority of studies estimate the incidence of side effects by subjective clinical evaluation.

In general, laser-induced pigmentary changes depend on the degree of preoperative pigmentation. (Haedersdal et al. 1999) Lighter skin types potentially experience more post-operative hyperpigmentation. Darker skin types experience more sub-clinical hypopigmentation. This finding is in accordance with the fact that laser light in dark skinned types is strongly absorbed by the epidermal melanin, leading to potential melanocytic damage (Anderson 1994). Conversely, thermal effects in lighter skin may provoke post-inflammatory hyperpigmentation.

Hypopigmentation

Transient post treatment hypopigmentation occurs in 10–17 % of patients (Grossman et al. 1996; Bjerring et al. 1998; Williams et al. 1998). The exact etiology of post-laser hair removal induced hypopigmentation is unclear, but may be related to the destruction of melanocytes, suppression of melanogenesis, or the redistribution of melanin in the keratinocytes.

Hyperpigmentation

Transient post treatment hyperpigmentation occurs in 14–25 % of patients (Grossman et al. 1996; Bjerring et al. 1998; Williams et al. 1998), and is normally related to melanocytic-induced stimulation. The causes of this hyperpigmentation include delayed tanning, epidermal injury, or an immediate pigment darkening phenomenon resulting from photo-oxidation of pre-existing melanin. The darkening is usually transient, lasting only 3–4 weeks and resolves without sequel in most individuals (McDaniel 1993; Wheeland 1995).

A potentially more serious hyperpigmentation resulting from epidermolysis and blistering can occur at energy thresholds higher than those associated with immediate pigment darkening. This can be associated with permanent dyschromia.

Dyschromia may also occur in individuals with a previous history of gold salt intake before or during the use of lasers. Such dyschromias may be permanent and previous or current use of gold salts should be considered a contraindication.

Pain

Laser and light source heat induced destruction of hair follicles is not pain free, as the hair follicle is well endowed with pain fibers arranged in a well-organized neovascular bundle. The intensity of pain varies with the delivered fluence, utilized wave length, pulse duration, spot size, repetition rate, laser interpulse spacing, and skin pigmentation. Regional body areas such as the lip and groin, and chronically sun-exposed and tanned areas, also have been associated with greater amounts of pain perception. In addition, with increasing pulse duration, heat diffusion is likely to raise the temperature around the follicle and increase the level of pain. Finally, pain can be perceived differently at different times of the month. During menstruation, the skin appears to be more sensitive to pain and laser hair removal can be more uncomfortable.

Scarring and Textural Changes

Despite the presence of severe macroscopic cutaneous damage, collagen and elastin networks in the dermis are found to be normal in the majority of the laser hair removal treated patients (Liew SH et al. 1999). Scarring can occur, but is rare.

Effects on Tattoos and Freckles

Lightening of tattoos, and loss of freckles or pigmented lesions, after laser assisted hair removal is common. Patients should be made aware of this possibility.

Acneiform Eruption

After treatment, a transient acneiform eruption can occur in anywhere between 3 and 16 % of treated patients. This seems to be more common

in patients treated with the Nd:YAG laser (Carter and Lanigan 2006).

Infections

Herpes simplex infections are uncommon after laser and light source treatment of hair removal, but may occur especially in patients with strong prior history of outbreaks. Eruptions most commonly are seen on or around the lip. Although the risk of bacterial infection is extremely low, it may occur if there is laser induce epidermal damage.

Plume

The plume generated by the vaporized hair shaft has a sulphur smell and in large quantities can be irritating to the respiratory tract. A smoke evacuator is advised.

The Future

The incredible amount of attention attracted by laser and light source hair removal techniques reflects a demand for more practical, tolerable, effective, and safer epilation technique. At this time, effective light and white hair removal techniques do not exists. Research into techniques that light activate hair may be a part of the future treatment of non-pigmented hairs.

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Ablative and Non-ablative Fractional Resurfacing

5

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Core Messages

- Fractionated laser resurfacing leads to improvement of photodamaged skin, rhytides and acne scars.
- In contrast to non-fractionated ablative laser resurfacing, fractionated ablative laser resurfacing is associated with lower risk of complications and less downtime.
- Compared to fractional non-ablative resurfacing, fractional ablative laser resurfacing is more effective and does not require as many treatments.
- When used with caution, fractionated ablative and fractionated non-ablative laser resurfacing is safe and effective for patients with higher Fitzpatrick skin types.

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History

Non-fractionated ablative resurfacing was first introduced in the mid-1990s. Technological advancements with carbon dioxide (CO_2) lasers had emerged to minimize their thermal impact on tissue and, subsequently, possible clinical uses were explored. Two types of CO_2 lasers were developed. The first utilized ultra-short pulse durations to minimize heat deposition in the tissue (Fitzpatrick et al. 2000). The other utilized the laser beam in a continuous wave (CW) mode in conjunction with a scanning device, to shorten the laser dwell time and, thereby, minimize thermal damage (Lask et al. 1995). These lasers were first used for the treatment of deep rhytides and acne scars; however, investigators soon discovered that superficial sun damage changes, including lentigines, as well as actinic keratoses, fine lines, and other superficial imperfections also improved. Additionally, the deposition of heat was noted to exert a tissue tightening effect, which softened deeper wrinkles (Fitzpatrick et al. 2000). The CO_2 laser proved to be very effective; however, as the technology expanded into the dermatologic and plastic surgeon's realm, it was found to have significant side effects, especially in inexperienced hands. Many patients experienced erythema that lasted for weeks to months as well as temporary hyperpigmentation, acne, and contact sensitivity to topical products. Yeast, bacterial, and viral infections were also a potential problem. Prolonged dyspigmentation and scarring, although infrequent, were also of great concern

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(Monheit 1995; Christian et al. 2000; Lewis et al. 1996; Nanni et al. 1998; Sriprachya-Anunt et al. 1997; Sriprachya-Anunt et al. 2002).

In an effort to decrease the risk/side effect profile, the use of erbium lasers was explored (Teikemeier et al. 1997; Zachary 2000). These short-pulsed lasers, with stronger water absorption at 2,940 nm were less injurious to deeper tissues; they ablated tissue but left little residual thermal damage (Walsh et al. 1989; Kaufmann et al. 1994). Unfortunately, it became apparent that this laser, although good for smoothing out the surface, did not lead to the same tightening effect as was noted with the CO_2 lasers (Fitzpatrick et al. 2000). Furthermore, the lack of residual thermal damage with the short pulsed Er:YAG laser allowed for a high rate of water loss from the skin surface, which produced greater immediate oozing and postoperative discomfort (Kaufmann et al. 1994; Ross 2009). The next level of advancement entailed increasing the pulse width of the erbium lasers to include some deposition of heat, which would allow tightening and improved coagulation (Pozner et al. 2000; Walsh 1989). In addition, lasers were developed that combined both erbium and CO_2 lasers to allow heat deposition by the CO_2 component as well as pure ablation by the erbium component. The potential benefit was great; however, side effects such as prolonged erythema, infection, bleeding, and postinflammatory pigmentation continued to be present (Lewis 1996; Tanzi et al. 2003).

A device utilizing another wavelength highly absorbed highly by water was subsequently developed. The erbium:yttrium-scandium-gallium-garnet (Er:YSGG) laser produces a 2,790 nm laser wavelength with a tissue absorption coefficient roughly five times that of the CO_2 10,600 nm wavelength and one third of that of the Er:YAG wavelength. When deployed with a pulse width of 200–800 μs, it shows an ablation threshold of about 3 J/cm^2 (Ross 2009). Given its unique water absorption coefficient, its laser beam offers a greater zone of coagulation than short-pulsed erbium devices but a narrower zone of coagulation than carbon dioxide systems. As such, it promised less bleeding and greater collagen remodeling than Er:YAG resurfacing but potentially fewer side effects such as pigmentation and scarring compared to CO_2 resurfacing. Early studies have shown promise for the treatment of photodamage, but its clinical superiority to CO_2 and erbium:YAG resurfacing has yet to be demonstrated (Ross 2009; Walgrave 2012).

To address the side effects associated with ablative resurfacing, a host of non-ablative technologies utilizing mid-infrared wavelengths emerged that targeted structures in the dermis and spared the epidermis. They included the 1,064 nm Nd:YaG, 1,320 nm Nd:YAG, and the 1,450 nm diode lasers. Although these devices significantly reduced downtime, their efficacy was often limited, with clinical benefit being mild to moderate at best (Ciocon et al. 2011; Goldberg 1997, 1999; 2000, 2001; Goldberg et al. 2002). Furthermore, these modest benefits were only appreciable after multiple treatments. For this reason, attention was turned in the early 2000s to developing devices that combined short post-procedure downtimes with greater and more immediate efficacy, using devices that achieved controlled but aggressive resurfacing.

In 2003, the innovative concept of fractional photothermolysis (FP) was reported (Huzaira et al. 2003) and followed by Manstein and colleagues in 2004 with their original prototype FP device (Manstein et al. 2004). With this modality, small columns of thermal injury known as "microthermal zones" (MTZs) were produced by light energy delivered in a pixilated fashion to the skin. This fractional emission of light differed from traditional ablative resurfacing, in which a uniform patch of epidermal and dermal injury was delivered by a flat, non-fractionated beam. With these initial prototype devices, the deep epidermis and dermis became necrotic in the individual microthermal zones, without being vaporized, and the stratum corneum remained histologically intact. This resulted in a "biologic bandage" on top of a zone of remodeled and coagulated collagen; as such, resurfacing with these initial fractional devices was termed "nonablative" and could be delivered using wavelengths only moderately absorbed by water (1,410, 1,440, 1,540, 1,550 nm) (Bogdan 2010).

Because fractional photothermolysis produces microscopic zones of thermal injury, the surrounding islands of normal tissue serves as a reservoir for re-epithelization (Laubach et al. 2006). More specifically, the photocoagulated collagen in the dermis serves as a stimulus for producing new collagen, while photocoagulated lower epidermis is replaced by the untreated epidermal periphery (Laubach et al. 2006). Histological studies demonstrate full epidermal healing occurring within the first 24 h after the procedure (Laubach et al. 2006). This rapid barrier restoration lowered the risk of infection, erythema, post-inflammatory pigmentation and other complications frequently associated with ablative resurfacing procedures (Bodgan 2010). Although results were far superior to the non-fractionated nonablative technologies, multiple treatments, typically in the range of five to seven, were needed.

Following the studies using non-ablative fractionated lasers, in 2007 Hantash et al. first described the use of an "ablative" CO_2 fractional photothermolysis device (AFP) (Hantash et al. 2007). Similar to the fractional non-ablative laser, the device produced an array of microthermal zones, but instead with a confluent pattern of ablation and coagulation extending from the stratum corneum through the dermis (Hantash et al. 2007). Various fractional ablative devices have been developed since the introduction of this prototype, using wavelengths highly absorbed by water. Among them are the fractionated the fractionated carbon dioxide (CO_2; 10,600 nm) laser, the fractionated erbium yttrium aluminum garnet (Er:YAG; 2,940 nm) laser, and most recently, the fractionated yttrium scandium gallium garnet (YSGG; 2,790 nm) laser (Ciocon et al. 2011). Most are FDA approved to treat wrinkles, rhytides, furrows, fine lines, textural irregularities, pigmented lesions, acne scars, and vascular dyschromia (Bodgan 2010).

In 2009, Hruza and colleagues introduced the fractional radiofrequency (RF) device, the first non-laser, non-light-based device capable of inducing fractional skin ablation, coagulation, necrosis, for skin rejuvenation (Hruza et al. 2009). Brightman applied the term "sublative rejuvenation" to this technology, as it produces limited epidermal disruption with coagulative effects concentrated in the mid to deep dermis. Compared to lasers, RF energy produces higher volumetric heating through tissue impedance, which allows the diffusion of heat to deeper tissues (Brightman et al. 2009). With the development of fractionated laser delivery, its application to the treatment of various skin conditions with mid to deep dermal pathology has been explored, including deep acne scars and rhytides. Furthermore, this technology holds the greatest promise for the fractional resurfacing of patients with darker skin types (Taub and Garretson 2011). Since the epidermis is mostly spared, fractional radiofrequency lowers the risk of scarring and post-inflammatory pigmentation. Below we review various fractional resurfacing devices and their use with regard to indications, benefits, risks, and treatment techniques.

Fractionated Resurfacing Currently Available Technology

Multiple devices utilizing ablative or non-ablative fractional photothermoysis are now available. These devices differ in the type of wavelength used (2,790, 2,940, and 10,600 nm for ablative fractional resurfacing devices and 1,410, 1,540, 1,550, and 1,927 nm for non-ablative resurfacing devices), pulse energy range, damage pattern (stamping, scanned, or continuous motion) and pulse width (Bodgan 2010). With regard to fractional ablative devices, increasing energy increases the width and depth of the zones of ablation and coagulation of tissue, which in turn, leads to an increase the time required for edema and erythema to resolve (Tierney et al. 2011). When treating areas with thinner skin (eyelids and neck), it is important to use lower energies (Tierney et al. 2011; Tierney and Hanke 2009). In general, long pulse durations result in more collateral heating of the tissue, which results in wider microthermal zones. Although this leads to improved coagulation and collagen remodeling, it may also leads to a higher risk of epidermal

injury, as well as the persistence of a visible grid-like pattern on the skin following treatment (Tierney et al. 2011).

Among the most widely used of non-ablative fractional photothermolysis devices (Fraxel re:store, Reliant Technologies, Mountain View, CA) is a fiber optic erbium doped YAG laser utilizing a wavelength of 1,550 nm. The laser hand piece is equipped with an "intelligent" optical tracking device that calculates the speed of the operator's hand against the background skin to adjust for the inconsistencies in operator hand speed. This ensures that the same number of microthermal zones are placed per given area, despite differences in hand velocity. (Ciocon and Rokhsar 2007). The laser is currently FDA approved for treatment of periorbital wrinkles, acne and surgical scars, skin resurfacing procedures, dermatologic procedures requiring the coagulation of soft tissue, as well as photocoagulation of pigmented lesions such as lentigines and melasma (Bogdan 2011).

The advantages to the fractional approach to resurfacing are numerous, both from a theoretical and practical perspective. First and foremost, unlike those treated with the ablative carbon dioxide or erbium laser, patients do not have open wounds, minimizing downtime. Second, potential complications associated with open wounds such as infection and hyper/hypopigmentation and scarring are minimized. Since a significant percentage of the epidermis is left intact, enough viable appendageal structures remain to promote wound healing (Ciocon and Rokhsar 2007). Third, water is the chromophore, so tissue interactions, both in the epidermis as well as the dermis, are relatively uniform. Finally, and most important, anatomic areas highly prone to scarring with traditional ablative resurfacing lasers such as the neck, chest, trunk, and hands can be safely and aggressively treated (Ciocon and Rokhsar 2007). Typically, with carbon dioxide/erbium laser resurfacing, one ablates tissue to a depth of approximately 200–400 μm during multiple pass procedures. Any deeper treatment risks the complication of scarring. With fractional photothermolysis, one can penetrate tissue to a greater depth safely, as entire epidermal and dermal ablation is not achieved. Because of these two factors, tissue can be safely resurfaced to a depth of 1,400 μm.

The efficacy of fractional nonablative photothermolysis for the treatment of photodamaged facial skin was first demonstrated in 2005 (Rokhsar and Fitzpatrick 2005). In this study, 12 patients with facial rhytides corresponding to Fitzpatrick scale 4–9 were treated with a first generation laser using fluences of 6–20 J at 1–4 week intervals with densities of 2000–300 MTZ/cm^2. Anesthesia was achieved through a topical 30 % lidocaine formulation. Each patient received an average of 4–5 treatments. Patients were assessed for improvement in texture, dyschromia and wrinkles on the face, neck and the chest. Significant improvement was seen in all parameters. Biopsies demonstrated new collagen formation. Side effects were minimal and limited to post-treatment erythema that lasted a few days, as well as mild edema.

In a subsequent study, the long-term efficacy of fractional non-ablative photothermolysis in treating both facial and non-facial photodamage, rhytides, and dyspigmentation was demonstrated (Wanner et al. 2007). Fifty patients with Fitzpatrick skin types I to III underwent a series of three consecutive treatments (2,000 MTZ/cm^2 at 8 mJ for facial areas; 1,500–2,000 MTZ/cm^2 at 8 mJ for non-facial areas, Fraxel 750 SR) spaced 3–4 weeks apart. Two blinded physicians assessed clinical improvement with a three-point quartile grading scale. The investigators reported a mean improvement of 2.23, 2.10, and 1.96 at 3, 6, and 9 months after treatment, respectively. Similar results were observed for non-facial areas, with a mean improvement of 1.85, 1.81, and 1.70 at 3, 6, and 9 months after treatment, respectively. An overall improvement of 51–75 % was found in 73 % (facial arm) and 55 % (non-facial arm) of patients 9 months after treatment. Adverse effects were limited and short-lived. The authors concluded that fractional photothermolysis was a safe and effective treatment for facial and non-facial photodamage, rhytides, and dyspigmentation with a favorable recovery and side effect profile.

Since the publication of these initial studies, second and third generation non-ablative fractional

photothermolysis models have emerged. Efficacy of these machines have been increased by fluence adjustments that allowed deeper and wider penetration of microscopic thermal zones, the addition of variable spot sizes, and hand piece modifications that allowed more uniform and consistent delivery of fractionated energy (Sherling et al. 2010). The newest of these fractional devices to emerge actually provides two wavelengths in the mid-infrared spectrum for the treatment of pigmentation and photodamage (Fraxel Dual, Solta Medical; Hayward, CA). This device combines a 1,550 nm laser wavelength with a 1,927 nm wavelength. With the first and second generation devices, four treatments were recommended; now the same correction with the dual wavelength device can usually be done in only three treatments. The 1,927 nm wavelength allows for a very superficial resurfacing which can eliminate pigmentation from melasma, hyperpigmentation, sun damage, and actinic keratoses with safety in all skin types and all parts of the body (Polder and Bruce 2012). It is thought that this device may be more effective in treating melasma than first and second generation systems, but results to this effect have not yet been proven in controlled clinical trials. However, company experts maintain that this third generation device provides superficial resurfacing similar to a superficial CO_2 laser resurfacing, without the downtime or wound care.

As with non-ablative fractional technology, there are a number of fractional ablative laser devices currently available. Among the most popular are those that incorporate fractional ablative carbon dioxide 10,600 nm wavelength technology. The major differences between these devices pertain to their depth of ablation and coagulation and to variations in their treatment handpieces, which determine the manner in which the treatments are delivered. One system (Fraxel re:pair, Solta Medical; Hayward, CA) utilizes a continuous motion (rolling) optical tracking system (Cohen and Henssler 2009). By adjusting its system according to the operator's hand speed, uniform and consistent microscopic thermal zones 135-μm in diameter can be delivered. Histologically, these microthermal zones consist of a superficial zone of ablation and a deeper contiguous zone of coagulation or residual thermal damage. Based on in vivo histologic studies of various fractional carbon dioxide laser devices by Kenkel et al., the coagulation zone of the laser with the rolling handpiece extends up to 1.6 mm into the dermis at 80 mJ (Farkas et al. 2010). The device is also equipped with a smoke evacuator and two tip sizes, 7 and 15 mm, the smaller being useful for the periorbital area, the nose, and upper lip and the larger for the cheeks, neck, forehead, and chest. Energy varies from 5 to 70 mJ, and density from 5 to 70 % based on the width of the coagulation zones.

Another device uses a scanned stamping technology attached to a smoke evacuator for the fractionated delivery of a 10,600 nm CO_2 laser wavelength (Deep Fx, Lumenis; Yokneam, Israel). The spot size for this laser is approximately 0.12 mm. Density ranges from 5 to 25 %, and energy ranges from 5 to 30 mJ. On the basis of in vivo histologic studies, the maximum depth of its ablative zone (at 20 mJ and using a single pulse) is approximately 500 μm while the depth of its coagulative zone is approximately 2,000 μm (Farkas et al. 2010). Maximum coverage rate for the fractional laser with a stamping handpiece is 98 mm^2/s, which is slower than the system with the rolling handpiece.

Finally, there is an additional modality, known as Active FX, which performs superficial fractional ablative skin resurfacing using a scanned stamping technology. The spot size for this mode is 1.25 mm, its density ranges from 55 to 100 %, and its energy ranges from 80 to 100 mJ. The ablative depth for this mode is from 80 to 100 μm in contrast to the 500 μm depth of the Deep Fx mode. Because it produces wider and shallower microthermal zones, delivering ablation primarily to the epidermis and papillary dermis, this superficial mode is better suited for superficial lesions of photoaging such as lentigines and dyspigmentation (Cohen and Henssler 2009).

Other fractional ablative devices include the fractionated erbium:YAG laser and the fractionated erbium: YSGG laser. Both have demonstrated efficacy for the treatment of photoaging and acne scars in small pilot studies. One fractional Er:YAG

device utilizes a 2,940 nm wavelength and 250 μm spot size with a variable treatment density from 1.5 to 30 % (Profractional, Sciton; Palo Alto, CA). Interestingly, this same device incorporates a sequential adjustable coagulation mode, which consists of three different treatment levels provided by long-pulse energy to create an extra-thermal effect. Coagulation levels 1, 2, and 3 correspond to 50, 100, and 150 μm of residual thermal damage around each microthermal zone, respectively. The addition of this tunable long pulse mode allows for the creation of simultaneous ablation and coagulation. In that respect, this fractional er:YAG laser can achieve clinical improvements similar to that of a fractional CO_2 laser, but with less bleeding and more collagen remodeling compared to patients treated with traditional fractional er:YAG resurfacing (Hu et al. 2011).

We published a study demonstrating the efficacy of a novel fractionated erbium:YSGG laser for the treatment of photodamage (Ciocon et al. 2011). It produces a 2,790 nm wavelength that has a greater water absorption coefficient than the 10,600 nm CO_2 wavelength but less than that of the 2,940 nm wavelength of erbium:YAG. Given its unique water absorption coefficient, its offers a greater zone of coagulation around each microthermal zone compared to fractionated short-pulsed erbium devices, but a narrower zone of coagulation compared to fractionated carbon dioxide systems. As such, it promises less bleeding and greater collagen remodeling than standard fractionated Er:YAG devices but potentially fewer side effects such as pigmentation and scarring compared to fractionated CO_2. We found this device highly effective for the treatment of facial photodamage and perioral rhytides using a single treatment with a high energy, high density protocol. Subsequent studies have shown its efficacy for the treatment of acne scars (Smith and Schachter 2011).

Few studies have been conducted, comparing the relative efficacy of currently available fractional ablative lasers. We recently published a split face comparison study comparing two fractional ablative carbon dioxide devices (Fraxel re:pair and Deep Fx modes) for the treatment of photodamage (Ciocon et al. 2011). In this study, both devices showed notable and comparable clinical improvement after a single treatment for facial photodamage, 3 months postoperatively. With regard to specific categories of improvement, there were no statistically significant differences in wrinkles, laxity, pigmentation, or overall appearance between the two devices. With regard to patient-measured parameters, significantly higher pain scores were associated with the laser with the stamping handpiece. In addition, procedure times were significantly shorter for the device with the rolling handpiece (Fraxel re:pair). In contrast, Dover et al. did a four quadrant, split-face comparison of four different fractional ablative lasers for the treatment of facial photodamage (Abbasi et al. 2010). No statistically significant differences were noted in terms of clinical efficacy, side effects, or downtime.

A recently introduced fractional radiofrequency device is the Matrix RF (Syneron Medical Ltd.). Matrix RF is the first bipolar RF-based aesthetic device capable of delivering ablative tunable RF energy to the skin in a non-homogenous fractional manner using an array of multi-electrode pins. This results in heating of the areas in direct contact with the pins and spares the zones between the targeted areas, which helps to maintain the skin integrity and serves as a pool of cells that promote wound healing. Hruza and colleagues delivered fractional RF treatment to the abdomen in individuals scheduled for abdominoplasty (Hruza et al. 2009). They used different tips at varying energy densities and coverage rates. Biopsies were performed *ex vivo* after abdominoplasty, and tissue samples were processed and stained, using hematoxylin and eosin. Another group of subjects received three facial treatments scheduled at 3- to 4-week intervals. Histological findings immediately after treatment revealed well-demarcated zones of ablation, coagulation, necrosis and subnecrosis up to a depth of 450 μm. Higher energy levels generated deeper effects. Subjects undergoing facial treatment had minimal pain and no permanent side effects or significant downtime. Investigators' assessments of improvement in skin texture correlated with subjects' evaluations and were greater than 40 % for approximately half of subjects. Eighty percent of

the subjects were satisfied with the results. High energy levels and low coverage rates produced excellent aesthetic results along with less pain.

Advantages

Fractional ablative and non-ablative photothermolysis carries multiple significant advantages, most importantly, decreased recovery times and risks of complications (Hantash et al. 2004; Berlin et al. 2009; Taub 2007; Tierney et al. 2011) when matched against traditional ablative laser resurfacing (Tierney et al. 2011). Some studies demonstrate that ablative fractional laser therapy may even be superior to traditional ablative resurfacing since a greater depth of penetration can be achieved (Taub et al. 2007; Tierney et al. 2009).

With regards to non-ablative fractional therapy, the advantages are numerous. For instance, patients do not develop open wounds, which reduces the risk of infection, dyspigmentation, and scarring in addition to minimizing downtime (Ciocon and Rokhsar 2007). One of the most significant advances in non-ablative FP is the ability to treat off the face areas, such as the neck, chest, back, and extremities—areas which can be associated with hypertrophic scarring if treated with traditional ablative or even fractionated ablative resurfacing (Ciocon and Rokhsar 2007; Avram et al. 2009; Fife et al. 2009). Finally, nonablative fractional photothermolysis and fractionated radiofrequency resurfacing are considered safe in patients with darker skin types since they do not target a chromophore and have minimal impact at the skin's surface (Brightman et al. 2009). The use of fractional ablative modalities is medium to dark skin types is also considered safe, particularly if pre-treatment regimens to minimize postinflammatory pigmentation are instituted, and treated areas are limited to the face (Sherling et al. 2010).

Disadvantages

Reports of mild complications including erythema, edema, acneiform eruptions, delayed purpura have been reported. Moderate complications include persistent erythema, bacterial infection, activation of herpes simplex, and post-treatment hyperpigmentation (Graber 2008). Hypertrophic scarring in areas with a decreased density of pilosebaceous units may occur when using high fluences and high densities as reported by Avram (Avram et al. 2009). In addition, the development of ectropion has also been reported when treating inside the orbit (Fife et al. 2009).

For the treatment of photodamage, nonablative fractional resurfacing treatment may require multiple treatments (five to seven) in comparison to fractional ablative resurfacing, which can accomplish similar results in one to two treatments. Furthermore, non-ablative fractional photothermolysis is much less efficacious for the management of deeper lines around the mouth or eyes in comparison to fractional ablative resurfacing (Geronemus 2006). Because minimal surface ablation occurs, radiofrequency treatment is less effective for superficial pigment changes; however it appears effective for acne scarring, deep wrinkles, and tissue laxity (Brightman et al. 2009).

Indications

The most common indications for fractional resurfacing include wrinkle, acne scars and cumulative photodamage. Fractional photothermolysis is currently FDA approved for treatment of periorbital wrinkles, acne and surgical scars, skin resurfacing procedures, dermatologic procedures requiring the coagulation of soft tissue, as well as photocoagulation of pigmented lesions such as lentigines and melasma (Geronemus 2006; Bogdan 2010; Hasegawa et al. 2006; Alster 2007; Behroozan et al. 2006; Rokhsar et al. 2005). Though these are the 'approved' uses, as research into this technology continues, there is an even wider array of clinical applications, such as matted telangiectasias (Glaich et al. 2007), atrophic scars (Alster et al. 2007), scar hypopigmentation (Glaich et al. 2007), striae distensae (Kim et al. 2008), neck skin tightening (Tierney and Hanke 2009), tattoo removal and pigmentary disorders such as vitiligo, among others (Shin et al. 2012).

Contraindications

There are few true contraindications. Scleroderma patients should be counseled that ablative resurfacing could exacerbate their disease although reports of successful treatment exist when using ablative laser resurfacing (Apfelberg 1998). Even though darker skinned patients have been treated effectively without post inflammatory pigmentary changes, the risk remains (Geronemus 2006), and patients still need to understand the potential for hyperpigmentation (Tanzi and Alster 2003), which is usually temporary but may be long-lasting. The use of hydroquinone preparations with vitamin A derivatives, glycolic acid and/or topical corticosteroids, and good sunscreen has minimized this problem in patients treated with ablative laser therapy. In addition, recent tanning, active herpes simplex or other infections or lesions of concern in the treatment field and the use of isotretinoin within the 6 months of treatment are all relative contraindications (Sherling 2010). Unrealistic expectations, the inability or unwillingness to perform wound care, and a history of keloid formation are also relative contraindications for fractional skin resurfacing.

Consent

Informed consent is mandatory and should include treatment options, potential risks and benefits. No guarantees should be made. A carefully written detailed consent that explains the above is suggested (Fig. 5.1).

Personal Laser Technique

A successful fractionated resurfacing procedure begins with a thorough preoperative evaluation, including a discussion of risks and benefits. This evaluation should pay careful attention to patient expectations, preoperative photographs, and counseling about the perioperative period. Medications are prescribed to minimize potential infection, including a prophylactic antibiotic (typically a first-generation cephalosporin), an antiviral (acyclovir or valcyclovir), and an antifungal medication. Although there is no consensus on a specific pretreatment regimen for skin types IV to VI, some physicians use topical hydroquinone and tretinoin for several months before treatment and discontinue the tretinoin 1 week before treatment and the hydroquinone 3 or 4 days before (Sherling et al. 2010). Topical steroids have also been used prior to treatment in patients with medium to dark skin types to minimize the possibility of post inflammatory pigmentation. A non-steroidal anti-inflammatory agent such as oral ibuprofen and an analgesic (hydrocodone) may also be prescribed to control post-operative discomfort. Patients are educated as to what to expect during the healing period; appropriate wound care for the first week is reviewed. Pre-operatively, patients apply topical anesthetic cream EMLA® (eutectic mixture of lidocaine and prilocaine) with occlusion 2½ h prior to the procedure time. Forty-five minutes before the procedure, EMLA® is reapplied under occlusion (Kilmer et al. 2003) (Figs. 5.2 and 5.3). Diazepam may also provided by mouth to control anxiety. Finally, regional nerve blocks (auriculotemporal, supraorbital, supratrochlear, infraorbital, mental) with 1 % lidocaine can also be performed.

Currently available fractional laser systems allow the operator to adjust the energy and density; some also allow adjustment of the pulse duration, whereas others have a fixed or automatically adjusting pulse duration (Tierney et al. 2011). Typically, low density/high fluence settings are used for treating conditions arising in the middle to deep dermis such as deep acne scars or rhytides, while more superficial conditions such as lentigines, fine lines, and melasma are treated with higher densities and lower fluences. The number of passes depends on the desired density. Continuous air cooling with a Zimmer® cooler is often employed as the laser is fired, to maximize patient comfort and minimize bulk heating. Older fractional non-ablative devices required the use of a blue dye or a lipophilic ointment just prior to resurfacing. Newer devices do not require this. Many fractional ablative

Ablative and Nonablative Fractional Laser Resurfacing

WHAT IS LASER SKIN RESURFACING?

The carbon dioxide (C02) laser has been used for more than 25 years for treating the skin. An intense beam of light is emitted, which heats and vaporizes skin tissue instantly. Recently developed Carbon Dioxide and Erbium Lasers are able to perform highly specific vaporization of tissue using powerfully focused light to precisely remove the layers of skin, vaporizing the ridges of scars and wrinkles and smoothing out the surface of the skin. In addition, the skin often tightens and collagen remodeling occurs with layers of new collagen replacing sun-damaged collagen. The CO2 laser tightens the skin more while the erbium laser is used more for sculpting. These lasers, and other similar devices have made laser resurfacing safer than was possible 25 years ago. Ablative Fractional treatments (usually 1-3) is generally more aggressive than non-ablative treatments (3-7)

BENEFITS

Fractional laser resurfacing may significantly reduce facial wrinkle lines and acne scarring. The length of time these benefits will last is unknown. Sun spots and brown spots are often removed as well.

RISKS AND DISCOMFORTS

The most common side effects and complications are explained below.

ERYTHEMA (redness of skin)

The laser-treated areas have a distinctive redness which is much more vivid than the areas not treated. This redness generally will last from several days to more than one month beyond the time required to heal the skin surface. This redness represents increased blood flow from healing as well as new growth of the superficial tissue and fades gradually week to week.

INFLAMMATION (swelling)

This is common and varies from person to person. Most patients swell moderately, but in some patients, swelling is severe; your skin may feel tight in the initial weeks following treatment.

HYPERPIGMENTATION (increased skin color)
This is common in those with dark complexions, and almost always is temporary.
It often responds to the post-treatment use use of hydroquinone, protective sunscreens, and topical retinoids.

Fig. 5.1 Informed consent before fractional resurfacing

HYPOPIGMENTATION (decreased skin color)

This has been uncommon and although is usually related to the depth of the peel, can occur for unknown reasons even when the procedure has been performed properly. In addition, removing sun damaged skin can return you to your natural lighter color similar to areas on your body that have not had long term sun exposure (i.e., underarms). Delayed hypopigmentation, something that occurred on a regular basis with older non-fractional technology, is extraordinarily rare after fractional laser treatments. .

SCARRING OR KELOIDS

Scarring is not anticipated as a consequence of this procedure, but any procedure in which the surface of the skin is removed can heal with scarring. This usually occurs because of some secondary factor which interferes with healing, such as infection, irritation, scratching, or poor wound care. Scarring from infection, irritation or scratching, does blend and ordinarily disappears in a few months, but some scarring may be permanent if it occurs. Hypertrophic scars or keloids in susceptible people may suddenly appear. Most of these respond to injections or special creams. Some scarring could be permanent. Some scarring may occur for no reason at all.

Notify your physician if you have ever used Accutane as this may increase your risk for scarring.

ALLERGIC REACTIONS

Allergic reactions or irritations to some of the medications or creams may develop. An increased sensitivity to wind and sun may occur, but is temporary and clears as the skin heals. If you have had a cold sore or herpes outbreak in or around the area to be treated, let us know as treatment can reactivate it.

EXPLANATION OF THE PROCEDURE

A personal interview and clinical examination will be conducted to obtain relevant facts about your medical history, dermatologic history and any medications you are currently taking or have taken in the recent past. Preoperative vitamin A and C creams may be started prior to the procedure. A sunscreen with UVB and UVA protection should be applied every morning. If you have a dark complexion, you may also need to apply a bleaching gel. You will begin taking an antiviral medication the night before or the morning of the procedure. On the day of the procedure, you will begin taking an antibiotic by mouth for a minimum of 5 days. A topical anesthetic cream will be applied for 2 hours before the procedure to decrease pain. Valium, Vicodin, Toradol or similar pain medication may be given as needed for pain. Injections to block the facial nerve endings may be performed just prior to the procedure. Please plan to have someone drive you home after the procedure.

Fig. 5.1 (continued)

NO GUARANTEES

It is possible that you may derive no benefits from the above-described procedure. While this procedure is effective in most cases, no guarantees can be made that a specific patient will benefit from treatment.
Do not sign this form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

CONSENT

MY SIGNATURE INDICATES THE FOLLOWING:

1)1 HAVE READ AND I UNDERSTAND THE INFORMATION OUTLINED ABOVE;

2) I HAVE DISCUSSED MY QUESTIONS WITH THE DOCTOR OR HER STAFF.

DATE.....NAME OF PATIENT.....SIGNATURE OF PATIENT.....

DATE.....NAME OF WITNESS.....SIGNATURE OF WITNESS.....

DATE.....NAME OF PHYSICIAN.....SIGNATURE OF PHYSICIAN.....

Fig. 5.1 (continued)

Fig. 5.2 EMLA with occlusion, preoperative

Fig. 5.3 EMLA with occlusion; the face is treated with the CO_2 laser in sections, as shown

devices come equipped with continuous suction to remove aerosolized particulate debris released during the resurfacing procedure. With regard to fractionated radiofrequency devices, a dry skin surface and close apposition of the laser tip with the skin is necessary to deliver an adequate energy pulse.

During treatment, appropriate eye wear protection should used by the patient and the operator. If resurfacing is to be performed close to the eyelid margin or within the bony orbit, corneal shields can be placed to protect the eyes. Shields are placed after topical numbing of the periorbial skin with EMLA cream. Tetracaine drops and eye lubricant are then used to anesthetize and moisten the eyes, before shield placement. Extreme caution should be used when using corneal shields as placement of the shields in combination with EMLA cream has been associated with corneal abrasion (Ogle 2009; Eaglestein 1999). In some cases symptoms of corneal abrasion can take hours after the procedure to manifest themselves, when the tetracaine so1ution wears off.

Non-ablative fractionated treatment tends to require multiple treatments, whereas ablative fractionated treatment does not (Figs. 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 5.10, and 5.11). It is recommended to treat the face in its entirety, as treatment of isolated areas such as the lip and around the eye could result in a undesired colored discrepancy between treated and untreated areas. Because fractional radiofrequency devices exert minimal effects on surface pigmentation, fractional radiofrequency treatments do not require treatment of the entire face to achieve a blended look. However, because of the benefits of overall tissue tightening, it may be worth considering (Brightman et al. 2009).

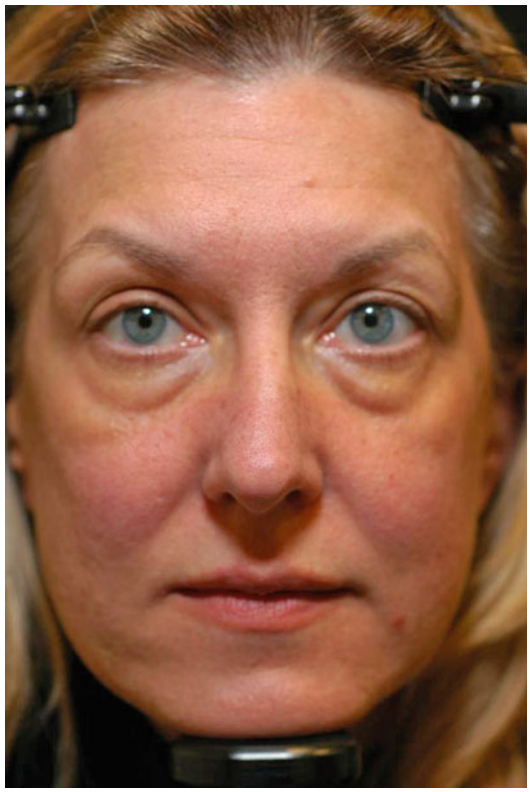

Fig. 5.4 Before fractional carbon dioxide laser resurfacing

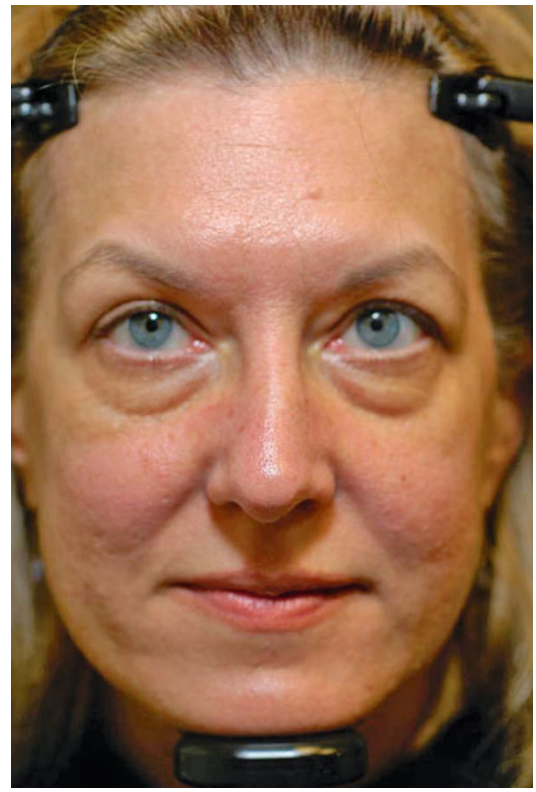

Fig. 5.5 After fractional carbon dioxide laser resurfacing

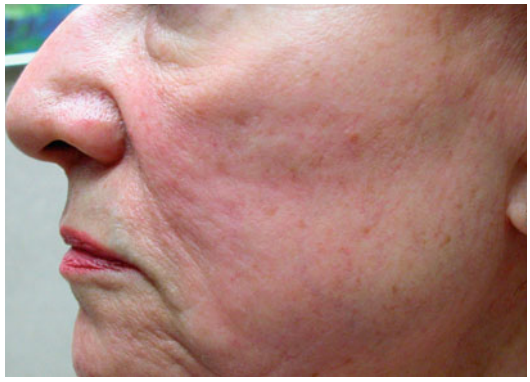

Fig. 5.6 Before fractional carbon dioxide laser resurfacing

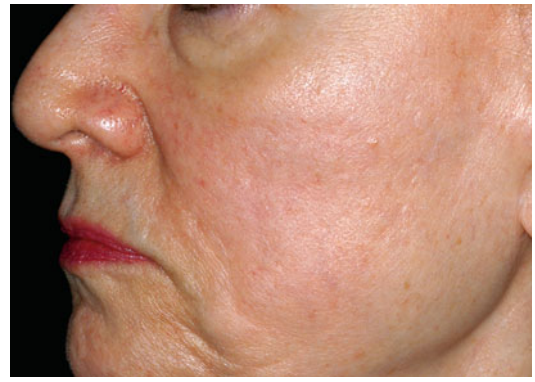

Fig. 5.7 After fractional carbon dioxide laser resurfacing

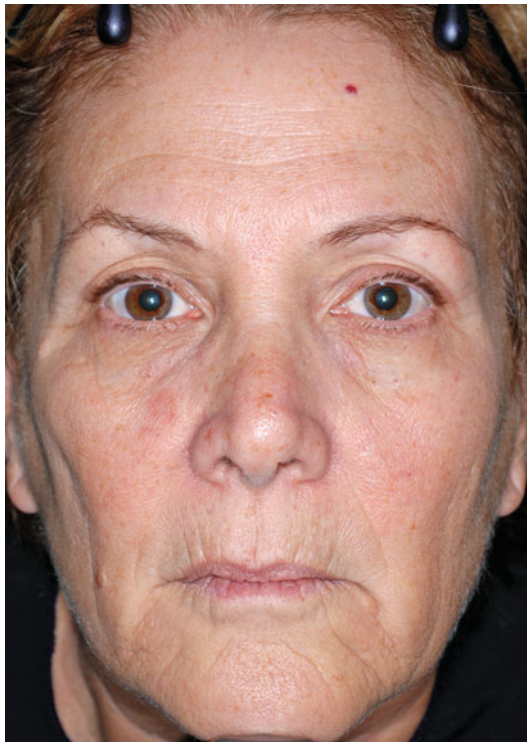

Fig. 5.8 Before fractional fractional erbium:YAG laser resurfacing

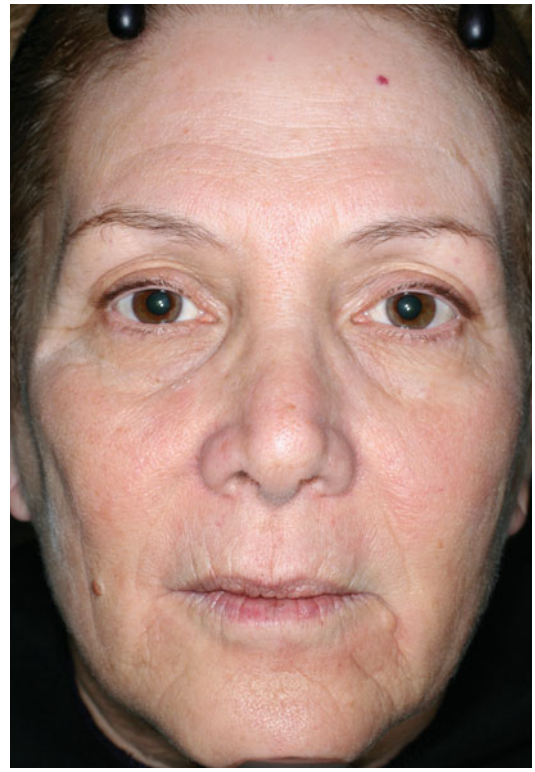

Fig. 5.9 After fractional erbium:YAG laser resurfacing to right side of face

Postoperative Care and Complications

Following fractional photothermolysis, patients are instructed to apply cool compresses to the areas as well as a bland topical emollient. Some authors have suggested that ointment-based emollients as opposed to cream or dimethicone-based emollients have been associated with a higher incidence of post procedure acneiform eruptions (Sherling et al. 2010). In addition, cold compresses are recommended for control of itching and to reduce swelling. It is also important to

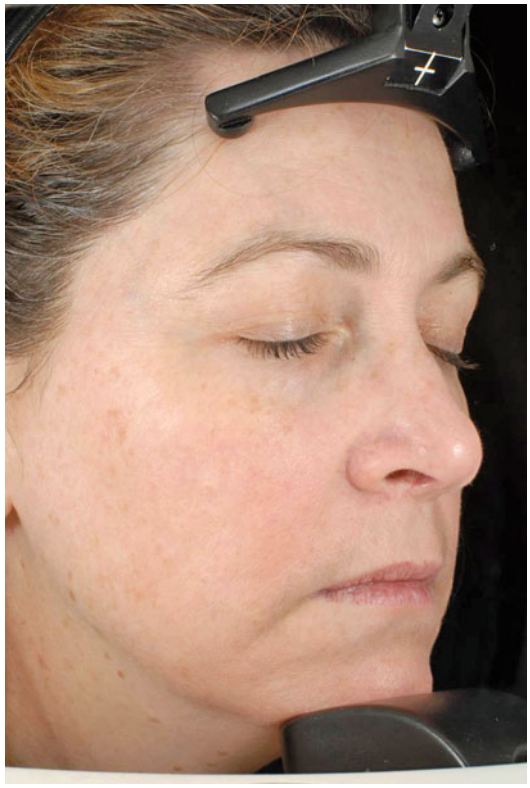

Fig. 5.10 Before fractional radiofrequency resurfacing

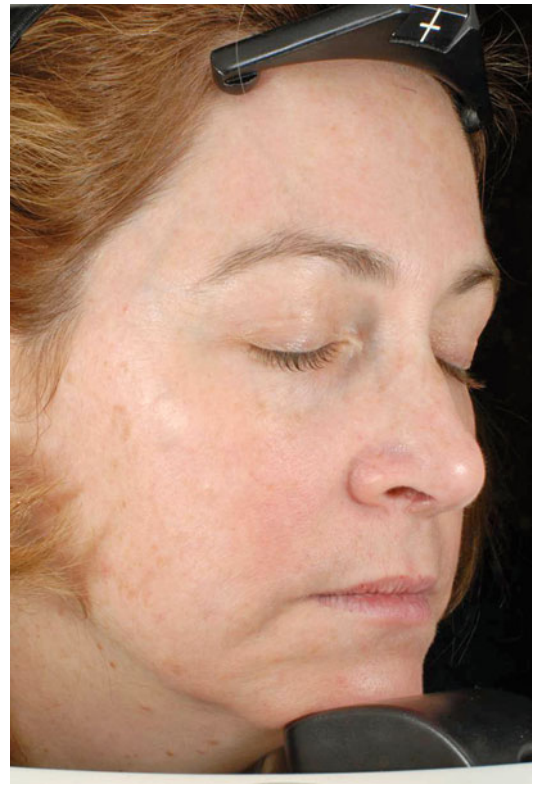

Fig. 5.11 After fractional radiofrequency resurfacing

instruct patient to avoid picking at their treated skin with respect to scabs, crusts, and coagulum (Tierney et al. 2011). Some have described using a dilute vinegar solution to assist in the removal of crust.

A survey study conducted by Fisher and Geronemus in 2005 revealed that 100 % of patients treated with fractional photothermolysis experienced post-treatment erythema, 82 % facial edema, 87 % dry skin, 60 % flaking, 37 % pruritus, 27 % transient pigmentary changes, and 10 % an acneiform eruption (Fisher and Geronemus 2005). Graber et al. then retrospectively reviewed the side effects and complications of FP as a result of 961 treatment sessions in 422 patients. In this study, 73 complications (7.6 %) were recorded: 18 acneiform eruptions, 17 herpes simplex virus outbreaks, 13 erosions, 8 instances of prolonged erythema, 7 instance of post-inflammatory hyperpigmentation, 6 instances of prolonged edema, 2 instances of dermatitis, and 1 instance each of impetigo and purpura (Graber et al. 2008). Post inflammatory hyperpigmentation usually resolved within 6–12 months and could be reduced by pretreatment regimens that include hydroquinone, topical steroids, and/or tretinoin.

Although rare, scarring may be a complication of both ablative and non-ablative FP and may occur in areas of bulk heating (i.e., temple, glabellar skin, infraorbital skin, and upper cutaneous lip). With respective to fractional ablative devices, recent reports of hypertrophic scarring of the neck and ectropion have emerged (Avram et al. 2009; Fife et al. 2009).

Results

Ablative fractional resurfacing leads to dramatic improvement in the overall quality of the skin including fine lines, deep rhytides, solar lentigi-

nes and elastotic changes. It is also very effective in smoothing other superficial irregularities such as actinic keratoses, nevi, benign tumors and acne scars. Although multiple treatments are needed for non-ablative fractionated resurfacing, the effects are modest when compared to ablative fractionated photothermolysis. Finally, Brightman and colleagues have reported noticeable improvement in deep and/or dynamic wrinkles and scars treated with fractionated radiofrequency (Brightman et al. 2009), but its relative efficacy compared to fractionated ablative systems has yet to be determined.

The Future

As the number of indications for treatment with fractional resurfacing continues to rise, newer approaches that include combination therapy with these devices will be explored. Beer reviewed the benefit of combining FP with botulinum toxin injections to enhance the results of the laser treatment, while Ruiz-Rodriguez combined the synergistic effects of fractional resurfacing and 5-aminolevulinic acid–photodynamic therapy (ALA-PDT) in the treatment of skin rejuvenation (Beer et al. 2007; Ruiz-Rodriguez et al. 2007). More recent studies, have suggested a role for combining fractional resurfacing with the topical application of platelet-enriched plasma for photorejuvenation (Shin et al. 2012). These combination therapies have demonstrated efficacy in pilot settings, but larger studies are needed.

Although a few small studies comparing the effect of non-ablative FP and ablative FP exist, more trials are needed to further delineate the difference between the two technologies. With the availability of multiple FP devices, standardized treatment regimens that control for differences in density and spot size, could revolutionize the field of laser therapy. Recently, Aljalan shared treatment recommendations using algorithms to treat acne scarring in patients with darker skin using both ablative and non-ablative fractionated lasers (Aljalan 2011). Finally, with continued experience with fractionated radiofrequency technology, the risk of treating patients with darker skin types for fear of post-procedure pigmentary changes may become an irrelevant issue (Taub and Garretson 2011).

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Lasers and Light Sources for Medical Dermatologic Conditions

6

Michael H. Gold

Core Messages

- Lasers and light sources have become more commonplace in the treatment of dermatologic medical diseases.
- ALA-PDT is a proven therapy for actinic keratoses and superficial non-melanoma skin cancers.
- ALA-PDT is being used to treat the signs of photorejuvenation with a variety of vascular lasers, blue light sources, and the intense pulsed light source.
- PDT is a useful therapy for acne vulgaris with blue light and other light sources as well.
- ALA-PDT is being used to treat moderate to severe acne vulgaris, andother sebaceous gland disorders with a variety of vascular lasers, blue light sources, and the intense pulsed light source.
- New lasers and light sources are being used to treat psoriasis vulgaris, vitiligo, other disorders of pigmentation, and hypopigmented stretch marks.

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Photodynamic Therapy

The treatment of superficial non-melanoma skin cancers and actinic keratoses (AKs) with lasers and light sources has entered a new era in dermatology with the advent of 20 % 5-aminolevulinic acid (ALA), a potent photosensitizer, and it's methyl ester (MAL). These photosensitizers have demonstrated an effective ability to work with lasers and light sources of appropriate wavelengths to selectively destroy a variety of cutaneous lesions. The term photodynamic therapy, or PDT, is now a treatment option which has, over the past several years, become an integral part of many clinicians therapeutic armamentarium. A review of what PDT is, its history and how it is being incorporated into dermatologist's offices today will follow.

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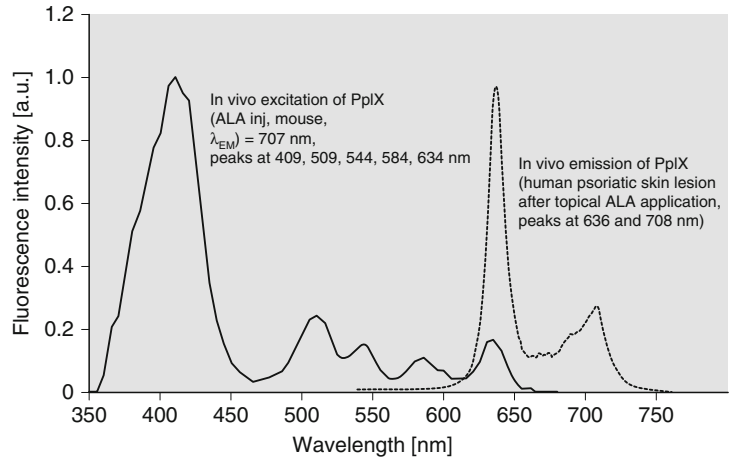


Fig. 6.1 Porphyrin absorption spectrum (©Dusa Pharmaceuticals)

History of Photodynamic Therapy

PDT is a treatment modality which involves the use of a photosensitizer, a light source which fits the absorption spectrum of the photosensitizer, and molecular oxygen, which when stimulated, will destroy a specific target tissue. To be effective in the process, the photosensitizer must be able to selectively penetrate more into the targeted tissue than the surrounding skin. ALA has been shown to be absorbed very well by actinically damaged skin, skin cancer cells, and by the pilosebaceous glands within the skin. The photosensitizer may be given exogenously or formed endogenously during normal biochemical pathways found within certain disease state pathways. An appropriate light source must be employed to activate the photosensitizer and the wavelength of that light must be within the appropriate wavelength of the photosensitizer (Fritsch et al. 1998; Stables 1999). Various lasers and light are being utilized by dermatologists for PDT and these devices have different wavelengths of light and thus different penetration depths into tissues. This may be important in determining the proper light source to use, i.e., utilizing blue light for AKs and red light for nonmelanoma skin cancers.

5-ALA, the most common drug used in dermatology for PDT, occurs naturally in cells as an intermediate product formed during the endogenous porphyrin synthesis process. 5-ALA acts as a prodrug and has been demonstrated by Kennedy et al. (1990) to effectively penetrate the stratum corneum and to localize in the target tissues previously described. Once localized into the appropriate cells within the target tissues, the 5-ALA is transformed into a highly photoactive endogenous porphyrin derivative, protoporphyrin IX (PpIX), which has an absorption spectrum of light in the 415 nm range to 630 nm (Fig. 6.1). MAL acts similarly in that it, too, is a prodrug, and is enzymatically converted to PpIX, the active form of the drug needed for successful PDT.

PDT can trace its routes back to 1900 when Raab (Kalka et al. 2000) found that Paramecium caudatum cells died quickly when exposed to light in the presence of acridine orange. In 1904 Von Tappeiner and Jodblauer (1904) first described the "photodynamic effect." His work involved the study of protozoa; he described oxygen-consuming chemical reactions and fluorescence patterns after the applications of analine dyes. Jesionek and Von Tappeiner (1905) followed in 1905 by utilizing 5 % eosin as a skin photosensitizer. He used artificial light and successfully treated human non-melanoma skin cancer, condylomata lata, and lupus vulgaris. The next 40 odd years found very little substantial studies being performed on PDT.

In 1948, Figge, Weiland, and Manganiello (1948) found that hematoporphyrin could be selectively absorbed in neoplastic tissues, embryonic tissues, and traumatized tissues. Their work led to the development of a purified synthetic compound, a hematoporphyrin derivative, which

then became the standard for PDT research and treatment in that time. Dougherty et al. (1978) reported in 1978 the hematoporphyrin derivative and its photo-activation with a red light source. This group described its effectiveness in treating a variety of cutaneous malignancies and other cancers as well. PDT has been studied and continues to be looked at for a variety of malignancies including lung, colon, esophagus, peritoneum, pleura, gastrointestinal tract, brain, eye and skin (Dougherty et al. 1998; Gomer et al. 1989; Dougherty 1993; McCaughan et al. 1992; Pass and Delaney 1992; Rowe 1988). A variety of non-oncologic applications utilizing PDT includes atherosclerosis (Saito et al. 1996), infectious diseases (Ben-Hur et al. 1997), and rheumatologic diseases (Ratkay et al. 1998; Hendrich and Siebert 1997), as well as skin concerns where the pilosebaceous units are involved. Svaasand et al. (1996) described a dosimetry model for PDT which again describes the necessary three steps for the PDT process to occur: (1) ALA diffusion through the stratum corneum and ability to penetrate the epidermis and dermis; (2) synthesis and production of the photosensitive PpIX from the exogenous ALA applied to the skin; and (3) the production of singlet oxygen when PpIX is properly irradiated with a wavelength of light which is absorbed by PpIX.

In the United States, PDT therapy emerged in the late 1990s as a treatment for non-hyperkeratotic AKs of the face and scalp. AKs are a problem which dermatologists encounter on a daily basis in their clinical practices. The Actinic Keratosis Consensus Conference of 2001 reported that AKs serve as a marker for photodamage and that their principle etiology is ultraviolet light, specifically ultraviolet B light. They found that AKs are associated with alterations of DNA that are associated with squamous cell carcinomas (SCCs), specifically mutations in the tumor suppressing gene p53 (Lefell 2000).

The conference reported that AKs are a carcinoma in situ and some of them will naturally regress, some will remain stable, or some will progress to the formation of SCCs. Which will regress or which will progress is not yet able to be determined; the natural history of AKs is unpredictable, and therefore all AKs should be treated in some fashion to prevent the potential onset of cutaneous malignancies. Conversion rates to SCCs have been reported from 0.1 to 20 %. Additionally, Hurwitz and Monger (1995) showed that 97 % of SCCs are associated with a nearby AK. Dinehart et al. (1997) found that nearby AKs were found in 44 % of cutaneous SCCs which had metastasized. These findings also support the concept that all AKs should be treated to prevent further potential conversion to SCCs.

Table 6.1 Treatment options for actinic keratoses

Surgical options for AK treatment	Cryosurgery Curettage Excisional surgery Diffuse superficicl destructive processes Chemical peels Dermabrasion Laser resurfacing ALA-PDT photodynamic therapy
Medical treatments for AKs	5-Fluorouracil Imiquimod Retinoids – tretinoin, adapalene, tazarotene Diclofenac

A variety of treatment options are currently available for the treatment of AKs. These include both medical and surgical options. Therapeutic modalities are shown in (Table 6.1). Most contend that the principle treatment for AKs involve a destructive process. ALA-PDT fits nicely into this destructive category for the treatment of AKs and has received a great deal of attention recently for the treatment of AKs and other cutaneous concerns.

In Europe, ALA research has focused on its use in treating not only AKs but in treating superficial cutaneous malignancies, from squamous cell carcinoma in situ (Bowen's Disease) to superficial basal (BCCs) and squamous cell carcinomas. Numerous clinical reports have been reported in the medical literature and are summarized in (Table 6.2) (Lui and Anderson 1993; McCaughan et al.

Table 6.2 Summary of lasers/light sources for the treatment of AKs, superficial cutaneous malignancies, squamous cell carcinomas

Indication	Author(s)	Year(s)	Sensitizer/light source	Results
Actinic keratoses	Kennedy et al.	1990, 1992	20 % ALA/filtered slide projector	Complete response in 90 %
	Wolf et al.	1993	20 % ALA/filtered slide projector	80–100 % response
	Morton et al.	1995	20 % ALA/filtered slide projector	80–100 % response
	Fijan et al.	1995	20 % ALA/filtered slide projector	80–100 % response
	Calzavara-Pinton	1995	20 % ALA/argon laser	100 % response
	Calzavara-Pinton	1997	20 % ALA/argon laser	84 % response on F/U from 1995
	Jeffes et al.	1997	10–30 % ALA/argon laser	91 % face/scalp; trunk/extremities 45 %
	Pinzi et al.	2000	20 % ALA/incoherent light source	100 % response
	Kurwa et al.	1999	20 % ALA/non-laser light	More rapid response than 5 FU/equivalent – results at 6 months
	Fritsch et al.	1997	20 % ALA/green light	Painless
Bowen's disease	Calzavara-Pinton et al.	1997	20 % ALA/argon laser	90–100 % response
	Pinzi et al.	2000	20 % ALA/tungsten filament lamp	90–100 % response
	Svamberg et al.	1994	20 % ALA/Nd:YAG dye laser	90–100 % response
	Cairnduff et al.	1994	20 % ALA/CVDL	97 % clearance at 2 month (35/36); 89 % at 18 month
	Morton et al.	1996	20 % ALA/filtered xenon lamp	Superior to cryotherapy in 20 pts.
	Morton et al.	2000	20 % ALA/non-laser light source	Red light more effective than green light
	Stables et al.	1997	20 % ALA/non-laser light source	Complete response in 3 patients
Basal cell carcinomas	Clzavara-Pinton et al.	1997	20 % ALA/argon laser	*The next 6 authors show following results*:
	Pinzi et al.	2000	20 % ALA/tungsten filament lamp	Superficial BCCs 87–100 % response
	Thissen et al.	2000	20 % ALA/Versalight	Nodular BCCs 10–80 % response
	Morton et al.	1998	20 % ALA/xenon lamp	
	Svamberg et al.	1994	20 % ALA/Nd:YAG-pumped dye laser	
	Wolf et al.	1993	20 % ALA/filtered slide projector	
	Kennedy et al.	1990	20 % ALA/filtered slide projector	93.7 % superficial BCC response; 19.4 % recurrence rate
	Carinduff et al.	1994	20 % ALA/CVDL	88 % superficial BCC response
	McCaughan	1999	3.0 mg/kg ALA IV/2 argon laser	100 % response rate
	Calzavara-Pinton	1993	20 % ALA argon pumped dye laser	100 % response rate
	Haller et al.	2000	20 % ALA/non-laser light source	–1 recurrence of 20 superfical BCCs; 16 month F/U
	Itoh et al.	2000	20 % ALA/halogen lamp	–16 pigment BCCs – good results
	Pennington et al.	1998	5 mg/kg IV ALA/coherent light	100 % response clinically; histological exam residual in 50 %

Indication	Author(s)	Year(s)	Sensitizer/light source	Results
Squamous cell carcinomas	Kennedy et al.	1990	20 % ALA/filtered slide projector	*The next 5 authors show the following results*:
	Calzavara-Pinton	1997	20 % ALA/argon laser	67–92 % response for superficial SCCs
	Pinzi et al.	2000	20 % ALA/tungsten filament lamp	0–67 % for nodular SCCs
	Calzavara-Pinton	1993	20 % ALA argon pumped dye laser	
	Wolf et al.	1993	20 % ALA/filtered slide projector	
	Pennington et al.	1988	5 mg/kg IV ALA/coherent light	High recurrence rates
	Fink-Puckes et al.	1998	20 % ALA/incoherent light source	High recurrence rates
	Fritsch et al.	1999	20 % ALA ointment/Wood's lamp	10/10 response superficial SCCs; 50 % nodular SCCs

1989; Bissonnette and Lui 1997). This table shows that a variety of lasers and light sources have been used to treat AKs, Bowen's Disease, BCCs, and SCCs. For AKs, response rates from 80 to 100 % are routinely reported. For Bowen's Disease, response rates from 90 to 100 % are reported with PDT. For BCCs and SCCs, 67–100 % of lesions treated respond to PDT. A variety of treatment protocols were followed by the authors listed in (Table 6.2) but most have used multiple treatment applications with sufficient follow-up to document the effectiveness of ALA-PDT in the treatment of cutaneous malignancies.

Currently Available Technology

The two main photosensitizers being utilized in this time frame are 20 % 5-ALA, known as Levulan,® manufactured by Dusa Pharmaceuticals, Wilmington, MA and the methyl-ester derivative of 5-ALA, Metvix,® made by PhotoCure ASA, Norway and distributed worldwide by Galderma, France. Both of these compounds have received extensive study over the last several years and will be summarized below.

U.S. Experience for Actinic Keratoses with ALA-PDT

In the United States, the 20 % 5-ALA product is currently the only marketed commercial product available for use by physicians (Ormrod and Jarvis 2000). It is a 20 % weight/volume ALA solution with 48 % ethanol. It is produced in the form of a kerastick, and is shown in (Fig. 6.2). The kerastick has a dermatologic applicator at one of its ends for accurate application of the ALA medicine. The applicator tip is attached to flexible plastic tubing which contains two glass vials. One of the vials contains the ALA in a powder form and the other glass vial contains the ethanol solvent. The vials on the kerastick are broken by light manual pressure to the tubing and then the contents are mixed by rotating the contents of the kerastick back and forth for several

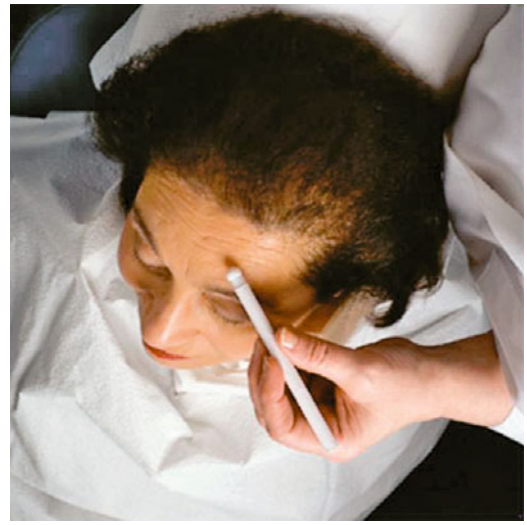
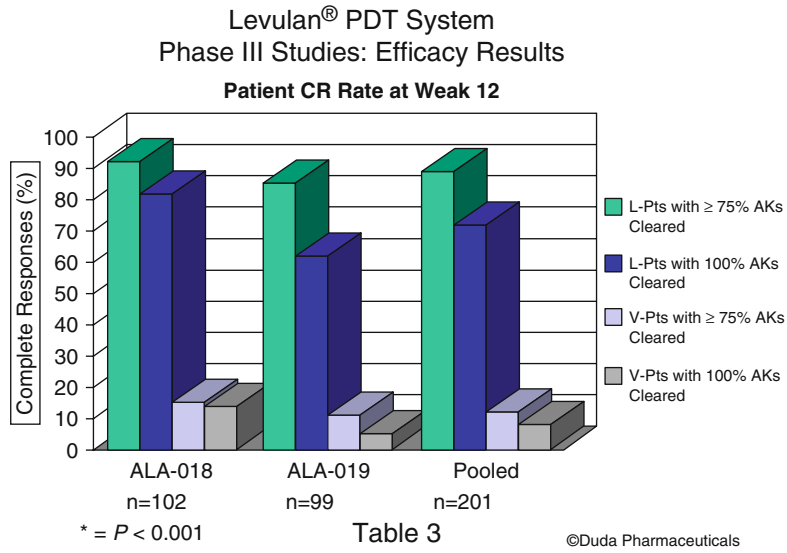


Fig. 6.2 Application of Levulan Kerastick (©Dusa Pharmaceuticals)

minutes, with 3 min being the recommended time frame for proper mixing of the medicine. Once fully mixed together, the ALA is ready for patient application. Preparation of the patient includes washing of the skin with a mild cleanser followed by one or two applications of the ALA. Some clinicians advocate the use of an acetone scrub or a microdermabrasion procedure to allow an even deeper penetration of the ALA. Once the drug has been incubated for the time period chosen, the ALA is washed off the skin and the patient is then ready for the appropriate light therapy.

The first clinical trial with the 20 % 5-ALA was a Phase II clinical trial reported by Jeffes et al. in 2001 (Jeffes et al. 2001). In this clinical trial, 36 individuals with non-hyperkeratotic AKs of the face and scalp were evaluated for its safety and efficacy. The patients had the ALA applied to the individual AK lesions. The drug was allowed to incubate on the individual lesions for 14–18 h without occlusion and the patient was then subjected to a blue light source (Blu-U™ wavelength 410–430 nm, Dusa Pharmaceuticals) for 16 min and 40 s. The blue light source provided a dose of 10 J/cm^2 to the affected lesions. The results of the trial showed that non-hyperkeratotic AKs were effectively treated with the ALA-PDT and the blue light source. Specifically, 66 % of the treated AKs responded to the therapy after one treatment.

Table 6.3 Levulan® PDT system Phase III studies: efficacy results



For those AKs which did not respond ($N=16$), they were retreated after 8 weeks. This improved the efficacy rate to 85 % at the 16 week follow-up period. The treatments were well tolerated by the participants in this trial. All patients noted burning and stinging during their light therapy and facial erythema was reported in 96 % of the participants; all resolved by the first 4 week follow-up.

This led to the Phase III clinical trial (Jeffes 2002) which was a placebo-controlled multicenter analysis looking at a larger number of individuals ($N=243$) using a similar protocol as reported in the Phase II trial. Two applications of either the ALA solution or a vehicle placebo were applied to the individual AK lesions; incubation times for the drug remained at 14–18 h; and the patients received 16 min, 40 s of blue light therapy. Results of the clinical trials showed significant differences between the active ALA and the placebo (Table 6.3); more than 70 % of the lesions were reported clear at 12 weeks. Lesions which were not clear were retreated at 8 weeks. At the conclusion of the study, 88 % of the patients with active medicine had a greater than or equal to 75 % response rate compared to 20 % in the vehicle/placebo group of patients. Clinical examples from the Phase III clinical trial are shown in (Fig. 6.3). Again, the treatments were well tolerated by the study participants. Patients noted that during their light therapy, there was stinging and burning and some of the patients did have associated erythema and edema from the therapy, with these symptoms being resolved at 1 week post the light treatment. No non-cutaneous adverse effects were seen in the Phase III trials. An important outcome of this trial was patient and physician assessment of improvement in the cosmetic appearance of the skin as a result of the ALA therapies. Ninety-four percent of the patients and 92 % of the investigators rated the cosmetic improvement as good to excellent.

A long-term clinical trial has looked at both efficacy and recurrence rates associated with ALA therapy (Fowler and Zax 2002). This study, reported by Fowler et al., showed that 69 % of 32 AKs studied in 4 individuals remained clear at the end of 4 years; 9 % were found to be recurrent; and the authors reported 22 % as "uncertain" as to whether the lesions were actually recurrent or new lesions developed.

New U.S. Indications for Photodynamic Photorejuvenation with ALA-PDT

Gold (2002) also reported on the use of 20 % 5-ALA for AKs with the blue light source. This paper looked at the role of ALA-PDT for photoaging and showed significant improvement in the

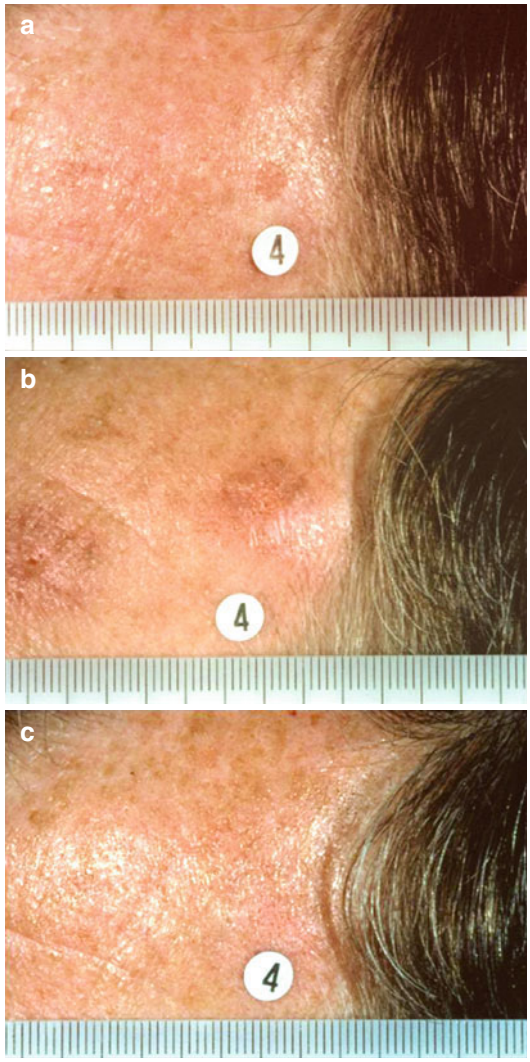


Fig. 6.3 (**a**) Pre-treatment. (**b**) 1 week after ALA-PDT tx. (**c**) 1 month after ALA-PDT tx (©Dusa Pharmaceuticals)

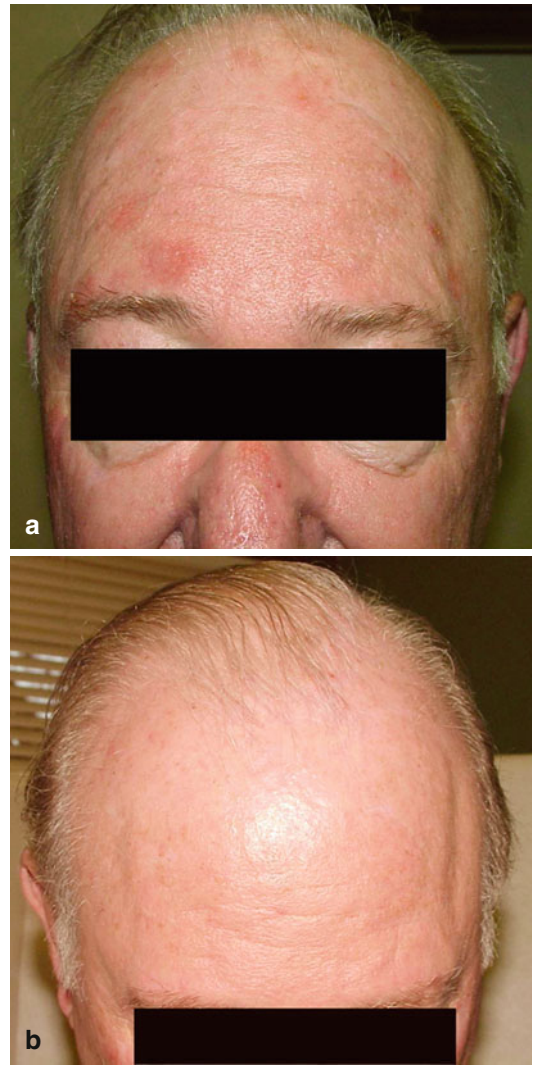


Fig. 6.4 (**a**) Immediately after blue light tx. (**b**) 1 month after treatment (© Gold Skin Care Center)

signs of photorejuvenation and cutaneous aging. Clinical examples are shown in (Figs. 6.4 and 6.5). Others then began to explore new ways which has redefined our current mind-set on the proper use of this therapy for photoaging and photorejuvenation. This has included the use of broad application of the ALA over the entire area which will be treated and the use of a variety of lasers and light sources which fit the absorption spectrum of protoporphyrin IX (Fig. 6.1). The light sources, which are being studied, include a variety of blue light sources, the pulsed dye vascular lasers, and the myriad of intense pulsed light (IPL) devices (Table 6.4). As well, shorter drug incubation times, with the average being 1 h incubation time, are now routinely being employed to help make the procedures more accessible to the patients being treated. This means that the patients need only to have therapy on 1 day versus 2 consecutive days, and with the newer light sources, this makes the therapy more tolerable to the patients by potentially lessening the adverse effect profile seen with the original Phase II and Phase III trial patients.

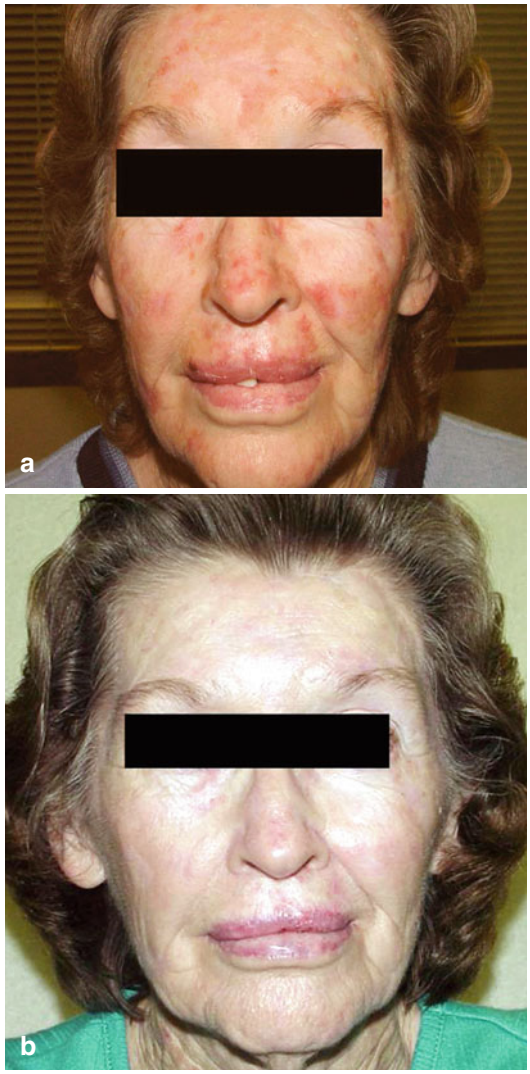


Fig. 6.5 (**a**) Before ALA-PDT blue light. (**b**) After 4 sessions ALA-PDT blue light (© Gold Skin Care Center)

Table 6.4 Lasers/light sources currently being used for photorejuvenation with 20 % 5-ALA

Blue light sources	Blue U™ (Dusa Pharmaceuticals)
	ClearLight™ (CureLight, Lumenis)
Pulsed dye vascular lasers	V-Star™ (Cynosure)
	Cynergy™ (Cynosure)
	V-Beam™ (Candela)
Intense pulsed light sources	Quantum™ (Lumenis)
	Vasculight™ (Lumenis)
	Lumenis One™ (Lumenis)
	Aurora™ (Syneron)
	ClearTouch™ (Radiancy)
	SkinStation™ (Radiancy)
	Estelux™ (Palomar)
	Medilux™ (Palomar)
	Isolaz (AesThera)

To support the notion of full face, short contact ALA therapy, a number of clinical investigators reported their successes with ALA for photorejuvenation. Photorejuvenation utilizing lasers and light sources have been successfully utilized over the past several years to non-invasively rejuvenate the skin improving facial telangiectasias, pigmentary dyschromias, and overall skin texture. Ruiz-Rodriquez et al. (2002) found that after 4 h of drug incubation, patients responded well to ALA therapy and photorejuvenation and associated AKs. Seventeen individuals were studied in this trial with 38 AKs being assessed as well. Two IPL sessions with ALA applied for the 4 h yielded excellent cosmetic results and an 87 % improvement in the parameters of photorejuvenation (wrinkling, skin texture, pigmentary changes, and telangiectasias), and improvement in the AKs as well. He called this new therapeutic approach "Photodynamic Photorejuvenation", a term which fully describes the use of ALA-PDT and lasers and light sources. Touma and Gilchrest (Touma et al. 2004) utilized IPL therapy with ALA in 18 individuals with full face, short contact therapy. They studied incubation of the ALA for 1, 2, and 3 h followed by exposure to a blue light source. They found that 1 h drug incubation was as efficacious as the original 14–18 h drug incubation time periods. The patients showed improvement in skin sallowness, fine wrinkling, and mottled hyperpigmentation with this therapy. Gold (2003) reported his experience with short contact, full face ALA therapy with the IPL in 10 patients. IPL settings included the use of a 550 nm cut-off filter, double pulsing with a 3.5 ms pulse delay, and fluence ranges from 20 to 34 J/cm^2. The patients in this clinical trial received 3 monthly IPL treatments and had follow-up visits at 1 and 3 months following the last IPL therapy. Results from this clinical trial showed that over 85 % of the targeted AKs responded to the therapy. In addition, there was a global improvement score of 90 %

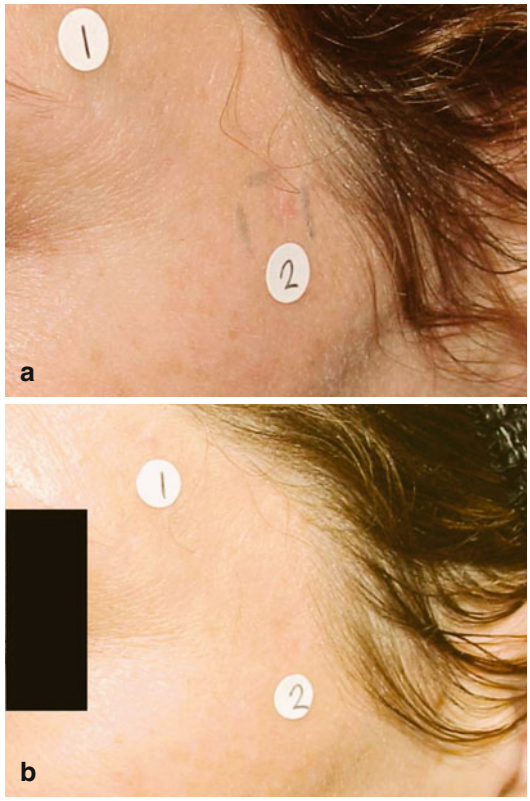


Fig. 6.6 (**a**) AK before ALA-PDT/IPL therapy. (**b**) AK area 1 month after ALA-PDT/IPL therapy (© Gold Skin Care Center)

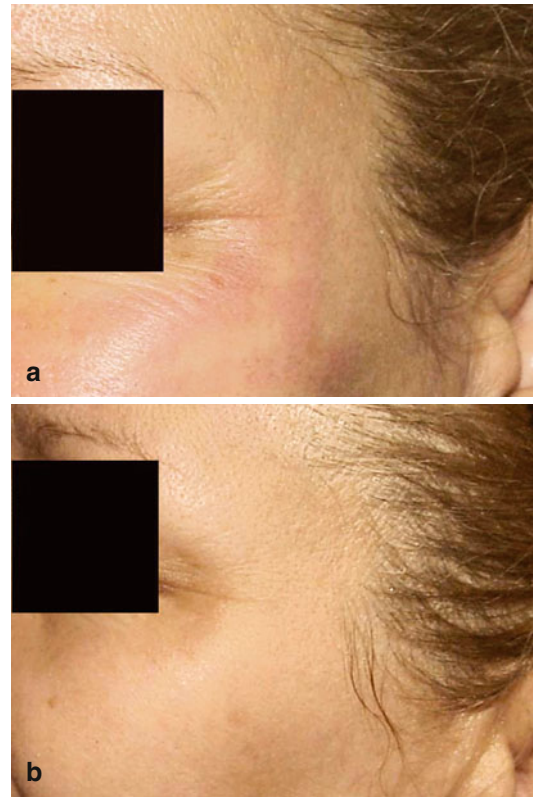


Fig. 6.7 (**a**) Crows feet immediately after ALA-PDT/IPL therapy. (**b**) Crows feet 1 month after ALA-PDT/IPL therapy (© Gold Skin Care Center)

greater than 75 % improvement compared to the baseline visits. Specifically, there was a 90 % improvement in crow's feet lines and wrinkles, 100 % improvement in tactile skin roughness, 90 % improvement in mottled hyperpigmentation, and a 70 % improvement in facial erythema. No adverse effects were reported; 30 % did have facial erythema and edema reported immediately after therapy which abated within 24–48 h. No patient in this clinical investigation reported any downtime from their day to day activities as a result of their therapies. Examples are shown in (Figs. 6.6 and 6.7). Other investigations include Goldman et al. (2002) who evaluated 32 patients with moderate photodamage and multiple AKs, again using short contact full face therapy and the blue light source. At the end of this clinical trial, there was a 90 % clearance of AKs, a 72 % improvement in skin texture, and a 59 % improvement in skin pigmentation. Of note, 62.5 % of the patients in this trial found this therapy less painful than cryotherapy. Avram and Goldman (2004) reported on 17 individuals using short contact full face ALA therapy and one IPL treatment. They used 1 h drug incubation and found that 68 % of the AKs treated responded after the one IPL treatment. In addition, they found that there was a 55 % improvement in facial telangectasias, 48 % improvement in pigmentary irregularities, and 25 % improvement in skin texture, all with just one IPL and ALA therapy.

The pulse dye lasers have also been shown to be useful in the photorejuvenation of the skin. By utilizing ALA, Alexiades-Armenakas and Geronemus (2003), evaluated both 3 h and 14–18 h drug incubations and found both successful in treating the AKs and in improving the parameters of photorejuvenation. This group uti-

lized a pulsed dye laser at 595 nm, with fluence ranges of 4–7.5 J/cm^2, 10 ms pulse durations, 10 mm spot sizes and 30 ms cryogen sprays. They evaluated 2,561 face and scalp AKs with clearances of 99.9 % at 10 days, 94.8 % at 2 months, and 90.1 % at 4 months. Torso lesions were also evaluated; 54.5 % response at 10 days and 74.4 % at 2 months. A similar study (Alexiades-Armenakas and Geronemus 2004) was performed in evaluating actinic chelitis with ALA-PDT and the pulsed dye laser – efficacy rates of 68 % at 12 months were reported utilizing this technique.

Five split-face clinical trials have been reported on the use of ALA-PDT for AKs and photorejuvenation. Alster et al. (2005) reported a split-face evaluation with ALA-PDT and an IPL light source. The patients treated with ALA-IPL had significant improvement as compared to the IPL treated side in the signs of photorejuvenation. Key (2005) reported his findings in a split-face clinical trial utilizing the pulsed dye laser and found the side treated with ALA-PDL responded better than the PDL alone. Marmur et al. (2005) looked at ALA-PDT in a split-face clinical trial in which they evaluated ultrastructural changes, especially the formation of Types I and III collagen following either ALA-IPL therapy or IPL therapy alone. They found that the ALA-IPL side had greater increases in Types I and III collagen as compared to IPL therapy alone. Dover et al. (2005) also reported their findings with ALA with an IPL in a split-face study. In their study, 20 patients had three split-face ALA-IPL treatments at 3 week intervals followed by two additional full face IPL treatments and a 4-week follow-up period. They found improvements in the global score for photoaging (80 % vs. 50 %), improvement in mottled hyperpigmentation (95 % vs. 65 %), and in the appearance of fine lines (55 % vs. 20 %). In their study, they found no differences in tactile roughness or skin sallowness between the two therapies. Gold (2006) also reported his findings in a split-face ALA-IPL clinical trial. Three split-face treatments were performed with follow-up visits at 4 and 12 weeks following the last treatment. Improvements were found in AKs (78 % vs. 53.6 %), crow's feet (55 % vs. 28.5 %), tactile skin roughness (55 % vs. 29.5 %), mottled hyperpigmentation (60.3 % vs. 37.2 %), and erythema (84.6 % vs. 53.8 %). These studies helped solidify ALA-PDT in most dermatologic circles as an effective therapy for AKs and photorejuvenation.

A 12 month evaluation looking at the recurrence rate of AKs (Tschen et al. 2006) showed that after ALA-PDT therapy, recurrence rates and formations of new AKs was significantly delayed. Redbord and Hanke (2007) looked at complication rates in 85 patients treated with ALA-PDT for AKs and photorejuvenation (247 total treatments). They found that the therapy was safe and effective with only a 2 % complication rate, with photosensitivity being the most common adverse event but overall ALA-PDT was well tolerated and efficacious.

Finally, Bissonnette et al. (2004) have looked at the safety and efficacy of large surface application of ALA in hairless mice. In their study, they looked at blue light therapy alone ALA therapy alone, or the combination of ALA and blue light with weekly applications being performed for 10 months. No tumors were formed during this trial period; therefore, ALA-PDT should be deemed not only efficacious but safe as well.

The European and Early USA Experience for Actinic Keratoses and Skin Cancers

The methyl ester derivative of ALA, known as Metvix, ® is available in Europe and several other countries and is currently FDA approved in the United States at the time of this writing but not yet available for commercial use in the United States. It is a compound which has had most of its clinical trials performed utilizing a red laser light source at 630 nm (Fig. 6.1). It has European Union approvals for the treatment of non-hyperkeratotic AKs of the face and scalp and BCCs which are unsuitable for conventional therapy. Recommendations for the use of the methyl-ALA include the gentle scraping or curettage of the effected lesion prior to the application of the methyl-ALA cream. This is then occluded for 3 h before the cream is removed and the area is subjected to the red laser light source. Several recent

clinical trials support the use of the methyl-ALA in the treatment of AKs. Freeman et al. (2003) studied the methyl-ALA cream in 204 individuals compared to cryotherapy and placebo. The methyl-ALA was found to have better response rates and cosmetic improvements compared to both cryotherapy and placebo. Pariser et al. (2003) studied the methyl-ALA cream in 80 individuals with AKs. They found an 89 % improvement in the AKs and a 90 % improvement in the cosmetic appearance. In their group of patients, 72 % of them preferred PDT over both cryotherapy and 5-FU therapy. Rhodes et al. (2004) recently completed a prospective randomized study of BCCs treated with either methyl-ALA or surgery in 101 patients. After 3 months of follow-up, there was a 98 % complete response rate with surgery versus a 91 % response rate with the methyl-ALA. After 12 months, there was a 96 % response rate with surgery and an 83 % response seen in the methyl-ALA group. The authors concluded that the cosmetic appearance was better in the methyl-ALA group compared to the surgical group. And at 24 months, there was one recurrence noted in the surgery group; 5 in the methyl-ALA group. Through two consensus papers written on MAL-PDT, most recommend two MAL-PDT treatments 1 week apart for the most successful therapeutic outcomes (Braathen et al. 2007; Morton et al. 2008).

Three cases of allergic contact dermatitis have also been published in association with the methyl-ALA cream. The authors in the first report (Wulf and Philipsen 2004) noted this response with the methyl cream but not with the 5-ALA solution. Harries et al. (2007) and Hohwy et al. (2007) have also reported allergic contact dermatitis cases with MAL-PDT's use.

The exact role of the methyl-ALA in the United States is still yet to be determined. A recent multicenter clinical trial (Pariser et al. 2008) showed its effectiveness in treating nonhyperkeratotic AKs of the face and scalp utilizing parameters and protocols as has been routinely performed in Europe (>85 % complete response rate). The red light source (Aktilite, Galderma) used in Europe is the recommended light source with MAL in the US as well. This work has led to the FDA approval for its use. MAL-PDT for superficial BCCs has not been approved and if used for this indication, will be considered off-label. Even though there is FDA approval, and most expect that MAL will be available in the US, as of this writing, it is not commercially available.

Several investigations have looked at pain associated with both ALA-PDT and MAL-PDT (Wiegell and Wulf 2006; Kashe et al. 2006). Unfortunately, these studies did not use commercially available ALA and used long ALA drug incubation times which are not the standard for care when ALA-PDT is utilized in the US. A recent commentary (Gold 2008) reviewed these clinical reports and described the difficulties in comparing the modalities.

In summary, ALA-PDT is a new therapeutic modality to enhance previously accepted lasers and light source technologies. With short contact, full face treatments, it appears that all parameters of photorejuvenation and associated AKs can be successfully treated with a reduced number of treatments. The exact number of lasers or light therapies has yet to be determined but will range from 1 to 3 and they will usually be performed at 1 month time intervals. Adverse events are kept to a minimum in this manner and patients routinely report no downtime from day to day activities utilizing ALA-PDT in this manner. Further research endeavors are required and are being conducted to further validate and define this new therapy for photorejuvenation and the associated AKs, or Photodynamic Photorejuvenation. Furthermore, where MAL-PDT fits into the US therapeutic armamentarium has yet to be determined – and how it will influence and effect how clinicians use PDT in the US.

Other Indications

The use of ALA-PDT is not limited to the treatment of AKs, BCCs, and SCCs. In fact, PDT therapy has long been recognized as an important treatment in acne vulgaris and other disorders of the pilosebaceous glands. Recent advances has made the use of a variety of lasers and light sources

and the use of ALA practical for those suffering from acne vulgaris and other pilosebaceous entities. Clinical trials will be reviewed showing the effectiveness of PDT for these entities.

Photodynamic Therapy for Acne Vulgaris

Acne vulgaris is perhaps the most common entity presented to dermatologists for treatment, accounting for over 30 % of all dermatology visits. It has been estimated that between 70 and 96 % of all individuals will suffer from acne vulgaris at some point in their lifetime. Recent evidence suggests that over 40 million American adolescents and 25 million American adults are affected by acne vulgaris (Leyden 1997).

In its simplest form, acne vulgaris is a disorder of the sebaceous glands, where hormonal activity causes dilation and then obstruction of the glands themselves, forming open and closed comedones. The obstruction of the sebaceous glands leads to the production and proliferation of bacterial growth within the sebaceous glands. The bacteria most commonly associated with the formation of acne vulgaris is *Propionobacterium acnes* (*P. acnes*). This clinically presents as inflammatory acne vulgaris lesions, namely papules, pustules, and cysts.

We are very fortunate to have very good medicines to treat those individuals suffering from acne vulgaris. Medicines remain the gold standard for acne vulgaris therapy. These include the topical and systemic antibiotics; the topical benzoyl peroxide medicines, the topical salicylic acid derivatives, and the variety of topical sulfa preparations seen in today's marketplace. Topical and systemic retinoids round out the medical armamentarium we have for those suffering from acne vulgaris. Despite the advances we have for our acne therapies, drawbacks to each group of medicines exist. Some of the topical medications are irritating to the skin and may cause clothes to stain. Most topical therapies are slow to achieve an acceptable onset of action, some requiring several months to become successful. Systemic antibiotics, the mainstay for inflammatory acne for many years, has recently seen reports of up to 40 % drug resistance to the commonly used systemic therapies – the tetracyclines, the erythromycins, and the sulfa derivatives (Leyden 1997; Gollnick et al. 2003). A recent report has even suggested that the long term use of systemic antibiotics in women may be associated with a higher incidence of breast cancer (Heckbert and Lampe et al. 2004).

Exposure to natural and artificial UV light has been reported successful in treating acne vulgaris over the years (Knulst and van Weelden et al. 1997). The exact mechanism for this response of the acne lesions to UV light is not fully understood but felt to be, in part to, destruction of the *P. acnes* bacteria in the sebaceous unit. This natural endogenous PDT reaction works well in the treatment of acne vulgaris; however, the damaging effects of UV light with regard to photoaging and the development of skin cancers precludes its regular use in today's medical environment.

The photodynamic reaction seen in the destruction of the *P. acnes* bacteria involves the natural production of porphyrins seen during the growth of the *P. acnes* during the inflammatory phase of the acne cycle. The porphyrins produced are principally PpIX and Coproporphyrin III, which have absorption spectra in the near ultraviolet range of light, in the blue light range, with peak absorption seen at 415 nm. The PDT reaction seen works through the photo-activation of the *P. acnes*' porphyrins with exposure to the appropriate light source. This causes the formation of singlet oxygen within the bacteria. Finally, destruction of the *P. acnes* bacteria will occur, with specific destruction of the acne lesion, leaving surrounding tissues and structures alone.

A variety of light sources have been used over the past century to treat acne vulgaris. These have included halogen, xenon, and tungsten light sources. More recent investigations have focused predominantly on blue light, and with the addition of ALA, blue light, vascular lasers, and the IPLs. These lasers and light sources focus on PDT and the destruction of the *P. acnes* bacteria. Still other lasers focus on destruction of the sebaceous gland and sebaceous gland activity output. Both groups will be reviewed.

The treatment of inflammatory acne vulgaris and the blue light source has seen extensive literature review over the past several years. Papageorgiou et al. (2000) reported his findings

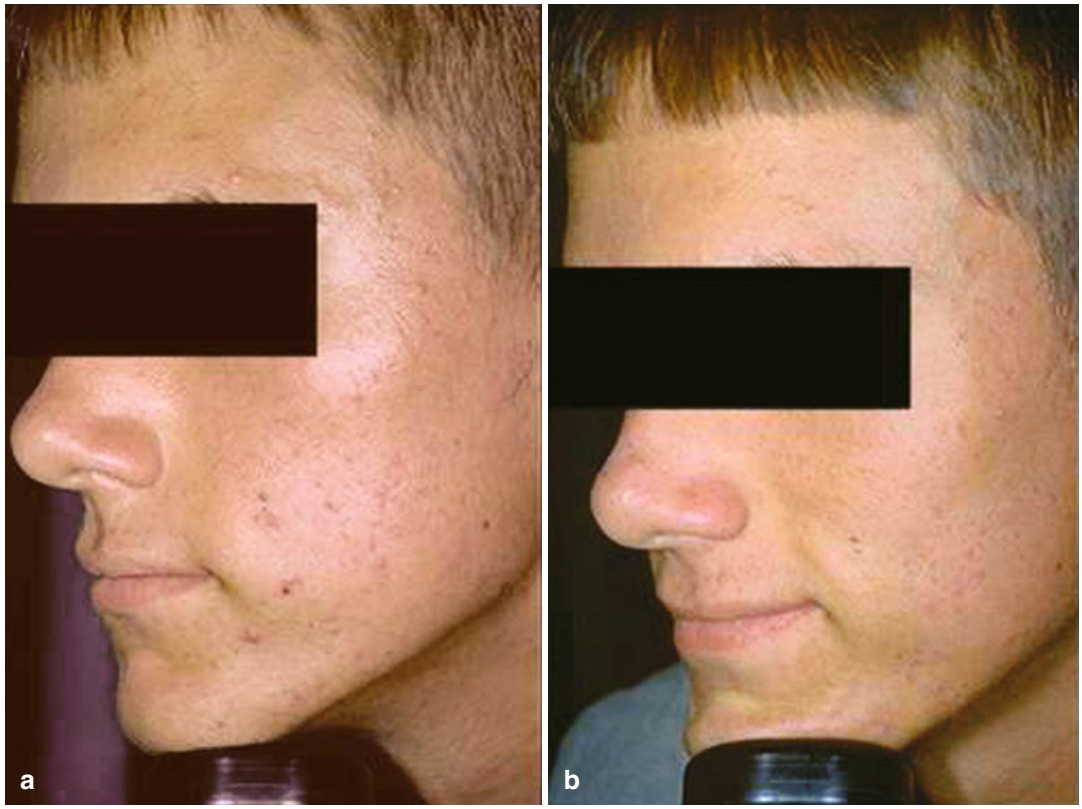


Fig. 6.8 (**a**) Acne: before blue light therapy. (**b**) Acne: post blue light therapy (© Gold Skin Care Center)

with a blue light source. He showed that 63 % of inflammatory lesions responded to blue light and 45 % of comedonal lesions also responded. Kawada et al. (2002) showed that 65 % of inflammatory acne lesions responded to the blue light therapy. A high-intensity blue light source (ClearLight™ CureLight, Israel) has also been evaluated for its effectiveness in the treatment of inflammatory acne vulgaris (Med Drug Lett Ther 2003; Elman et al. 2003). Investigators have shown between 60 and 75 % improvements with the high-intensity blue light source. Most of the clinical trials used two treatments per week for 4 weeks with appropriate 1 and 3 month follow-ups. These clinical trials had, on average, a 20 % non-responder rate. Gold (2003) reported his findings with the blue light source and 40 individuals with mild to moderate inflammatory acne vulgaris. Treatments were conducted two times per week with the high-intensity blue light source for 4 weeks, with follow-up at 1 and 4 months. The results of this trial showed that 43 % improvement in the inflammatory acne lesions; all patients were included in the analysis, responders and non-responders. Clinical examples are shown in (Figs. 6.8 and 6.9). Another blue light source, the Blu-U™ (Dusa Pharmaceuticals), has also been cleared for the treatment of mild to moderate inflammatory acne vulgaris lesions. A recent investigation of this blue light source showed that blue light therapy was more effective than topical 1 % clindamycin solution in treating inflammatory acne vulgaris during a 4 week treatment period and a 4 month follow-up time period (Gold 2004).

A variety of IPLs are also being used for the treatment of acne vulgaris. The mechanism of action for IPLs is similar to blue light therapy; destruction of the *P. acnes* bacteria leading to a PDT effect. The SkinStation™ by Radiancy was

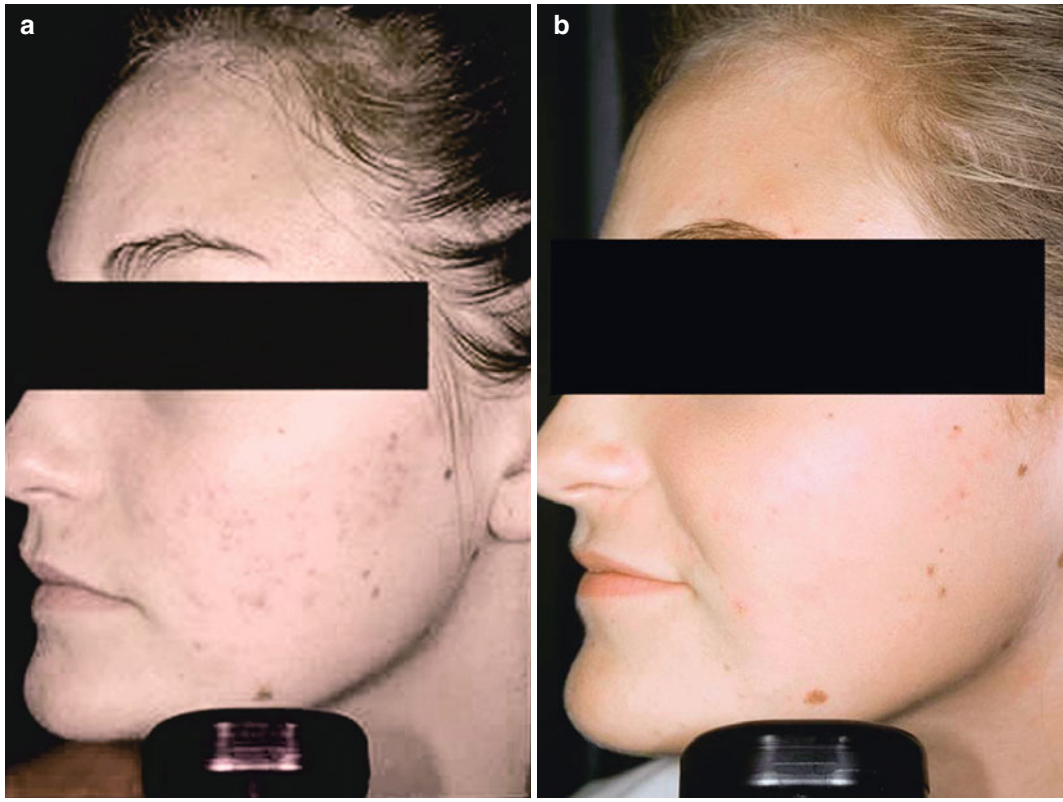


Fig. 6.9 (**a**) Acne: before blue light therapy. (**b**) Acne: post blue light therapy (© Gold Skin Care Center)

evaluated by Elman and Lebzelter (2004). Eighty-five percent of their patients showed greater than 50 % improvement in their acne lesions. Fifteen to twenty percent of the patients, however, were non-responders. Recently, a newer IPL, the Isolaz (AesThera, California) has shown effectiveness in several clinical trials in treating both non-inflammatory and inflammatory acne vulgaris (Shamban et al. 2008; Gold and Biron 2008).

Other investigators have looked at other laser systems which work through the destruction of the sebaceous glands themselves. Lloyd and Mirkov (2002) evaluated the use of the 810 nm diode laser with application of indocyanin green. The indocyanin green is selectively absorbed into sebaceous glands and can be destroyed with exposure to the 810 nm diode laser. Paithankar et al. (2002) have studied the 1,450 nm laser for the treatment of inflammatory acne lesions. Their clinical evaluations have shown significant destructions of the sebaceous glands with this therapy and long-lasting resolution of the acne lesions.

From these initial clinical trials and evaluations, a group of investigators have begun to look at the use of ALA as an enhancer for the laser and light therapies. Hongcharu et al. (2000) looked at broad band light (500–700 nm) using ALA with a 3 h drug incubation period in 22 individuals. The results of the trial showed significant clinical clearance noted after 4 weeks which persisted up to 20 weeks with multiple treatments with the ALA or up to 10 weeks with one ALA treatment. Adverse effects included an acneform folliculitis, post-inflammatory hyperpigmentation, superficial peeling, and crusting. Itoh et al. (2000) reported on the use of ALA and a 635 nm pulsed excimer-dye laser in an intractable case of acne vulgaris on the face. The ALA was incubated for 4 h under occlusion. The treated area remained clear of the

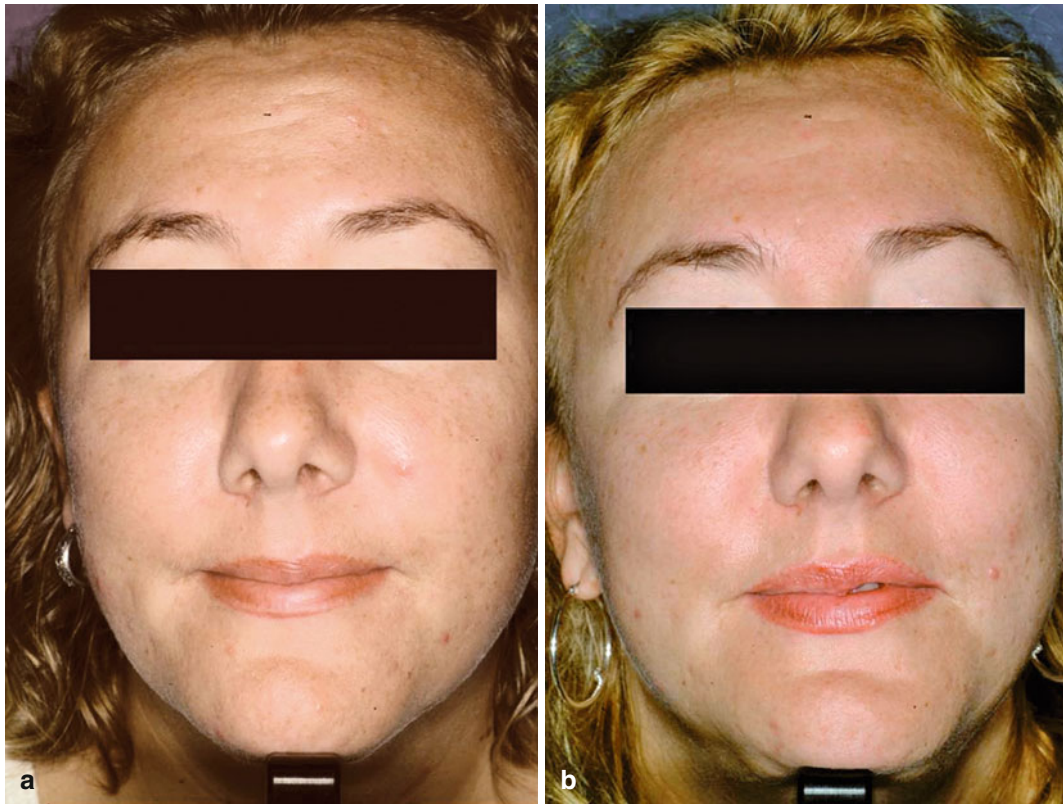


Fig. 6.10 (**a**) Acne: before ALA-PDT/IPL therapy. (**b**) Acne: post ALA-PDT/IPL therapy (© Gold Skin Care Center)

acne lesions during the 8 month follow-up period. A classic PDT reaction (erythema, edema, and crusting) were seen following the therapy. A second trial from Itoh et al. (2001) looked at a single ALA treatment in 13 individuals. Polychromatic visible light with a wavelength of 600–700 nm, 17 mW/cm^2, and 13 J/cm^2. The facial appearance of all patients improved and new acne lesions were reduced at 1, 3, and 6 months. During the following 6 months, acne lesions did reappear and seborrhea, reduced during therapy, also returned. Again, a classic PDT reaction occurred following the therapy with erythema, edema, and crusting noted in the patients following treatments.

Goldman (2003) reported on the use of short contact ALA-PDT and the IPL device or blue light device for the treatment of acne vulgaris and sebaceous gland hyperplasia. Treatments were noted to be pain free and without adverse effects. Relative clearing of the acne lesions were seen after 2–4 weekly treatments. Gold (2003) evaluated ten patients with moderate to severe acne vulgaris utilizing short contact, full face ALA-PDT and the high-intensity blue light source. Four weekly treatments showed a response of approximately 60 % (versus 43 % with the blue light source alone). Sessions were well tolerated with no adverse effects. Goldman and Boyce (2003) studied acne vulgaris with the blue light source with and without ALA in 22 individuals. Blue light therapy was performed twice per week for 2 weeks with a follow-up at 2 weeks; blue light plus ALA was performed two times at 2 weeks intervals with a follow-up at 2 weeks post the final treatment. There was a greater response in the ALA-PDT/blue light group than blue light alone with no significant adverse effects seen in either group of patients. Gold (2004) has been evaluating a new IPL for moderate to severe acne vulgaris with ALA-PDT. Twenty patients were

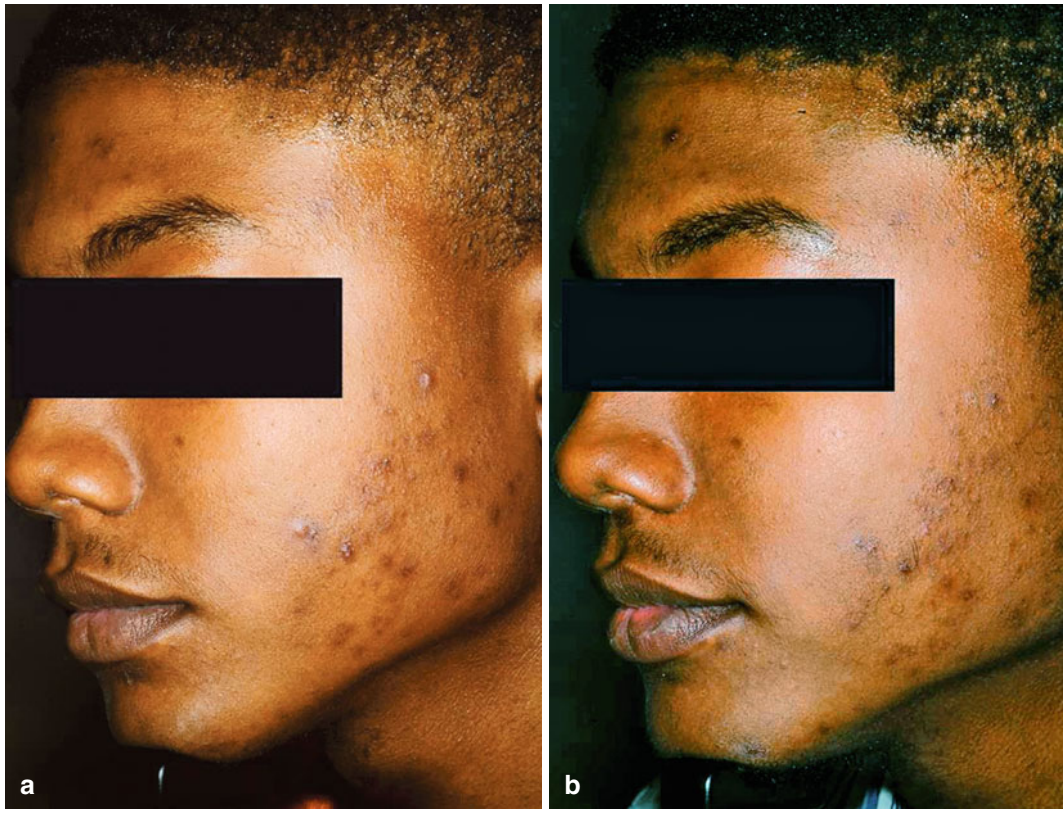


Fig. 6.11 (**a**) Acne: before ALA-PDT/IPL therapy. (**b**) Acne: post ALA-PDT/IPL therapy (© Gold Skin Care Center)

evaluated and results show significant improvement in inflammatory acne lesions; similar to previous studies performed by the author with blue light and ALA. Examples are seen in (Figs. 6.10 and 6.11).

Two recent split-face clinical trials (Santos et al. 2005; Rojanamatin and Choawawanich 2006) have recently been published utilizing ALA-IPL for the treatment of inflammatory acne vulgaris. In both of these clinical trials the ALA-IPL treated side improved significantly as compared to the IPL treated side.

MAL-PDT has also been used to treat inflammatory acne vulgaris utilizing protocols similar to what is routinely performed for MAL-PDT. Wiegell and Wulf (2006) were the first to report on the use of MAL-PDT in inflammatory acne vulgaris in 20 individuals. They found the treatment successful (68 %) but adverse events, including postulation within 24 h, and pain, were common in their patients. Horfelt et al. (2006) also have reported their use with MAL-PDT and inflammatory acne vulgaris – with a 54 % response rate in the 30 patients evaluated. Again, pain was the major adverse event reported in this clinical trial.

The combination of short contact, full face ALA-PDT treatments with blue light sources, IPLs, and other lasers and light sources appears to provide a synergistic effect to effectively treat patients suffering from moderate to severe inflammatory acne vulgaris. The combination therapy has been shown to be safe and it appears to work at a faster rate than lasers or light therapy alone and with fewer treatments required. This combination therapy may eliminate the need of more intensive systemic therapies in some of our patients. A recent Phase III clinical trial utilizing ALA-PDT and blue light failed to show significance in reducing inflammatory acne vulgaris, as compared to blue light alone. The future of ALA-PDT

for inflammatory acne vulgaris appears in question at this time in gaining regulatory approval, although many consider it still a very viable therapy.

The future of MAL-PDT for inflammatory acne vulgaris also is not known at this time. The pain associated with the therapy as it is performed today may need to be modified to make it more "user friendly." Clinical trials with MAL-PDT for inflammatory acne vulgaris are ongoing at this time.

Photodynamic Therapy for Hidradenitis Suppurativa

Several other medical conditions are also being treated with ALA-PDT. Gold et al. (2004) reported on the successful use of ALA-PDT and the high-intensity blue light source in the treatment of hidradenitis suppurativa (HS). Four individuals with recalcitrant HS were treated with short-contact ALA and between 3 and 4 sessions of the blue light source. The treatments were given at 1–2 week intervals. Seventy-five to one hundred percent of the HS lesions responded to this therapy and remained clear during the 3 months follow-up period. An example is seen in (Fig. 6.12).

A second report, in Europe (Strauss et al. 2005) failed to show the effectiveness of their non-commercial ALA in the treatment of HS. Their patients, for the most part, were unable to tolerate the therapy, due to pain predominantly. A long drug incubation time was used by this group. A subsequent clinical study in the US, by Rivard and Ozog (2006) did confirm the results of Gold et al. that by using ALA-PDT and a short drug incubation, HS can be successfully treated and maintained.

Photodynamic Therapy for Sebaceous Gland Hyperplasia

Sebaceous gland hyperplasia is an entity which has had numerous therapeutic modalities used for therapy. These have included cryotherapy, excision, electrodessication, laser vaporization, and oral isotretinoin use. These therapies are often associated with lesional recurrences or undesirable adverse side effects. The first report of the use of ALA-PDT in the treatment of sebaceous gland hyperplasia was by Horio et al. (2003) in which a slide projector used as a light source successfully made sebaceous gland hyperplasia lesions smaller. Alster and Tanzi (2003) reported on the use of ALA and the 595 nm pulsed dye laser in the treatment of sebaceous gland hyperplasia lesions. Ten patients received short contact ALA drug incubation (1 h) and one or two treatments at 6 week intervals. Results showed that seven individuals had clearing of the targeted sebaceous gland hyperplasia lesions with one ALA-pulsed dye laser treatment and three patients required two treatments for lesion clearing. Follow-up in this group of patients was for 3 months. Matched lesions on the same patient served as controls; some were treated with pulsed dye laser and some not treated at all. The treatments were well tolerated by the study participants. Richey and Hopson (2004) evaluated ten patients with short-contact ALA-PDT and the blue light source. Patients

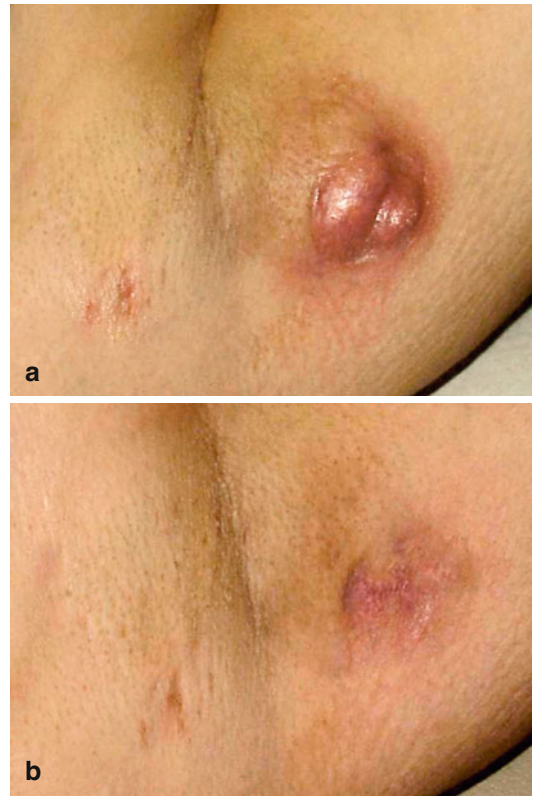


Fig. 6.12 (**a**) HS: before ALA-PDT blue light. (**b**) HS: 3 months post ALA-PDT blue light (© Gold Skin Care Center)

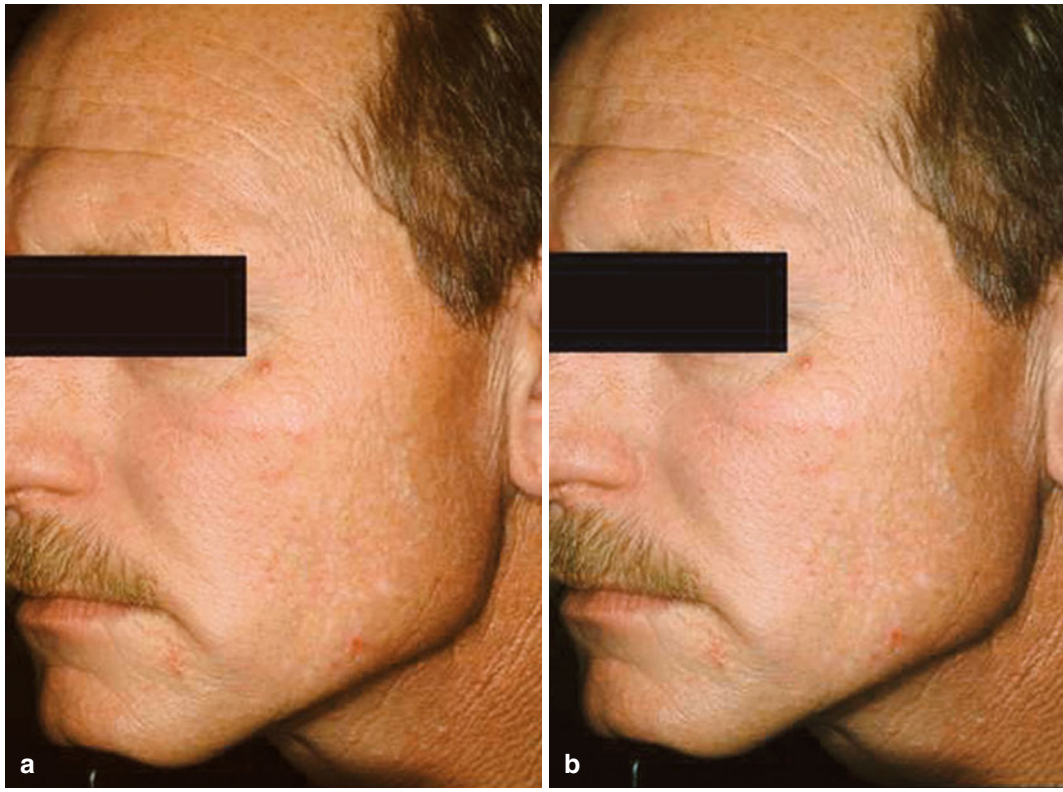


Fig. 6.13 (**a**) Sebaceous gland hyperplasia: before ALA-PDT/IPL therapy. (**b**) SBH: after ALA-PDT/IPL therapy (© Gold Skin Care Center)

were given 3–6 one times per week treatments and were followed for 6 months. Seventy percent of all lesions responded to the therapy and all patients showed at least a partial response to this therapy. Recurrence rates of up to 10–20 % of lesions were seen within 3–4 months of the final treatment. Gold (2004) has examined short-contact ALA-PDT in a group of patients who received either IPL therapy or the high-intensity blue light source. Results from 4 weekly therapies show both therapies useful in the treatment of sebaceous gland hyperplasia, with 50 % of lesions responding during the treatment and follow-up period of 3 months. A clinical example is seen in (Fig. 6.13).

Advantages

ALA-PDT therapy is an important new treatment modality which enhances already proven and successful laser and light source treatments. It must be remembered that, at the time of this writing, ALA-PDT is the only commercially available photosensitizer available. Its only FDA approval is for the treatment of nonhyperkeratotic AKs of the face and the scalp utilizing a blue light source with a 14–18 h drug incubation time period. The clinical trials presented for AKs, photorejuvenation, acne vulgaris, HS, and sebaceous gland hyperplasia, and the methodology used by the investigators are all being performed as off-label clinical trials when used in the short-contact, full-face mode. Clinicians can use medicines in an off-label format; patients should be made aware of the off-label use of these treatments and proper informed consents should be made prior to the actual treatments (Fig. 6.14). Research into entities being treated with ALA-PDT is growing and more investigations will follow in the months and years to come.

Patient's Informed Consent

Informed Consent for ALA-PDT

CLIENT CONSENT FOR LEVULAN PHOTODYNAMIC TREATMENT

Levulan (Aminolevulinic acid 20%) is a naturally occurring photosensitizing compound which has been approved by the FDA and Health and Welfare Canada to treat pre-cancerous skin lesions called actinic keratosis. Levulan is applied to the skin and subsequently "activated" by specific wavelengths of light. This process of activating Levulan with light is termed Photodynamic Therapy. The purpose of activating the Levulan is to improve the appearance and reduce acne rosacea, acne vulgaris, sebaceous hyperplasia, decrease oiliness of the skin, and improve texture and smoothness by minimizing pore size. Any pre-cancerous lesions are also simultaneously treated. The improvement of these skin conditions (other than actinic keratosis) is considered an "off-label" use of Levulan.

I understand that Levulan will be applied to my skin for 30- 60 minutes. Subsequently, the area will be treated with a specific wavelength of light to activate the Levulan. Following my treatment, I must wash off any Levulan on my skin. I understand that I should avoid direct sunlight for 24 hours following the treatment due to photosensitivity. I understand that I am not pregnant.

Anticipated side effects of Levulan treatment include discomfort, burning, swelling, blistering, scarring, redness and possible skin peeling, especially in any areas of sun damaged skin and pre-cancers of the skin, as well as lightening or darkening of skin tone and spots, and possible hair removal. The peeling may last many days, and the redness for several weeks if I have an exuberant response to treatment.

I consent to the taking of photographs of my face before each treatment session. I understand that I may require several treatment sessions spaced 1-6 weeks apart to achieve optimal results. I understand that I am responsible for payment of this procedure, as it is not covered by health insurance.

I understand that medicine is not an exact science, and that there can be no guarantees of my results. I am aware that while some individuals have fabulous results, it is possible that these treatments will not work for me. I understand that alternative treatments include topical medications, oral medications, cryosurgery, excisional surgery, and doing nothing.

I have read the above information and understand it. My questions have been answered satisfactorily by the doctor and his staff. I accept the risks and complications of the procedure. By signing this consent form I agree to have one or more Levulan treatments.

Name	Signature
Date	Witness

Fig. 6.14 Informed Consent for ALA-PDT

Informed Consent for Psoriasis Laser/Light Therapy & Disorders of Hypopigmentation

CONSENT FOR ULTRAVIOLET LIGHT TYPE B- PHOTOTHERAPY

Phototherapy involves the exposure of the involved skin to a short-wave ultraviolet light known as UVB. UVB occurs naturally in sunlight; it is the part of the sunlight, which causes sunburns.

The dosage of UVB will be determined on many factors such as type of skin, disease, age, and type of equipment. The time is gradually increased until the desired result is achieved. At all times, while inside the phototherapy light box, special protective eyewear must be worn. Men will also protect their scrotum area.

The side effects to ultra-phototherapy B are, during treatment the psoriasis can sometimes get temporarily worse before getting better. The skin may itch and get red due to overexposure (sunburn). The long-term risk in developing skin cancer(s) from long-term exposure to UVB is unknown. Also, long-term exposure can cause freckling and loss of skin elasticity.

During the course of therapy, your skin will be evaluated.

***Also, I agree that any pictures taken of me can be used for either teaching or publication unless I notify the staff in writing that they are not to use my pictures. ***

_____

I hereby state that I have read and understand the above information. All my questions have been answered, and I hereby consent to the proposed UVB phototherapy treatment.

_____ _____

Patient's Signature Witness

_____

Date

Fig. 6.15 Informed Consent for laser/light therapy for psoriasis and disorders of hypopigmentation

Psoriasis and Disorders of Hypopigmentation

Psoriasis Vulgaris

Psoriasis vulgaris is another medical dermatology disease which has recently been shown to be successfully treated with a new generation of lasers and light sources. Psoriasis is a chronic, non contagious skin disease which affects between 1 and 3 % of the population, or about 7 million people in the United States. It is the seventh most common reason patients seek dermatologic care, and numerous studies have indicated significant quality of life issues associated with patients having psoriasis. Psoriasis is characterized by a silver-scaled erythematous plaque-like eruption with predilection sites being areas of trauma, such as the elbows, knees, and scalp. Psoriasis varies in severity from mild to moderate to severe disease. Mild psoriasis vulgaris usually means disease activity of less than 2 % body surface area; moderate disease between 2 and 10 %; and severe, greater than 10 % body surface area. Genetics, biochemical pathways, and the immune system are known to be involved in the pathogenesis of psoriasis. Faulty immune signals accelerate the growth cycles in skin cells, which pile up on the skin surface faster than the body can shed them – 3–4 days instead of the normal 28 days. Much of the recent evidence into the pathogenesis of psoriasis suggests that psoriasis is a T-cell mediated disease (Callen et al. 2003).

Currently Available Technology

A variety of treatment options exist for patients suffering from psoriasis. Most of the treatments are safe and effective, and can improve the condition of the skin and reduce the symptoms associated with psoriasis, mainly swelling, redness, flaking and itching. These therapies, seen in (Table 6.5), are used to induce remissions in the skin. A step-ladder approach to psoriasis therapy is commonly used by most clinicians, as shown in (Table 6.5). Under Step 2, Phototherapy, a variety of new lasers and light sources are being evaluated for the treatment of psoriasis.

The major light sources being used for the treatment of psoriasis are the phototherapy light sources: BClear™ (Lumenis), ReLume (Lumenis), and the MultiClear™ (CureLight); and the excimer lasers and light sources including Xtrac™ (PhotoMedix) and the Pharos Ex 308 (RA Medical Systems). Clinical trials with the XTrac™, a 308 nm excimer laser, have shown significant clearing of psoriatic plaques. Feldman (2002) reported on a multicenter analysis with 124 patients at 5 centers. Seventy-two percent of patients demonstrated 75 % or greater clearance in 6.2 treatments or less. Eighty-four percent achieved improvement of 75 % or better after ten treatments. Trehan and Taylor (2002) also showed significant clearance using the excimer laser in 11 patients in 1 month of therapy; 5 patients remained disease free at a 4 month follow-up. Clinical examples with the excimer device are shown in (Figs. 6.16 and 6.17). The BClear™ is a narrowband UVB device which delivers the UVB in a focused, fiber-optic delivery system. This allows the UVB to be delivered only to diseased tissue and leaving healthy tissue alone. This gives the potential to have the number of sessions needed for successful UV therapy to be reduced and, by targeting healthy skin, gives

Table 6.5 Treatment options for psoriasis vulgaris

Step 1: Topical therapy	Topical corticosteroids Topical coal tar Topical calcepotriene (vitamin D) Topical vitamin A derivatives Topical anthralin Topical salicylic acid Natural sunlight
Step 2: Phototherapy/ lasers	Ultraviolet B (UVB) light Narrowband UVB BClear™ - ReLume (Lumenis) Xtrac™ (PhotoMedex) Excimer Laser PUVA (psoralen plus ultraviolet A light)
Step 3: Systemic medications	Methotrexate Oral retinoids Cyclosporine Biologic drugs Alefacept (Amevive®) Efalizumal (Raptiva®) Etanercept (Enbrel®) Infliximab (Remicade®)

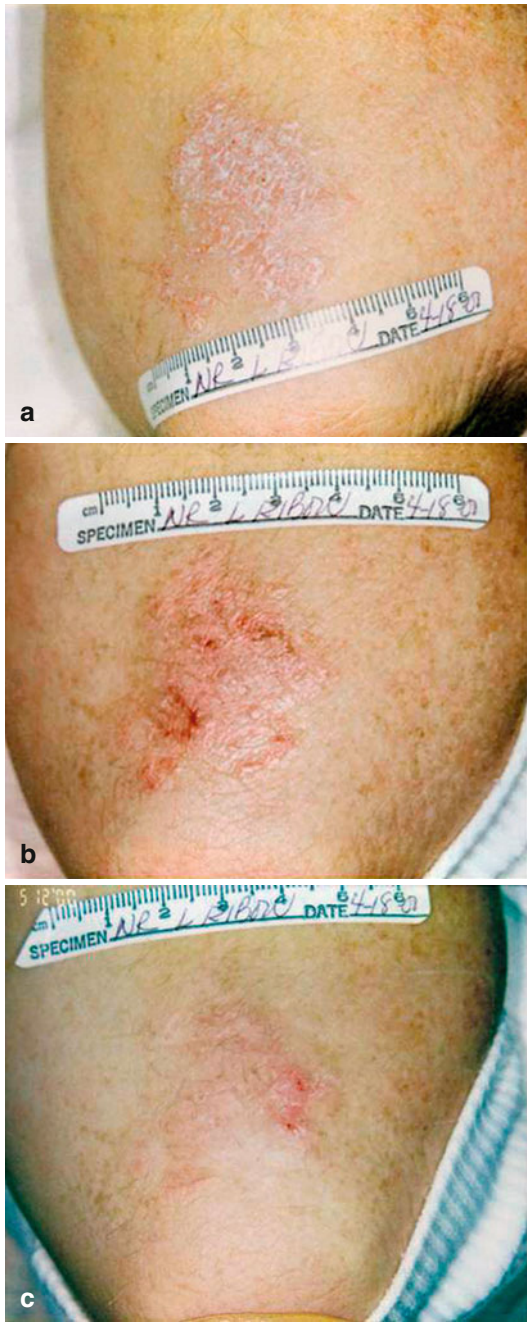


Fig. 6.16 (**a**) Psoriasis: pre-excimer laser. (**b**) Psoriasis : post 3 excimer laser treatments. (**c**) Psoriasis : post 6 excimer laser treatments (© PhotoMedex)

a reduction for potential adverse effects and for the development of skin cancers. This device produces UVB light in the 290–320 nm range with peak energies at 311 and 314 nm. The device

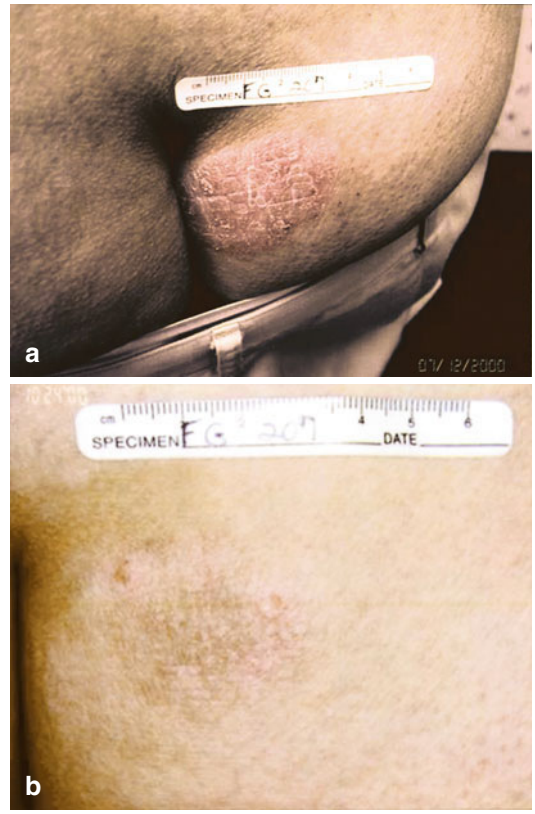


Fig. 6.17 (**a**) Psoriasis: pre-excimer laser. (**b**) Psoriasis: post 10 excimer laser treatments (© PhotoMedex)

may deliver light either in a single pulse mode or continuous pulse mode. Pulse widths of 0.5, 1.0, 1.5, and 2.0 s exist. Fluences range from 50 to 800 mJ and spot sizes up to 16×16 mm exist for the device. Several clinical trials by C. Dierickx (2002, personal communication) and E. Tanghetti (2002, personal communication) have shown significant clearances with this targeted UVB system. Clinical examples with the targeted UVB system are shown in (Figs. 6.18 and 6.19). The BClear and the ReLume are no longer commercially available, although many still utilize this device for psoriasis.

Disorders of Hypopigmentation

Vitiligo

A variety of leukodermas of the skin is also being treated with the excimer devices and targeted

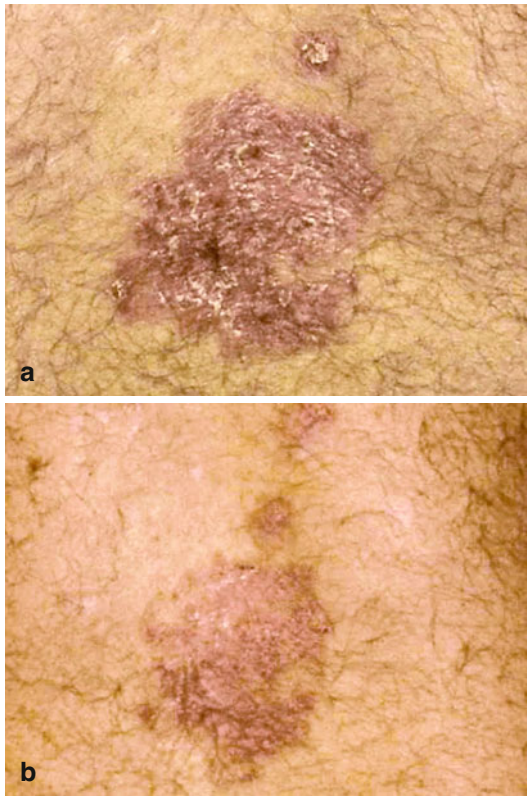


Fig. 6.18 (**a**) Psoriasis: pre-narrowband UVB targeted therapy. (**b**) Psoriasis: post 10 narrowband UVB targeted therapy (©Gold Skin Care Center)

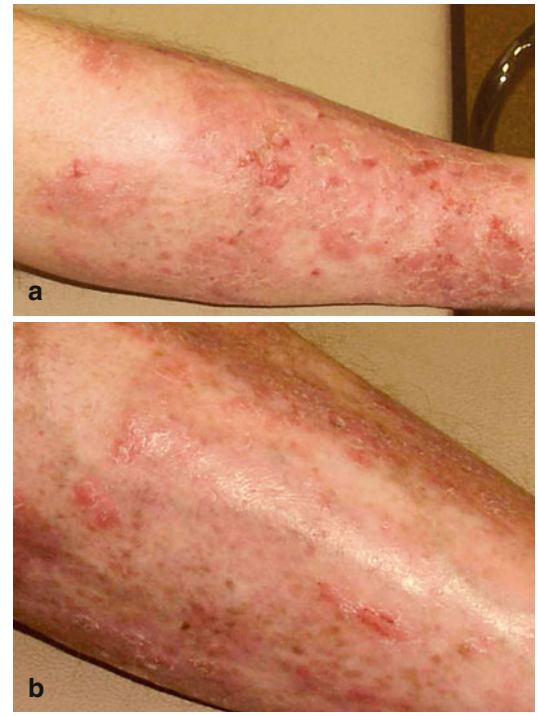


Fig. 6.19 (**a**) Psoriasis: pre narrowband UVB targeted therapy. (**b**) Psoriasis: post 10 narrowband UVB targeted therapy (©Gold Skin Care Center)

UVB systems. Leukodermas of the skin are defined as loss of skin pigment from a disease process (i.e., vitiligo) or secondary to an injury pattern to the skin (including loss of pigment from burns, surgical procedures, and following laser resurfacing procedures). Other skin concerns, such as idiopathic guttate hypomelanosis and hypopigmented stretch marks are also being evaluated with these machines. Vitiligo is a pigmentation disorder in which melanocytes in the skin, mucous membranes, and the retina of the eye may be destroyed. As a result, white patches of skin can appear on different parts of the body. Even hair may be affected in vitiligo and turn white. The cause of vitiligo is unknown; genetics may play a role and vitiligo is often associated with autoimmune diseases. Vitiligo affects between 1 and 2 % of the world population, or between 40 and 50 million people worldwide. All races are equally affected with vitiligo and both sexes are also equally affected. A variety of therapies are available in an attempt to repigment those affected with vitiligo. These are shown in (Table 6.8). The 308 nm excimer laser has shown promising results in the treatment of vitiligo. Spencer et al. (2002) looked at 18 patients with vitiligo. Twenty-three patches of vitiligo from 12 patients received at least 6 treatments with the excimer laser and showed a response rate of 57 %. Eleven patches from 6 patients received 12 treatments and had an 82 % response rate. An example of the treatment of vitiligo with the excimer laser is shown in (Fig. 6.20). The targeted narrowband UVB device used for repigmentation is called the ReLume™ (Lumenis). It is a similar device to the narrowband UVB device used for psoriasis; its fluences range from 50 to 400 mJ. Initial clinical reports support its usefulness in the treatment of vitiligo. An example of the targeted UVB device in the treatment of vitiligo is seen in (Fig. 6.21).

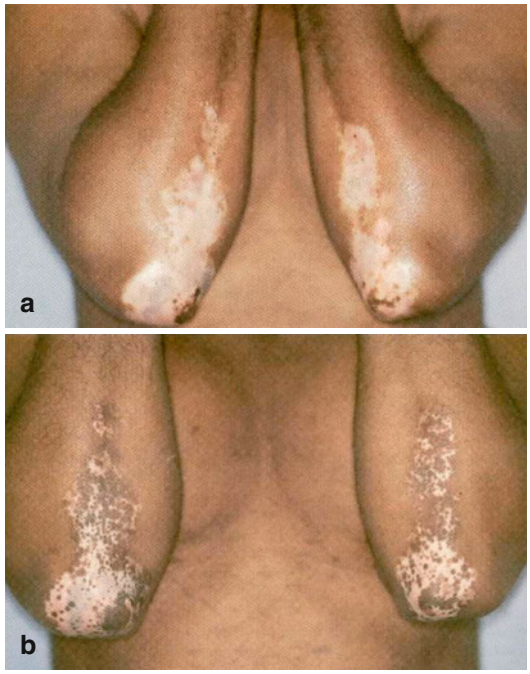


Fig. 6.20 (**a**) Vitiligo: pre excimer laser. (**b**) Vitiligo: post 10 excimer laser treatments (©PhotoMedex)

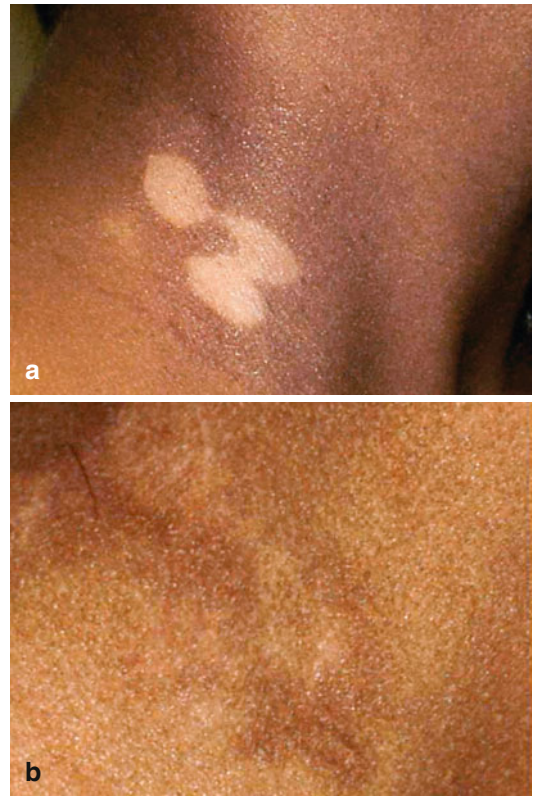


Fig. 6.21 (**a**) Vitiligo: pre narrowband UVB targeted therapy. (**b**) Vitiligo: post 4 narrowband UVB targeted therapy (©Gold Skin Care Center)

Hypopigmented Stretch Marks

Hypopigmented stretch marks are an interesting and potentially exciting field of study. Stretch marks are often seen in dermatologic and cosmetic clinics. Vascular stretch marks are easy to treat with a variety of vascular lasers and IPLs. Hypopigmented stretch marks are more difficult to treat. Goldberg & Associates (Sarradet et al. 2002) presented data with regard to 10 patients receiving 10 patients with the 308 nm excimer laser. Repigmentation was noted in all study participants; acceptable results were seen in 70 % of the individuals. The targeted UVB device has had several reports which showed up to 70–80 % repigmentation in hypopigmented scars and stretch marks. Gold (2004) recently reported on a group of 50 individuals with hypopigmented stretch marks and with 10 treatments found between 30 and 40 % repigmentation. Examples of the repigmentation by the targeted UVB device are shown in (Figs. 6.22 and 6.23).

Recently, the laser community has been introduced to the fractional laser devices, both the nonablative and the ablative modes. There has been much speculation that these may be useful for the treatment of hypopigmented stretch marks and several clinical trials are underway which will delineate which of these might be affective and the appropriate parameters needed.

Disadvantages

The lasers and light sources used in the treatment of medical dermatologic skin concerns have a low incidence of adverse effects. The use of ALA-PDT has had a "PDT effect" described after prolonged drug incubation and exposure to light sources. This PDT effect of erythema, edema, and crusting has been shown to last up to 1 week after light exposure; this has been minimized with the use of short contact full face therapy. Lasers and light sources can cause erythema, blisters, burns and, on occasion, scarring – all

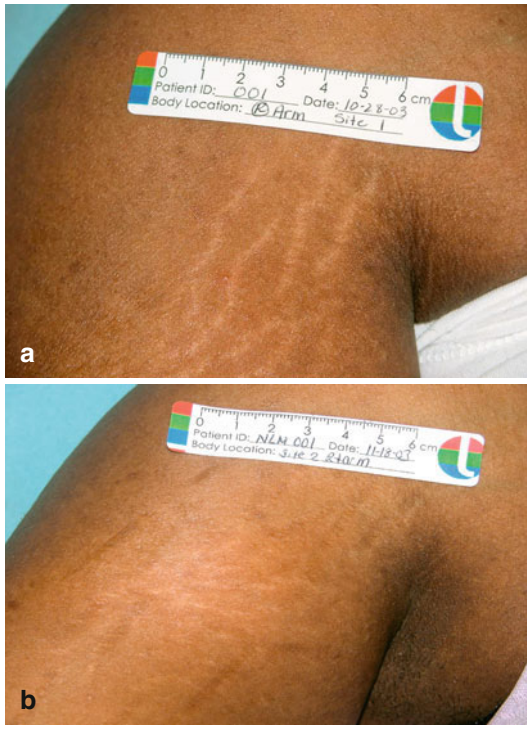


Fig. 6.22 (**a**) Hypopigmented stretch marks: pre narrowband UVB targeted therapy. (**b**) Hypopigmented stretch marks: post 4 narrowband UVB targeted therapy (©Gold Skin Care Center)

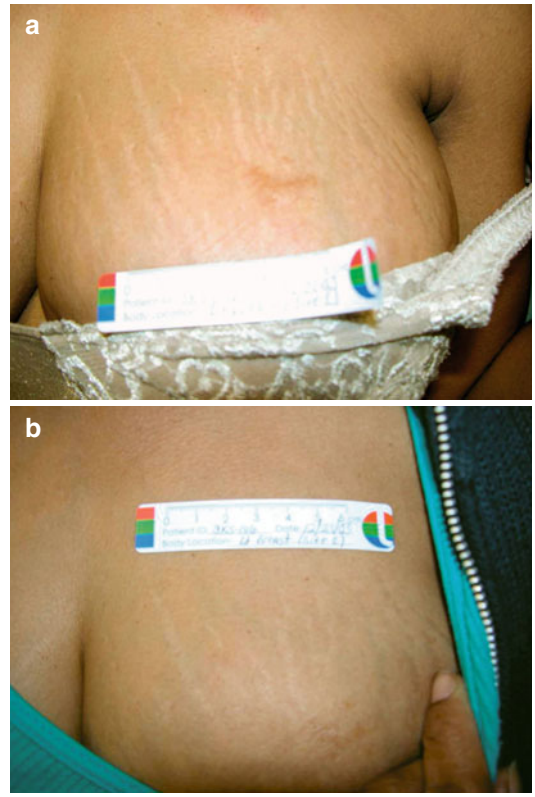


Fig. 6.23 (**a**) Hypopigmented stretch marks: pre narrowband UVB targeted therapy. (**b**) Hypopigmented stretch marks: post 4 narrowband UVB targeted therapy (©Gold Skin Care Center)

physicians must be aware of the devices they use and learn the technology intimately to minimize any potential adverse risk. Conversely, if a complication arises, the physician must be comfortable in treating such adverse events.

The lasers and light sources being utilized for psoriasis vulgaris and disorders of hypopigmentation have shown themselves to be very safe and devoid of major complications. Fractional lasers also appear very safe, with only minimal side effects reported thus far.

Contraindications

Contraindications are rare when utilizing lasers and light sources with ALA-PDT. Similarly, contraindications are rare for the lasers and light sources used for psoriasis vulgaris and disorders of hypopigmentation. As with all laser and light treatments, patient expectations are a major concern for all these therapies. The treatments work over time and will require multiple visits to achieve the proper results. Maintenance therapies will also be required in most instances.

Most laser physicians would not recommend the use of oral isotretinoin when performing laser and light treatments. Whether this is an absolute contraindication is open for debate, but caution should be used if oral isotretinoin is used during these laser or light procedures.

Personal Laser Technique

ALA-PDT Technique

The technique which we use in our office varies depending upon the condition which we are treating. The two most common uses of ALA-PDT in our office setting is for photodynamic photorejuvenation and for the treatment of moderated to

Table 6.6 Lasers/light sources for ALA/photorejuvenation

Machine	J/cm^2	Other parameters
Quantum™ IPL	22	Program depending on skin type – default parameters for pulse width and delay
Vasculight™ IPL	32	Double pulsed; 3.5, 3.5 20 ms delay
Lumenis One ™	15–25	560 nm filter Double pulse (4.0/4/0 ms with 20 ms delay) Single pass with no overlap
Levulan incubation of 30–60 min		

Table 6.7 Acne vulgaris treatment with ALA-PDT

Machine	Time on
Blu-U ™	16 min; 40 s
Skin Station ™	10 % power
ClearLight ™	18 min
Incubation of 30 min to 1 h	

Table 6.8 Psoriasis and hypopigmented disorders (B ClearTM – RelumeTM)

B Clear™ – Relume™	Psoriasis	Starting with MED testing based on Fitzpatrick skin type	
MED settings			
Test spot #	Skin phototypes I–II	Skin phototypes III–IV	Skin phototypes V–VI
1	100	150	200
2	130	190	250
3	170	230	300
4	200	270	350
5	230	310	400
6	260	350	450
7	300	400	500
We start treatment after reading MED's 24 h after administering them.			
We initiate treatment at 3 times the MED.			
B Clear™ – Relume™	Vitiligo and hypopigmented scars	Start at 100 J, increase by 10 % at each visit	

severe acne vulgaris. Both techniques will be described.

ALA-PDT for photodynamic photorejuvenation utilizes the Levulan® Kerastick™, and the following light sources: blue light, the intense pulsed light source, and the pulsed dye laser. The preparation prior to the procedure is the same for each device. The areas to be treated are cleaned with a mild facial cleanser. For increased penetration of the ALA, those with moderate to severe actinic damage, a vigorous acetone scrub or a microdermabrasion procedure is performed prior to application of the ALA. The ALA is prepared as previously described. The ALA is applied to the entire area being treated in an even distribution and allowed to incubate for approximately 1 h prior to laser/light therapy. Before the procedure is performed, the ALA is washed off the face with the mild cleanser. The choice of light source is up to each practitioner – head to head clinical trials have not been performed to determine if one light source is superior to another; in my experience, all work well and deliver the desired results. The lasers/light sources available at our office for photodynamic photorejuvenation and the settings we utilize for this therapy are shown in (Table 6.6). We explain to our patients that treatments are performed once a month for up to four treatments, with the actual number determined by the patient's response to the therapy.

For the treatment of moderate to severe acne vulgaris, the procedures previously outlined are once again utilized. The light sources we utilize in our office setting when treating acne vulgaris with ALA-PDT are listed in (Table 6.7). For our acne patients, we typically treat patients every other week for up to four visits, all dependent on the patient's response to the therapy.

Medicines and other skin care products are very important in all situations with ALA-PDT, and again, maintenance therapies will be required.

Psoriasis Vulgaris and Disorders of Pigmentation Techniques

The two main light sources utilized in our office, for psoriasis vulgaris and disorders of hypopigmentation are the narrowband UVB source and the excimer laser. Multiple therapies with each modality are required and maintenance therapies will be needed. (Tables 6.8 and 6.9) list the light sources utilized in our office and the settings used for each condition.

Table 6.9 Psoriasis and hypopigmented disorders (XTRACTM)

XTRAC™	Psoriasis	Start with MED administration with settings below	
MED settings:			
MED values	MJ/cm² delivered	Determining first dose:	
1	100	Thick plaque: 3× MED	
	150	Thin plaque: 2× MED	
3	200		
4	250		
5	300		
6	350		
XTRAC™	Vitiligo	Start with MED with same parameters as above	
Suggested starting dosage for:		Then use chart that follows: mJ/cm² MED and treatment dose multiplier levels (shown as integer or as a percentage value)	
Periocular		100 mJ = 1 MED × 1 (MULT) *or* MED × 100 % (MULT)	
Face, scalp, ear, neck, axilla bikini		150 mJ = 2 MED × 1 (MULT) *or* 2 MED × 100 % (MULT)	
Arm, leg, trunk		200 mJ = 3 MED × 1 (MULT) *or* 3 MED × 100 % (MULT)	
Wrist		250 mJ = 4 MED × 1 (MULT) *or* 4 MED × 100 % (MULT)	
Elbow		300 mJ = 5 MED × 1 (MULT) *or* 5 MED × 100 % (MULT)	
Knee		350 mJ = 1 MED × 1 (MULT) *or* 6 MED × 100 % (MULT)	
Hands, feet		400 mJ = 3 MED × 1 (MULT) *or* 3 MED × 200 % (MULT)	
Finger, toes		600 mJ = 5 MED × 1 (MULT) *or* 5 MED × 200 % (MULT)	
Subsequent doses:			
Erythema < 24 h	Erythema 24–48 h	Erythema 48–60 h	Erythema 60–72 h
Treat fluence should be increased by 50 mJ	Treatment fluence should be kept at same fluence as previous treatment.	Treatment fluence should be decreased by 500 mJ	Treatment should be postponed and next treatment decrease by 100 mJ

Post-operative Care

ALA-PDT Post-operative Care

Home Care Instructions for Patients Following ALA-PDT Photodynamic Skin Rejuvenation

Day of Treatment

1. If you have any discomfort, begin applying ice packs to the treated areas. This will help keep the area cool and alleviate any discomfort, as well as help keep down any swelling. Swelling will be most evident around the eyes and is usually more prominent in the morning.
2. Remain indoors and avoid direct sunlight.
3. Spray on Avene™ Thermal Spring Water often.
4. Apply Cetaphil™ moisturizing cream.
5. Take analgesics such as Advil® if necessary.
6. If given any topical medications, apply twice daily to the treated area.

Days 2–7

1. You may begin applying make-up once any crusting has healed. The area may be slightly red for 1–2 weeks. If make-up is important to you, please see one of our aestheticians for a complimentary consultation.
2. The skin will feel dry and tightened. Cetaphil™ moisturizer should be used daily.
3. Try to avoid direct sunlight for 1 week. Use a total block Zinc Oxide based sunscreen with a minimum SPF 30.

Psoriasis and Disorders of Hypopigmentations Post-operative Care

Post-op Care for ReLume™

ReLume is a UVB light source. Therefore, some redness may occur to the treated areas.

1. If redness occurs, you may use ice packs or Aloe-Vera gel to the treated areas.

2. Avoid sunlight for the first couple of days after treatment. You may use sunscreen if you must be outdoors.

Complications

Complications reported with these therapies are rare and have been covered with each individual trial in which any complications were described.

The Future

A variety of medical concerns are now being treated with lasers and light sources. The advent of ALA-PDT has heralded a new era for dermatologists and laser surgeons beyond AKs, BCCs, and SCCs. Now "Photodynamic Photorejuvenation" is a common term and photorejuvenation treatments are being enhanced with the use of ALA-PDT. Other entities, including acne vulgaris, hidradenitis suppurativa, and sebaceous gland hyperplasia are being treated with lasers, light sources, and ALA-PDT. As well, lasers and light sources are being used to treat psoriasis vulgaris, vitiligo, and other hypopigmented disorders, including hypopigmented stretch marks. Lasers and light sources have moved into the medical dermatology world – making this a very exciting time for laser physicians.

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Index

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