3rd Edition

PROCEDURES IN COSMETIC DERMATOLOGY

Series editor Jeffrey S Dover

Associate editor Murad Alam

Expert CONSULT

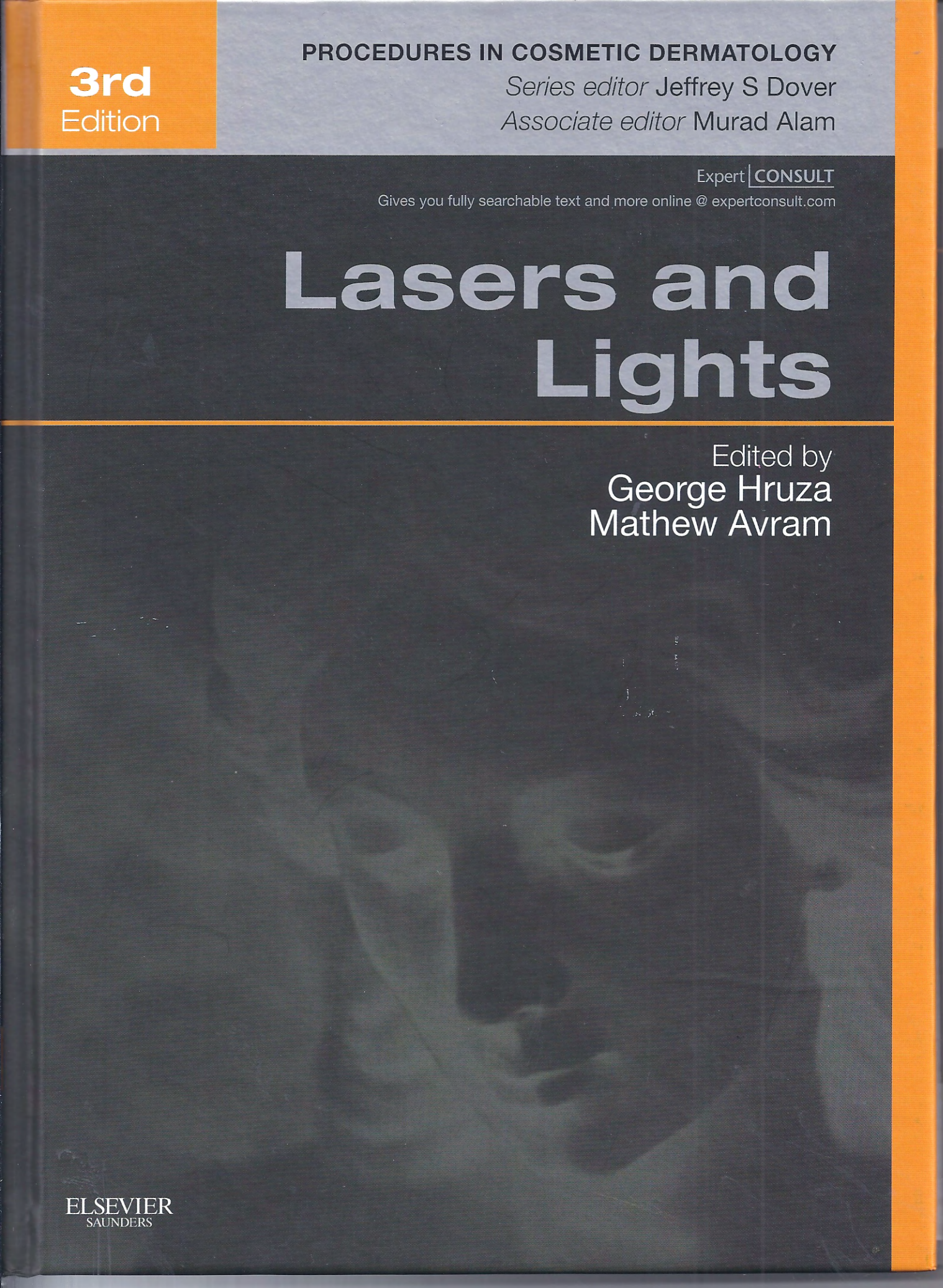
Gives you fully searchable text and more online @ expertconsult.com

Lasers and Lights

Edited by

George Hruza

Mathew Avram



ELSEVIER
SAUNDERS

3rd Edition

PROCEDURES IN COSMETIC DERMATOLOGY

Lasers and Lights

Edited by

George J. Hruza MD, MBA

Clinical Professor, Dermatology, Saint Louis University, Saint Louis;
Medical Director, Laser & Dermatologic Surgery Center, Chesterfield, MO, USA

Mathew M. Avram MD, JD

Assistant Professor of Dermatology, Harvard Medical School;
Affiliate Faculty, Wellman Centerfor Photomedicine;
Director, Massachusetts General Hospital Dermatology Laser & Cosmetic Center, Boston, MA, USA

Series Editor

Jeffrey S. Dover MD, FRCPC, FRCP

Associate Professor of Clinical Dermatology, Yale University School of Medicine, New Haven, CT;
Adjunct Professor of Medicine (Dermatology), Dartmouth Medical School, Hanover, NH;
Adjunct Associate Professor of Dermatology, Brown Medical School, Providence, RI;
Director, SkinCare Physicians, Chestnut Hill, MA, USA

Associate Editor

Murad Alam MD

Professor of Dermatology, Otolaryngology, and Surgery;
Chief, Section of Cutaneous and Aesthetic Surgery,
Northwestern University, Chicago, IL, USA

SAUNDERS

ELSEVIER

London New York Oxford St Louis Sydney Toronto 2013

3 Laser treatment of pigmented lesions and tattoos

Kavita Mariwalla, George J. Hruza

Summary and Key Features

- Just as placement of tattoos has gained popularity, so has the number of people interested in their removal
- Black and blue tattoos are the easiest to fade with the most predictable results, whereas multicolored tattoos are the most difficult
- Of the various benign pigmented lesions that can be treated with laser, the easiest to treat are lentigines while the most difficult are the nevi of Ota, Ito, and Hori
- Pigment-specific lasers such as the quality-switched (QS) ruby (694 nm), QS alexandrite (755 nm), and QS Nd:YAG (532 nm and 1064 nm) continue to be the workhorse systems for both tattoo and pigmented lesion removal
- QS lasers remove tattoo pigment through photoacoustic injury, breaking up the ink particles and making them more available for macrophage phagocytosis and removal
- Fractional photothermolysis has provided expanded options for pigmented lesion removal in the last decade, though generally more treatment sessions are required and the cost is higher
- In general, patients with Fitzpatrick skin phototypes I–III have a better response than those with skin phototypes IV–VI as the lasers used for pigment removal can also damage epidermal pigment
- Topical anesthesia is helpful when treating dermal pigmented lesions and tattoos
- Factors to consider prior to estimating the number of treatment sessions a patient will need for tattoo removal include: Fitzpatrick skin phototype, location, color, amount of ink used in the tattoo, scarring or tissue change, and ink layering
- As with any procedure, patient selection and preparation are important to success and photographs of the lesions should be taken prior to each treatment session
- Side effects of laser treatment for pigmented lesions include textural change, scarring, pruritus, hypo- or hyperpigmentation, and immediate pigment change
- Tattoos with white or red ink carry an increased risk of paradoxical darkening after laser treatment, which is why test spots should be carried out prior to the first treatment session
- Caution should be exercised prior to treatment of a tattoo with an allergic reaction as the dispersed ink particles can elicit a systemic response
- For pigmented lesions such as melasma and postinflammatory hyperpigmentation, pre- and postoperative treatment should include hydroquinone and topical retinoids
- Postoperative care includes gentle cleansing and a bland emollient while the skin heals

Introduction

Tattooing has become increasingly popular in recent times, with an estimated 7–20 million people in the USA with at least one. In a 2008 online survey conducted by Harris Interactive, an estimated 14% of all adults in the USA have a tattoo, which corroborates with phone survey results from 2004 in which Laumann & Derick found tattoo prevalence in 26% of males and 22% of females. Interestingly, 17% of those with tattoos considered removal. With advances in laser- and light-based technology, as well as their availability, many patients are not only looking to rid themselves of tattoo ink but also seeking removal of benign pigmented lesions.

In this chapter, we will discuss the use of laser for removing tattoos and ameliorating the appearance of benign pigmented lesions. Although the target for both is pigment, the management of lightening and removal for each condition is distinct.

Pigment removal principles

Quality-switched ('QS') lasers have traditionally been the workhorse laser systems for the removal of pigmentation

and tattoos. The laser treatment of pigmented lesions is based on the concept of selective photothermolysis; in essence the chosen laser must emit a wavelength that is specific and well absorbed by the intended target. In the case of tattoos, the chromophore is exogenously placed ink found either within macrophages or extracellularly throughout the dermis. In the case of benign pigmented lesions, the intended chromophore is melanin found within melanocytes, keratinocytes or dermal macrophages. Destruction of this pigment is thought to occur mainly through photoacoustic injury. Because the target particles are small, it is important to use pulses of energy that are extremely short to minimize collateral thermal injury to the normal surrounding tissue. For this reason, QS lasers, with energy pulses in the nanosecond range, enable energy to be deposited very quickly. The intense heat transients cause some particles to shatter and kill the cells in which the pigment resides. The rupture of pigment-containing cells eventually triggers phagocytosis and the packaging of pigment fragments for lymphatic drainage and scavenging by dermal macrophages. For epidermal pigment, the pigment-containing cells are killed with the laser pulses resulting in epidermal necrosis and subsequent sloughing and replacement with normal epidermis.

QS lasers used for pigmented lesions include the QS ruby (694 nm), the QS alexandrite (755 nm) and the QS Nd:YAG (532 and 1064 nm) though it is also possible to use the long-pulsed ruby, alexandrite and diode lasers, or intense pulsed light (see Ch. 5). Within the last decade, fractional photothermolysis ('FP') has gained popularity for its ability to treat pigmented conditions such as melasma, solar lentigines, nevus of Ota, and postinflammatory hyperpigmentation (see Ch. 6).

Lesion selection

Just as important as patient selection is evaluation of the lesion itself. Tattoos can be divided into amateur, professional, cosmetic, medical, and traumatic categories. In amateur tattoos, a steel needle is used to deposit ink, which may be at various depths of the skin, whereas in professional tattoos, a hollow needle is used to inject ink into the dermal layer of skin. Amateur tattoos typically contain pigment of unknown sources such as ash, coal, or India ink **(**Fig. 3.1**)**. On the other hand, professional tattoo artists often combine ink pigments to achieve novel colors and shading. Cosmetic tattoos using skin-colored tones are important to distinguish, as are medical tattoos such as those used as radiation markers. For traumatic tattoos, it is important to understand the nature of the injury that caused it so as to be aware of the type of material implanted in the skin prior to treatment.

It is critical when treating pigmented lesions other than tattoos that the lesion itself be evaluated for malignancy. Lasers should not be used for any kind of melanoma, as even with in situ melanoma recurrence rates are very high. Similarly, we recommend against the removal of dysplastic nevi with lasers even though studies have shown no significant increase in carcinogenic markers after laser stimulation of melanocytes.

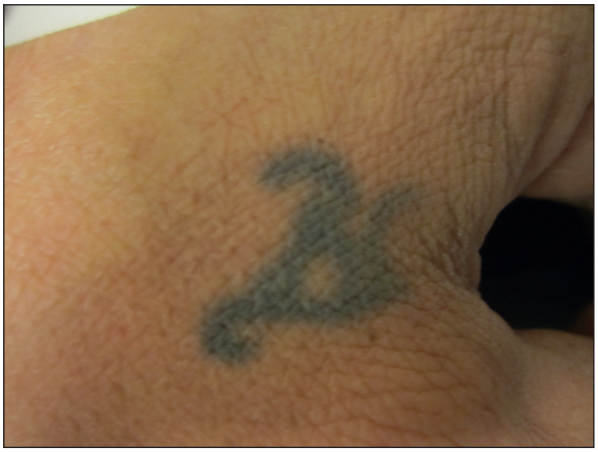


Figure 3.1 Amateur tattoo placed on the hand in a person with Fitzpatrick skin phototype IV.

Patient selection in general

At initial consultation for removal of a pigmented lesion, it is important to take a thorough medical history including a history of allergy to anesthetics (both topical and injectable), current medical conditions, and medications. If a patient is currently taking isotretinoin, laser treatment should be delayed until medication completion as, theoretically, there is a potential for increased scarring and delayed healing. In addition, it is important to note if the patient was ever treated with systemic gold therapy (e.g. rheumatoid arthritis therapy) as this is an absolute contraindication to QS laser treatment since darkening of gold-containing skin is immediate and irreversible. Prophylaxis is appropriate in patients with a history of herpes simplex virus if treating near the trigger point. A history of keloidal scarring and a tendency toward postinflammatory hypo- or hyperpigmentation should also be documented.

Patient selection for tattoo removal

Though tattoos are increasingly popular, they often become a source of personal regret as up to 50% of adults older than 40 with tattoos seek their removal. It is critical that a thorough history of the tattoo be taken prior to deciding upon a treatment plan to establish appropriate patient expectations (Box 3.1). Kirby et al recently published a scale to help practitioners estimate the number of treatment sessions needed for tattoo removal to appropriately guide patients who often enter the laser removal process of their tattoos with uncertainty and misconceptions (Table 3.1). In the scale, numerical values are assigned to six parameters: (1) Fitzpatrick skin phototype, (2) location, (3) color, (4) amount of ink used in the tattoo, (5)

minutes, this gray converts to erythema. In dermal lesions, the immediate whitening is less vivid.

A snapping sound is common with QS laser use as pigment particles and the cells that contain melanin or tattoo particles are heated and explode. The lesion is fully covered with laser pulses. The immediate whitening keeps additional light from entering the skin due to reflection. Pulse stacking should be avoided as this may increase the risk of scarring and unnecessary thermal injury. If significant energy is absorbed by a pigmented lesion, pinpoint bleeding may occur, as occasionally occurs with tattoos.

Pearl 4

After tattoo treatment, the lesion often turns a gray-white. When treating a multicolored tattoo with more than one laser wavelength, the additional treatment pass should be carried out only after the whitening has fully dissipated, which may take 10–20 minutes.

CASE STUDY 1

Uneven tissue response in a black tattoo

AR is a 39-year-old man with an amateur tattoo on the hand. The tattoo appears black and the patient reports that his 'friend put it there'. The patient does not have a tan. After icing the area for 15 minutes, the tattoo is treated with the QS Nd:YAG laser at a fluence of 3.0 J/cm^2. The tattoo responds immediately and turns white and then erythematous. Unlike the rest of the tattoo, the central portion develops an erosion immediately upon treatment. This occurred because, in amateur tattoos, pigment is not placed at a uniform depth or in a uniform concentration. The tattoo was treated from the periphery to the center. While the periphery responded well, it was too much energy for the center, which led to immediate epidermal sloughing and pinpoint bleeding (Figs 3.1 and 3.2).

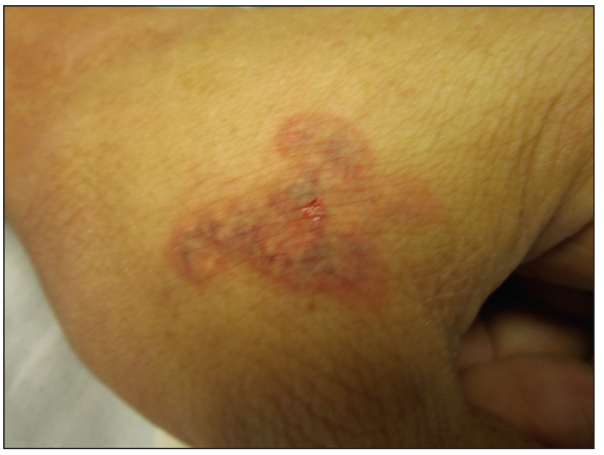


Figure 3.2 Amateur tattoo immediately after treatment with the QS Nd:YAG laser showing punctuate bleeding.

Performing 2–4 treatments of a tattoo all in one day (waiting for the immediate whitening to fade between treatments) seems to increase the degree of fading achieved in one visit.

Patients and equipment for dark-blue or black tattoo treatment

Fitzpatrick skin phototypes I–III

In lighter-skinned patients (in the absence of a tan or bronzer), the practitioner has several options (Table 3.2). The QS alexandrite (755 nm), the QS ruby (694 nm), and the QS Nd:YAG (1064 nm) lasers are all effective for dark-blue and black tattoos (Fig. 3.3). In the case of traumatic tattoos that appear black, it is important to know the origin of the trauma since such tattoos may react with a small explosion (e.g. gun powder tattoo) after laser treatment.

Fitzpatrick skin phototypes IV–VI

In darker-skinned patients, lasers having longer wavelengths are generally safer as they spare the epidermis to a greater degree than shorter-wavelength lasers. Thus, the QS Nd:YAG (1064 nm) is the laser of choice.

Patients and equipment for red tattoo treatment

The optimal laser wavelength for removing red tattoo ink is 532 nm (QS frequency-doubled Nd:YAG). This wavelength can cause both hyperpigmentation and hypopigmentation in darker-skinned patients so treatment should be limited to phototype I–III patients. It should be noted that red tattoo ink is often the culprit for allergic reactions after tattoo placement and granulomatous reactions in the tattoo itself (Fig. 3.4). Laser removal of the red ink can cause greater dispersion of the antigen resulting in urticaria or a systemic allergic reaction. In these cases, an ablative CO_2 or Er:YAG laser can be employed to vaporize the tattoo (Fig. 3.5). If a QS-laser is employed, the patient should be covered with systemic corticosteroids and antihistamines and the laser surgeon should proceed with caution (Case study 2).

Table 3.2 Laser choices based on tattoo ink color

QS laser	Black	Blue	Green	Red
Alexandrite 755 nm	X	X	X	
Ruby 694 nm	X	X	X	
Nd:YAG 1064 nm	X	X	X	
Nd:YAG 532 nm				X
Nd:YAG 650 nm			X	

tattoos, the presence of pastel colors such as light blue, turquoise, yellow, light green, lavender, and pink should also raise suspicion of white ink additives. Treatment may result in immediate and permanent tattoo darkening in white and even in red tattoos. The laser pulse can reduce ink from rust-colored ferric oxide (Fe_2O_3) to jet-black ferrous oxide (FeO). Similarly, white ink made up of titanium dioxide (TiO_2, T^{4+}) can be reduced to blue Ti^{3+} upon laser treatment. Such post-treatment darkening appears immediately. For this reason, a single small inconspicuous test spot is recommended to ensure that this complication does not occur. Even after testing, it is appropriate to obtain the patient's written consent that they understand tattoo ink darkening may still occur during future treatments and that it may be permanent. The darkening usually becomes apparent once the immediate whitening has faded. If pigment darkening does occur in a decorative tattoo, it may be improved with subsequent treatment with the QS Nd:YAG laser operated at 1064 nm.

Thermal injury and scarring

Textural changes can be minimized through use of a large spot size and appropriate spacing of treatments at 6–8 weeks. Significant thermal injury and subsequent scarring are rare (~5%) when treating dermal pigmented lesions if the proper laser guidelines are followed and the appropriate treatment parameters are used. When they do occur, they are most likely to happen on the chest, outer upper arm and ankle. Ideal wound care with normal saline cleansing and application of petrolatum with a non-stick gauze dressing may prevent infection and help to minimize scarring. In spite of these efforts, if scarring does occur, subsequent treatment with a series of pulsed dye laser treatments, a series of injections of low-dose triamcinolone acetonide directly into the scar or topical application of silicone gel sheeting along with scar massage over a period of several weeks may help to improve the appearance of the scar. Cobblestone texture seen within 2 weeks of treatment is a sign of incipient scarring, and may be reversed with twice daily application of class I topical corticosteroids. Scarring after QS laser treatment of epidermal lesions is extremely rare.

Special situations

Tattoo granulomas

Allergic granulomas to tattoo ink are probably most commonly seen to the cinnabar in red-colored inks. In these situations, the use of any of the QS lasers is not recommended as it may worsen the allergic reaction and produce systemic symptoms or even anaphylactic reactions. The use of an ablative laser, such as the carbon dioxide or Er:YAG laser, can be employed to remove the offending ink and also destroy the granulomas at the same time. Biopsies should be considered before laser treatment to rule out sarcoidosis, infectious granulomas such as atypical mycobacterial infections, and other entities.

Table 3.3 Tattoo pigments used to create specific tattoo colors

Tattoo color	Source
Black	Carbon, iron oxide, India ink, lead, gunpowder
Red	Cinnabar (mercuric sulfide), cadmium selenide, sienna, azo dyes
Green	Chromium oxide, malachite green, hydrated chromium sesquioxide, lead chromate
Blue	Cobalt aluminum
Brown	Ochre
Yellow	Cadmium sulfide, ochre, curcumin yellow
Violet	Manganese violet
White	Titanium dioxide, zinc oxide

Multicolored tattoos

When treating a tattoo of multiple colors, especially black, red, or green, more than one laser may be required to maximize the degree of improvement. In these situations, the black outline of the tattoo is usually first treated with infrared light from the QS Nd:YAG laser operated at 1064 nm. Once that portion of the treatment has been completed, the green light from the frequency-doubled QS Nd:YAG laser operated at 532 nm is used to treat the red portions of the tattoo. If green tattoo ink is also present, red light from the Q-switched ruby or alexandrite lasers is used. Alternatively, the QS Nd:YAG with a 650 nm wavelength dye-containing handpiece can be used as well. Care should be taken to avoid overlapping the treatment pulses as much as possible by matching the size of the laser beam to the amount of the tattoo color being treated. By using this technique, it is often possible to treat the entire tattoo at one time resulting in more rapid resolution of the different colors than if they were treated individually at different visits. Other colors respond unpredictably to specific wavelengths with the treatment done mostly by trial and error. If prominent immediate whitening in the tattoo ink is noted, that laser wavelength will tend to achieve fading of that color (Table 3.3).

Further reading

Adrian RM, Griffin L 2000 Laser tattoo removal. Clinics in Plastic Surgery 27:181-192

Anderson RR, Geronemus R, Kilmer SL, et al 1993 Cosmetic tattoo ink darkening. A complication of Q-switched and pulsed-laser treatment. Archives of Dermatology 129(8): 1010-1014

Anderson RR, Parrish JA 1983 Selective photothermolysis: precise microsurgery by selective absorption of pulsed radiation. Science 220(4596):524-527

Armstrong ML, Roberts AE, Koch JR et al 2008 Motivation for contemporary tattoo removal a shift in identity. Archives of Dermatology 144:879-884

Laser hair removal

Omar A. Ibrahimi, Suzanne L. Kilmer

4

Summary and Key Features

- Laser hair removal is the most commonly requested cosmetic procedure in the world
- The extended theory of selective photothermolysis enables the laser surgeon to target and destroy hair follicles, thereby leading to both permanent and temporary hair removal
- The ideal candidate for laser hair removal (LHR) is fair skinned with dark terminal hair; however, LHR can today be successfully performed in all skin types
- Thin hairs and hairs with white, blond and red color are extremely difficult to treat with laser hair removal devices
- Wax epilation should be avoided prior to laser hair removal treatments
- Lasers pose a safety risk to both the patient and device operator
- Informed consent should be reviewed with every patient prior to treatment
- Wavelengths, spot size, pulse duration, and skin cooling are key variables that can be used to tailor laser–tissue interactions for a given patient
- Roughly 15–30% of hairs can be removed with each treatment session using ideal parameters. Remaining hairs are often thinner and lighter in color
- The most common complication is pigmentary alteration, which can be temporary or permanent

Introduction

The non-specific damage of human hair follicles with a laser was noted over 50 years ago. However, it was not until the theory of selective photothermolysis was proposed by two Harvard dermatologists, Rox Anderson and John Parrish, that the concept of selectively targeting a particular chromophore based on its absorption spectra and size was realized. In 1996, this group also reported the first successful use of a normal-mode ruby laser for long-term and permanent hair removal.

Removing unwanted body hair is today a worldwide trend, and hair removal using laser or other light-based technology is one of the most highly requested cosmetic procedures. Prior to the advent of laser hair removal (LHR), only temporary methods for removing unwanted hair were available such as bleaching, plucking, shaving, waxing, and chemical depilatories. Threading, a form of epilation using a cotton thread, is a common practice in some cultures. In addition to not providing permanent hair removal, these methods are also inconvenient and tedious. Electrolysis is a technique in which a fine needle is inserted deep into the hair follicle and uses electrical current, thereby destroying the hair follicle and allowing for permanent hair removal of all types of hair. However, this technique is impractical for treating large areas, extremely tedious, operator dependent, and with variable efficacy in achieving permanent hair removal. Eflornithine (α-difluoromethylornithine or DFMO) is a topical inhibitor of ornithine decarboxylase that slows the rate of hair growth and is currently FDA cleared for the removal of unwanted facial hair in women. In this chapter, we provide a detailed overview on LHR including discussion of hair follicle biology, the science behind LHR, key factors in optimizing treatment, and future trends.

Basic hair biology

The hair follicle is a hormonally active structure (Fig. 4.1) that is anatomically divided into an infundibulum (hair follicle orifice to insertion of the sebaceous gland), isthmus (insertion of the sebaceous gland to the insertion of the arrector (erector) pili muscle), and inferior (insertion of the arrector pili to the base of the hair follicle) segments. The dermal papilla provides neurovascular support to the base of the follicle and helps form the hair shaft.

Every hair follicle is controlled by a programmed cycle that is dependent on the anatomical location. The hair cycle consists of anagen, catagen, and telogen phases. Anagen is characterized by a period of active growth where the hair shaft lengthens. A catagen transition period follows in which the lower part of the hair follicle undergoes apoptosis. A resting period, telogen, then ensues, and regrowth occurs when anagen resumes. Hair regrowth (entry into another anagen cycle) is dependent on stem cells within or near the hair bulb matrix. Slow-cycling stem cells have also been found in the follicular bulge

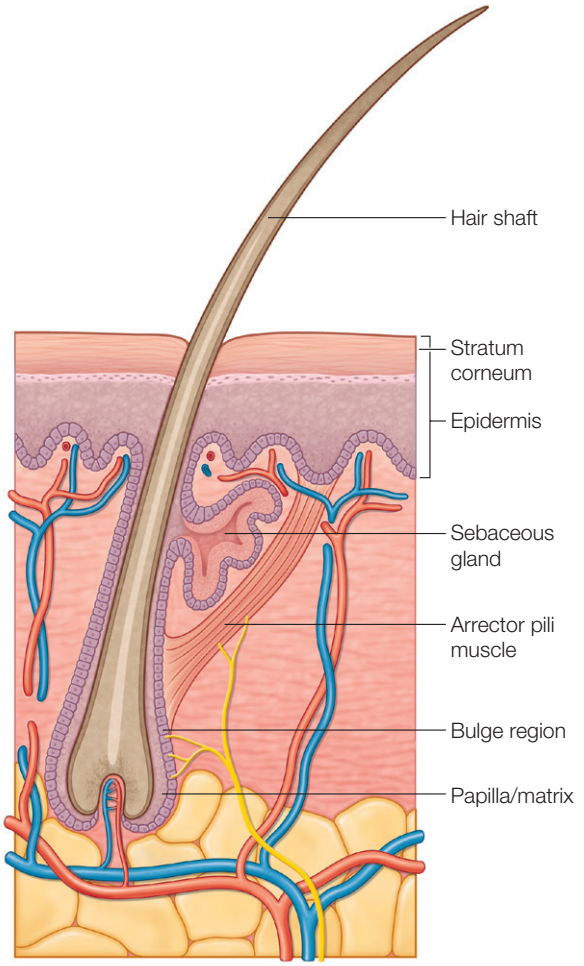


Figure 4.1 Hair follicle anatomy. *Reproduced from Tsao SS, Hruza GJ 2005 Laser hair removal. In: Robinson JK, Hanke CW, Sengelmann RD, Siegel DM (eds) Surgery of the Skin. Elsevier Mosby, Philadelphia, p 575-588.*

arising off the outer root sheath at the site of the arrector pili muscle attachment.

The main types of hair include lanugo, vellus, and terminal hairs. Lanugo hairs are fine hairs that cover a fetus and are shed in the neonatal period. Vellus hairs are usually non-pigmented, and have a diameter of roughly 30–50 μm. Terminal hair shafts range from 150 to 300 μm in diameter. The type of hair produced by an individual follicle is capable of change (e.g. vellus to terminal hair at puberty or terminal to vellus hair in androgenic alopecia).

The amount and type of pigment in the hair shaft determine hair color. Melanocytes produce two types of melanin: eumelanin, a brown-black pigment; and pheomelanin, a red pigment. Melanocytes are located in the upper portion of the hair bulb and outer root sheath of the infundibulum.

Definitions of what constitutes excessive or unwanted body hair depends on cultural mores, but can usually be classified as either hypertrichosis or hirsutism. Hirsutism is the abnormal growth of terminal hair in women in male-pattern (androgen-dependent) sites such as the face and chest. Hypertrichosis is excess hair growth at any body site that is not androgen dependent. Additionally, the use of grafts and flaps in skin surgery can often introduce hair to an area that causes a displeasing appearance or functional impairment.

Mechanism of LHR

The theory of selective photothermolysis enables precise targeting of pigmented hair follicles by using the melanin of the hair shaft as a chromophore. Melanin has an absorbance spectrum that matches wavelengths in the red and near-infrared (IR) portion of the electromagnetic spectrum. To achieve permanent hair removal, the biological 'target' is the follicular stem cells located in the bulge region and/or dermal papilla. Due to the slight spatial separation of the chromophore and desired target, an extended theory of selective photothermolysis was proposed that requires diffusion of heat from the chromophore to the desired target for destruction. This requires a laser pulse duration that is longer in duration than if the actual chromophore and desired target are identical. Temporary LHR can result when the follicular stem cells are not completely destroyed, primarily through induction of a catagen-like state in pigmented hair follicles. Temporary LHR is much easier to achieve than permanent removal when using lower fluences. Long-term hair removal depends on hair color, skin color, and tolerated fluence. Roughly 15–30% long-term hair loss may be observed with each treatment when optimal treatment parameters are used (Fig. 4.2). A list of laser and light devices that are currently commercially available for hair removal is given in Table 4.1.

Key factors in optimizing treatment

LHR has revolutionized the ability to eliminate unwanted hair temporarily and permanently in many individuals of all skin colors. Proper patient selection, preoperative preparation, informed consent, understanding of the principles of laser safety, and laser and light source selection are key to the success of laser treatment. An understanding of hair anatomy, growth and physiology, together with a thorough understanding of laser–tissue interaction, in particular within the context of choosing optimal laser parameters for effective LHR, should be acquired before using lasers for hair removal.

Patient selection

A focused medical history, physical examination, and informed consent, including setting realistic expectations and potentials risks, should be performed prior to any

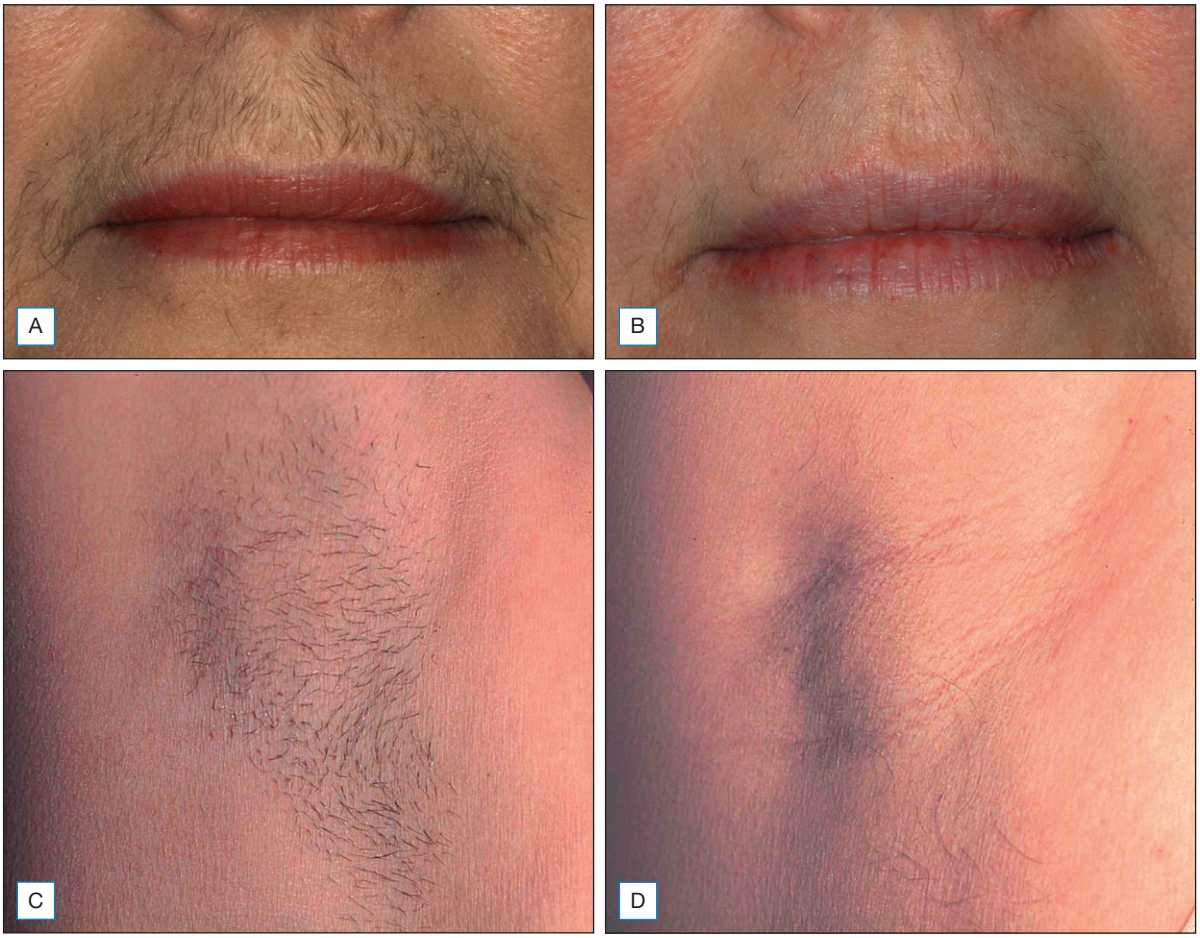


Figure 4.2 Laser hair removal is safe and effective. (**A**) The upper cutaneous lip of a hirsute female. (**B**) Appearance of same subject following only three treatments with a long-pulsed 755 nm alexandrite laser used with a 12 mm spot size, 16 J/cm^2, 3 ms pulse duration and DCD setting of 30/30/0. (**C**) Axilla of an adult female. (**D**) Following four treatments with a long-pulsed diode laser with a large spot size and vacuum-assisted suction. The fluence used was 12 J/cm^2 and the pulse duration was 60 ms. Both of the above subjects achieved excellent hair reduction and further benefit would likely be attained with additional treatments.

Table 4.1 Commercially available lasers and light sources for hair removal*

Laser/light source	Wavelength (nm)	System name	Pulse duration (ms)	Fluence (J/cm^2)	Spot size (mm)	Other features
Long-pulsed ruby	694	RubyStar® and Ruby Star+® (Aesclepion, Germany)	4	Up to 24	8, 10, 12, 18	Contact cooling
Long-pulsed alexandrite	755	Apogee® (Cynosure, Westford, MA, USA)	0.5–300	2–50	5–15	Cold air or integrated cooling, can add 1064 nm Nd:YG module to form Apogee Elite®
		Arion® (Quantel Derma, Germany)	5–140	Up to 40	6–16	Cold air cooling
		ClearScan ALX® (Sciton, Palo Alto, CA, USA)	Up to 200	Up to 140	3, 6, and 30 × 30	Contact cooling

Continued

Table 4.1 Commercially available lasers and light sources for hair removal—cont'd

Laser/light source	Wavelength (nm)	System name	Pulse duration (ms)	Fluence (J/cm^2)	Spot size (mm)	Other features
		Coolglide® (Cutera, Brisbane, CA, USA)	0.1–300	5–300	10	Contact cooling
		Elite® (Cynosure)	0.5–300	25–50	5–15	Cold air cooling, available with 1064 nm Nd:YAG, EliteMPX® model can simultaneously treat with 755 nm alexandrite and 1064 nm Nd:YAG
		EpiCare LP/LPX® (Light Age, Somerset, NJ, USA)	3–300	22–40	7–16	Dynamic cooling
		GentleLASE® (Syneron-Candela, Wayland, MA, USA) GentleMax® (Syneron-Candela)	3 0.25–300	Up to 100 Up to 600	6–18 1.5–18	Dynamic cooling, comes with 1064 Nd:YAG
		Ultrawave 755/II/III® (AMC Aesthetics and Advance Aesthetic Concepts, Plattsburgh, NY, USA)	Up to 100	Up to 125	Up to 16	Available with 532, 1064, and 1320 nm Nd:YAG
Diode	800–810	F1 Diode® (Opusmed, Canada)	15–40	Up to 40	5, 7	Chiller tip
	808, 980	Leda® (Quantel Derma)	6–60	Up to 60	50 × 12, 10 × 12	Contact cooling
	810, 940	MeDioStar XT® (Aesclepion)	5–500	Up to 90	6, 12	Integrated scanner with cold air cooling
	800	LightSheer Duet® (Lumenis, Israel)	5–400	10–100, 4.5–12	9 × 9, 22 × 35	Chilltip for smaller handpiece, vacuum skin flattening for larger handpiece
	810	Soprano XL® (Alma Lasers, Buffalo Grove, IL, USA)	10–1350	Up to 120	12 × 10	Contact cooling
Long-pulsed Nd:YAG	1064	Acclaim® (Cynosure)	0.4–300	35–600	1.5–15	Cold air or integrated cooling, can add 755 nm alexandrite module to form Apogee Elite® (Cynosure)
		ClearScan® YAG (Sciton)	0.3–200	Up to 400	3, 6, and 30 × 30	Contact cooling
		CoolGlide® CV/XEO/Excel/ Vantage (Cutera)	0.1–300	Up to 300	3–10	Contact cooling
		Cynergy® (Cynosure)	0.3–300	Up to 600	1.5–15	Cold air
		SP and XP Dynamis®, XP Focus®, XP Max® (Fotona)	0.1–50	Up to 300	2–10	n/a
		GentleYAG® (Syneron-Candela, Wayland, MA)	0.25–300	Up to 600	1.5–18	Dynamic cooling
		Gemini® (Cutera)	1-–100	Up to 990	2, 10	Available with 532 nm KTP
		LightPod Neo® (Aerolase, Tarrytown, NY, USA)	0.65–1.5	Up to 312	2	

the patient and laser surgeon. Goggles are not interchangeable between lasers or IPL devices of different wavelengths. Furthermore, because of the risk of retinal damage from the deeply penetrating wavelengths used for LHR, one should never treat a patient for LHR within the bony orbit.

CASE STUDY 3

A 35-year old female with Fitzpatrick skin type II and jet-black hair presents to you for laser hair removal. During the consultation, she states her primary concern is that she would like to have her eyebrows shaped permanently. She is inconvenienced by her current regimen of waxing every several weeks.

The patient is an ideal candidate for LHR with her fair skin and dark hair. Almost any hair removal laser would be appropriate for use. The issue of concern in this case is the location of treatment. Caution must be taken when treating near the eye, as there is a risk of damage to retinal pigment.

Device variables

Wavelength

The chromophore for laser hair removal is melanin. Within the hair follicle, melanin is principally located within the hair shaft, although the outer root sheath and matrix area also contain melanin. Melanin is capable of functioning as a chromophore for wavelengths in the red and near-IR portion of the electromagnetic spectrum, and can be targeted by ruby, alexandrite, diode and Nd:YAG lasers, as well as IPL devices.

The long-pulsed ruby laser (694 nm) was the first device used to selectively target hair follicles, resulting in long-term hair loss. The long-pulsed ruby laser can be safely used in Fitzpatrick skin phototypes I–III. Table 4.1 lists the long-pulsed ruby lasers that are commercially available.

The long-pulsed alexandrite (755 nm) laser has been shown to be effective for long-term hair removal in multiple studies. The long-pulsed alexandrite laser can be safely used in Fitzpatrick skin phototypes I–IV, although some experts limit the use of the long-pulsed alexandrite laser to Fitzpatrick skin phototypes I–III. A few studies have demonstrated the safety of the long-pulsed alexandrite laser in a large cohort of patients with Fitzpatrick skin phototypes IV–VI. Combination treatment of alexandrite and Nd:YAG lasers provides no added benefit over the alexandrite laser alone. The commercially available long-pulsed alexandrite devices are summarized in Table 4.1.

The long-pulsed diode (800–810 nm) laser (LPDL) has also been extensively used for LHR. The diode laser can be safely used in patients with Fitzpatrick skin phototypes I–V and has good long-term efficacy for LHR.

The long-pulsed Nd:YAG laser has been thought to offer the best combination of safety and efficacy for Fitzpatrick skin phototype VI patients. Long-term hair reduction with 18-month follow-up showed 73.6% clearance following four treatments at 2-month intervals.

IPL is composed of polychromatic, non-coherent light ranging from 400 to 1200 nm. Various filters can be used to target particular chromophores, including melanin. Long-term (>1 year) hair removal has not been convincingly demonstrated to date. Various reports have demonstrated short-term efficacy. One study of patients treated with a single IPL session reported 75% hair removal 1 year after treatment. Two studies providing a head-to-head comparison of IPL versus either the long-pulsed alexandrite laser or Nd:YAG laser both found the IPL to be inferior to laser devices for hair removal. In contrast, a study of hirsute women, some with a diagnosis of polycystic ovarian syndrome, who underwent a split-face treatment with six IPL or LDPL show statistically equivalent reductions in hair counts at 1 (77% versus 68%, respectively), 3 (53% versus 60%, respectively) and 6 months (40% versus 34%, respectively) after the final treatment.

Pearl 5

One should always evaluate the patient's Fitzpatrick skin type when evaluating a patient for LHR. Darker skin types require longer wavelengths, which pose a lower risk of side effects from the absorption of energy by epidermal melanin.

Fluence

Fluence is defined as the amount of energy delivered per unit area and is expressed as J/cm^2. Higher fluences have been correlated with greater permanent hair removal, but are also more likely to cause untoward side effects. Recommended treatment fluences are often provided with each individual laser device for non-experienced operators. However, a more appropriate method of determining the optimal treatment fluence for a given patient is to evaluate for the desired clinical end point of perifollicular erythema and edema seen within a few minutes of treatment (Fig. 4.4). The highest possible tolerated fluence that yields this end point without any adverse effects is the best fluence for treatment. Fluences that cause epidermal disruption are too high and should be reduced.

Pearl 6

When treating a patient for LHR for the first time, it may be prudent to try several test spots at varying fluences to determine the optimal settings. The highest tolerable fluence without epidermal damage will yield the greatest amount of hair clearance per treatment.

Pulse duration

Pulse duration is defined as the duration in seconds of laser exposure. The theory of selective photothermolysis

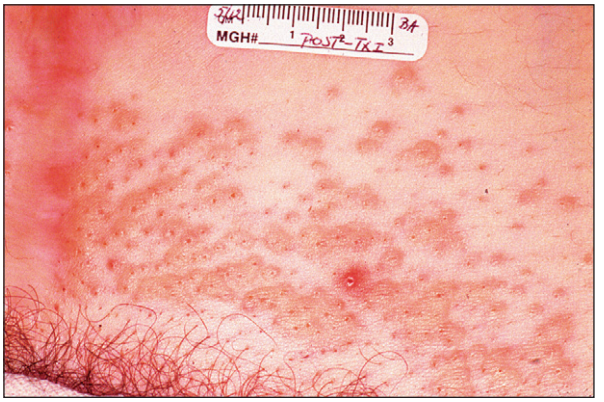


Figure 4.4 Formation of perifollicular eythema and edema immediately after laser treatment.

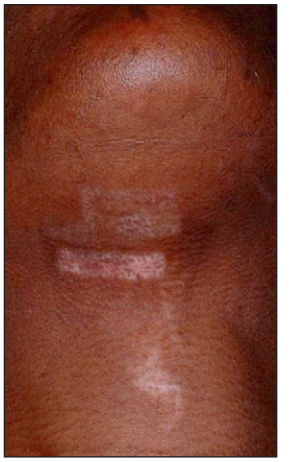


Figure 4.5 Inadequate contact cooling resulting in postinflammatory hypopigmentation in a patient with type V skin. *Photograph courtesy of Nathan Uebelhoer.*

enables the laser surgeon to select an optimal pulse duration based on the thermal relaxation time (TRT). Terminal hairs are about 300 μm in diameter, and thus the calculated TRT of a terminal hair follicle is about 100 ms. However, unlike many other laser applications, the hair follicle is distinct in that there is a spatial separation of the chromophore (melanin) within the hair shaft and the biological 'target' stem cells in the bulge and bulb areas of the follicle. The expanded theory of selective photothermolysis takes this spatial separation into account and proposes a thermal damage time (TDT), which is longer than the TRT. Shorter pulse widths are also capable of removing hair, and it is unclear which is more effective in producing permanent hair removal. Longer pulse widths are likely more selective for melanin within the hair follicle and can minimize epidermal damage as the pulse widths are greater than the TRT of the melanosomes in epidermal keratinocytes and melanocytes.

Pearl 7

When treating darker Fitzpatrick skin types, a longer pulse duration is preferred as the pulse duration exceeds the thermal relaxation time of the epidermal melanin, and minimizes the risk of epidermal damage.

Spot size

The spot size is the diameter in millimeters of the laser beam. As photons within a laser beam penetrate the dermis they are scattered by collagen fibers, and those that are scattered outside the area of the laser beam are essentially wasted. Photons are more likely to be scattered outside of the beam area for smaller spot sizes, whereas in a larger spot size the photons are likely to remain within the beam area following scatter. A double-blind, randomized controlled trial of a long-pulsed alexandrite laser for LHR of the axillary region comparing 18 and 12 mm spot sizes at otherwise identical treatment parameters showed a 10% greater reduction in hair counts with the larger spot size. Recently, a prospective study using a LDPL with a large 22 × 35 mm handpiece at low fluences and no skin cooling was shown to have similar long-term hair removal efficacy to published studies of LPDLs with smaller spot sizes using higher fluences and skin cooling. Thus, larger spot sizes are preferable to smaller spot sizes.

Pearl 8

Using the largest possible spot size allows for optimal penetration and minimizes the number of pulses it takes to cover a treatment area, thereby translating to faster treatment courses.

Skin cooling

The presence of epidermal melanin, particularly in darker skin types, presents a competing chromophore to hair follicle melanin, which can be damaged during LHR (Fig. 4.5). Cooling of the skin surface is used to minimize epidermal damage as well as pain, while permitting treatment with higher fluences. All of the skin-cooling methods function by acting as a heat sink and removing heat from the skin surface. The least effective type of cooling is the use of an aqueous cold gel, which passively extracts heats from the skin and then is not capable of further skin cooling. Alternatively, cooling with forced chilled air can provide cooling to the skin before, during, and after a laser pulse. Currently, most of the available LHR devices have a built-in skin cooling system, which consists of either contact cooling or dynamic cooling with a cryogen spray. Contact cooling, usually with a sapphire tip, provides skin cooling just before and during a laser pulse. It is most useful for treatments with longer pulse durations (>10 ms). Dynamic cooling with cryogen liquid spray precools the skin with a millisecond spray of cryogen just before the laser pulse. A second spray can be delivered

Non-ablative laser and light skin rejuvenation

5

Travis W. Blalock, E. Victor Ross

Summary and Key Features

- Non-ablative skin resurfacing is a safe and effective means of improving many aspects of photoaged skin
- While non-ablative skin resurfacing provides modest results, it also provides minimal downtime
- Non-ablative resurfacing alters cellular and non-cellular components of the skin without causing an open wound
- Patient selection requires careful consideration of medical factors as well as patient expectations
- Non-ablative modalities rarely require more than local anesthesia
- When performed with thoughtful consideration, complications are rare
- Photodynamic therapy has been utilized to maximize laser–tissue interaction and subsequent improvement in photoaging
- Treatment of types IV–VI skin requires adjustment of laser parameters to minimize pigment alteration
- Patients can generally return to their normal activities in 1–2 days following treatment with non-ablative modalities
- For patients with limited available downtime, multiple treatments 2–3 months apart may provide an improved result

Introduction

With the advancement of laser and non-laser light sources, the focus of skin rejuvenation is optimizing efficacy while minimizing recovery times. The gold standard for rejuvenation, at least for fine wrinkles, has been ablative modalities. Although ablative tools can achieve predictable cosmetic enhancement, the risks of scarring, infection, dyspigmentation, and prolonged recovery time make these modalities less attractive. Patients increasingly try to balance efficacy of skin rejuvenation within the context of downtime. Non-ablative skin rejuvenation normally mitigates the need for advanced anesthesia and can often be performed with only topical anesthesia. Thus, non-ablative modalities have enjoyed a greater role in skin rejuvenation.

A clear definition of non-ablative skin rejuvenation is important as the term is sometimes used haphazardly. In its most pure form, non-ablative rejuvenation improves skin quality without physical removal or vaporization of the skin. Ablative modalities, via vaporization, remove a portion, or all, of the epidermis and sometimes may remove parts of the dermis. This chapter focuses exclusively on non-fractional methods of non-ablative skin rejuvenation.

The dermis (and/or deeper epidermis) can be selectively damaged by two basic approaches:

1. Targeting discrete chromophores in the dermis and/or at the dermal epidermal junction, or
2. Using mid-infrared lasers in the range of 1.3–1.55 μm wavelengths, where water absorption is weak enough that relatively deep beam penetration is allowed (there is only 50% beam attenuation at depths of 300–1500 μm).

Treatment of photodamage can be divided into various categories, and treatment protocols are based on a logical approach founded on the laser–tissue interactions delineated above. The goal should be to maximize skin rejuvenation, from reducing telangiectasias and lentigines to enhancing dermal remodeling.

The laser and non-laser systems used for non-ablative rejuvenation are a heterogeneous group of devices that emit wavelengths in the visible (400–760 nm), near-infrared (760–1400 nm), or mid-infrared (1.4–3 μm) ranges, radiofrequency (RF) devices, intense pulsed light (IPL) devices, as well as light-emitting diode (LED) devices (Box 5.1). Each of these modalities can induce dermal remodeling, as well as target other components, without epidermal ablation. Most investigators believe that photothermal heating of the dermis: (1) increases collagen production by fibroblasts and (2) induces dermal matrix remodeling by altering glycosaminoglycans as well as other components of the dermal matrix. Others believe that the laser/light interaction with molecular cellular components alters the cellular function of enzymes as well as cellular structural components. Altering the different components of cells, from enzymes to cellular wall

Box 5.1
Devices used in non-ablative skin resurfacing

- Visible light/vascular lasers
  - 532 nm potassium titanyl phosphate (KTP)
  - 585 nm/595 nm pulsed dye
- Near-infrared lasers
  - 1064 nm Q-switched neodymium:yttrium-aluminum-garnet (Nd:YAG)
  - 1064 nm long-pulsed neodymium:yttrium-aluminum-garnet (Nd:YAG)
  - 1320 nm neodymium:yttrium-aluminum-garnet (Nd:YAG)
- Mid-infrared lasers
  - 1450 nm diode
  - 1540 nm erbium:glass
- Intense pulsed light (IPL) (500–1200 nm)
- Radiofrequency (RF) systems
- Light-emitting diode (LED)

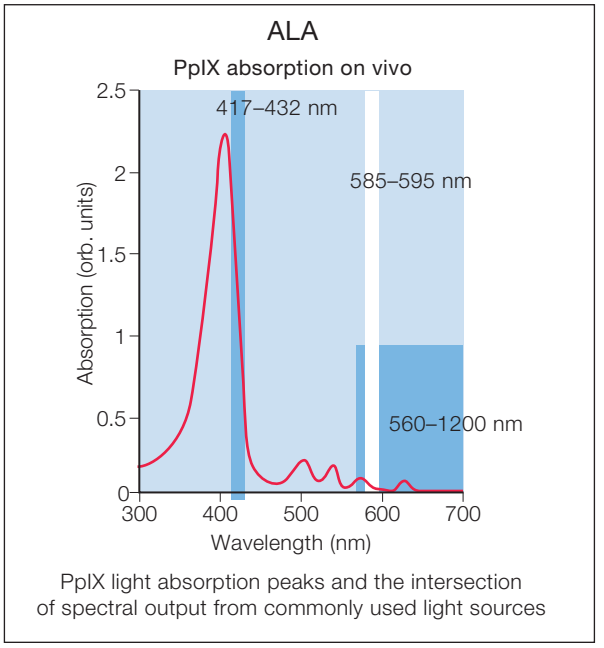


Figure 5.1 Protoporphyrin IX absorption: due to the multiple absorption peaks of protoporphyrin IX, multiple lasers and light sources can be used to augment the effects following application of porphyrin precursors to the skin.

constituents to nucleic acids, may then alter the environment and productivity of a given cell.

Photodynamic therapy (PDT) with aminolevulinic acid (ALA) has been show to augment the effects of laser or other light sources. Multiple laser and light sources have been used for photoactivation of protoporphyrin IX, leading to improved skin rejuvenation (Fig. 5.1).

Non-ablative skin rejuvenation is commonly used to reverse photoaging in the dermis. This damage is directly correlated with the patient's age and extent of ultraviolet exposure. Ultraviolet B (UVB) light alters nucleic acids as it interacts with epidermal keratinocytes, inducing cellular atypia. Over time, longer-wavelength ultraviolet A (UVA) light causes increases in oxygen radical formation, inducing alterations in the normal homeostasis of vessel formation, apoptosis, pigment generation by melanocytes, immune cell dysregulation, cytokine dysregulation, alteration of dermal matrix composition, and disruption in the transcription, translation, and replication of the cellular genetic code. Histological changes that accompany the clinical findings of photoaging include an atrophic epidermis, loss of the rete pattern, elastic fiber clumping in the papillary dermis, haphazard and reduced collagen production, and increased vasculature. These UV-induced changes correlate with the clinical appearance of photoaged skin, including skin laxity, atrophy and fragility, increased rhytid formation, telangiectasia, and alteration in the overall color, texture, and consistency of the skin. Thus the goal of rejuvenation is to replace damaged epidermal or dermal constituents with more robust, newly created ones. Physicians attempt to alter the quality of the keratinocytes and the pigment production of melanocytes, two key components of epidermal photodamage. Dermal photodamage rejuvenation typically has concentrated on improving the quality and inhibiting the degeneration of fibroblasts. Studies have shown an increase in antioxidant capacity and collagen synthesis after millisecond and nanosecond 532 nm and 1064 nm laser irradiation in fibroblast cell cultures.

Richard Glogau, MD developed a classification scale to chart the progression of clinical photoaging (Table 5.1). One can follow a patient from an early age, with relatively strong homogeneity of skin coloration and minimal wrinkles, to a more aged patient, with wrinkles at rest and a more heterogeneous skin coloration.

As one would expect, treating a Glogau grade I patient with current non-ablative modalities will achieve a higher percentage of photoaging correction versus more severely photodamaged patients. While ablative skin rejuvenation may achieve superior restoration of normal skin structures, especially for the Glogau grade III or IV patient (see Table 5.1), the downtime and potential risks are prohibitive for many patients. Nevertheless, as non-ablative technologies evolve, restoration of young, healthy skin with diminished risks and negligible recovery times is increasingly possible. The remainder of the chapter will focus on patient selection for non-ablative skin rejuvenation and discussion of the different devices.

Patient selection

Patient selection for non-ablative skin rejuvenation begins with an assessment of the degree and type of photoaging (see Table 5.1). The ideal patient is Glogau grade II or III with mild to moderate photodamage. Non-ablative therapies initiate new collagen formation (collagen I and collagen III) and might be appropriate in a Glogau grade I patient to prevent photodamage progression. Alternatively, a patient and/or a physician expecting dramatic

Table 5.1 Glogau photoaging classification

Grade	Classification	Typical age	Description	Skin characteristics
I	Mild	20s or 30s	No wrinkles	Early photoaging: mild pigmentary change, no keratoses, minimal wrinkles, minimal or no makeup
II	Moderate	30s or 40s	Wrinkles in motion	Early to moderate photoaging: early solar lentigines, keratoses palpable but not visible, parallel smile lines begin to appear, wears some foundation
III	Advanced	50s	Wrinkles at rest	Advanced photoaging: obvious discolorations, visible telangiectasias, visible keratoses, wears heavier foundation always
IV	Severe	60s and older	Only wrinkles	Severe photoaging: yellow-gray skin color, prior skin malignancies, wrinkles throughout – no normal skin, makeup 'cakes and cracks'

change following a non-ablative rejuvenation procedure in a Glogau grade IV patient may be disappointed.

Sadick divides patients in a different manner, where cosmetic deficiencies are based on the histological location of solar damage. His selection process takes into account epidermal (type I) damage (Fig. 5.2) and dermal/subcutaneous (type II) damage (Fig. 5.3), and subsequently treatment is tailored to laser selectivity of the damage.

Another important factor in patient selection is the patient's Fitzpatrick skin type. Fitzpatrick IV, V, and VI skin types may not be optimal candidates for particular non-ablative rejuvenation modalities that selectively heat melanin. The most common adverse result for non-ablative rejuvenation in darker skin patients is hyperpigmentation, a condition that usually resolves after 4–8 weeks (but can persist longer in some circumstances) with appropriate application of suppressors of melanin synthesis. Mid-infrared lasers, which minimize direct melanin targeting, can be used in patients with darker skin types. However, higher fluences in these patients may result in thermal damage and bulk heating, which can also result in dyspigmentation. Non-cryogen cooling devices can minimize bulk heating, whereas cooling devices that employ cryogen spray may induce pigmentary alterations similar to liquid nitrogen. See Chapter 10 for a detailed discussion of laser and non-laser light sources for the treatment of darker skin types.

Beyond skin type and amount of photodamage, there are some patients who might be excluded from non-ablative lasers and light sources based on medical criteria (Box 5.2). Oral retinoid use, recent rejuvenation procedures, infection, and active dermatitides are reasons to consider deferring a non-ablative rejuvenation procedure. Most likely oral retinoids will not affect the outcome, but no controlled study has investigated their effect on non-ablative skin resurfacing. Many texts advocate waiting a period of 6–12 months, most likely representing an extrapolation from ablative resurfacing wait times. Some cutaneous laser experts have used non-ablative devices 1 month following retinoid use without adverse outcomes.

Physicians must also consider the wavelength of the device. For example, devices that utilize visible light (i.e. LED devices, etc.) may exacerbate a phototoxicity/photosensitivity or a systemic condition that is photosensitive, like cutaneous lupus (although in a recent study only 7% of SLE patients reacted to visible light) (Fig. 5.4). On the other hand, some lasers may confer a protective quality. There is increasing evidence that IPL can activate fibroblasts as well as confer protection from future UV-induced skin damage.

Fillers and neurotoxins most likely are not affected by non-ablative modalities and can be administered in the same session. However, the non-ablative resurfacing should be performed last. This order will minimize the risk of neurotoxin diffusion, which should cease by 1 hour after the injection, and will reduce the possibility of edema obscuring endpoints in optimal filler placement.

Visible light and near-infrared/vascular lasers (Table 5.2)

Visible light lasers and near-infrared lasers are commonly used to treat vascular and pigmented lesions. Treatment of vascular lesions with visible light lasers can achieve histological correction of dyspigmentation, overall skin texture, dermal matrix abnormalities, and solar elastosis. Clinical improvement of solar lentigines, scars, including keloids and hypertrophic scars, and photoaging have all been observed. Orringer et al have reported increases in type I procollagen messenger RNA and subsequent dermal matrix remodeling following one treatment with a pulsed dye laser. Whether this is secondary to thermal alterations of cellular milieu or to vascular-injury-induced cytokines, the result is dermal remodeling, reversal of photoaging, and partial rhytid correction.

The first laser designed to exploit the principle of selective photothermolysis was the flashlamp-pumped pulsed dye laser (PDL). The laser was optimized to treat port-wine stains. As the understanding of treatment of vascular lesions has progressed, so has the configuration of the PDL, in both composition of the dye (rhodamine) and

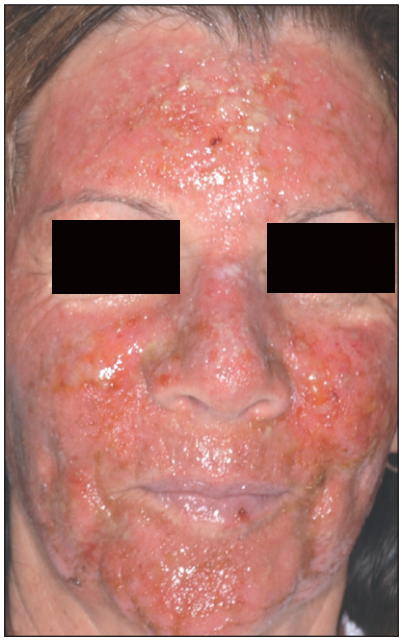


Figure 5.4 Photosensitivity reaction following photodynamic therapy. The patient is shown 6 days after photodynamic therapy. Reaction resolved after 3 weeks.

Other wavelengths that target hemoglobin in blood vessels have been shown to rejuvenate skin. The long-pulsed 755 nm alexandrite laser (Case study 1), the 810 nm diode, and the 1064 Nd:YAG lasers are used for deeper and larger-caliber vessels. The subsequent 'coincidental' dermal remodeling correlates to the depth of penetration of each respective laser. Weng et al have demonstrated that collagen synthesis by fibroblasts and antioxidant enzymes were significantly increased following irradiation with the 532 nm, 1064 nm Q-switched Nd:YAG, and 1064 nm long-pulse Nd:YAG lasers. The 1064 nm Nd:YAG laser induces deeper remodeling than the 532 nm laser due to its lower degree of dermal scattering and chromophore absorption at 1064 nm. Thus, some physicians use multiple lasers, such as the 532 nm laser to treat dyschromia and telangiectasia, and following it with a pass with the 1064 nm laser to obtain some deeper remodeling in the same treatment session.

Pearl 1

Combination treatment results in improved treatment results. The authors note improved outcomes with patients treated with combination using the 532 nm and 1064 nm lasers during the same treatment session. By using combination treatment, multiple chromophores can be targeted, with the 532 nm laser treating lentigines and telangiectasias, while the 1064 nm laser, by nature of its absorption spectrum, augments the rhytid correction of the 532 nm laser.

Table 5.2 Commonly used visible light / vascular lasers in non-ablative resurfacing*

Wavelength (nm)	Laser type	Energy	Pulse duration
532	Flash/arc lamp pumped KTP	Up to 950 J/cm^2	5–100 ms
532	Diode-pumped KTP	0.1–5 W	5–1000 ms
585–595	Pulsed dye	Up to 40 J/cm^2	0.45–40 ms, 350 ms
755	Alexandrite	1–50 J/cm^2	0.5–300 ms
808	Diode	Up to 170 J/cm^2	Up to 1000 ms
940	Diode	Up to 900 J/cm^2	5–625 ms
532/1064	Q-switched Nd:YAG	Up to 16 J/cm^2/Up to 37 J/cm^2	5–20 ms
1064	Nd:YAG	Up to 990 J/cm^2, 120 J	0.1–300 ms

KTP = potassium titanyl phosphate; Nd:YAG = neodymium:yttrium-aluminum-garnet.
*This table represents a wide range of available lasers with some utility in non-ablative resurfacing. As each device has unique properties and settings, please refer to each specific device's manual for exact information to optimize patient treatment.

CASE STUDY 1

A Caucasian female in her early 60s presents for total facial rejuvenation with request to focus on lentigenes, telangiectasias, and overall facial rejuvenation (Fig. 5.5A). The long-pulsed alexandrite 755 nm laser was used at a fluence of 36 J/cm^2 using an 8 mm spot size and a 3 ms pulse duration to treat the patient's forehead, cheeks, nose, and chin. At 6 weeks following her treatment, significant improvement in hyperpigmented macules, telangiectasias, and an overall more youthful appearance is appreciated (Fig. 5.5B).

Near-infrared lasers have been used in a motion technique for skin rejuvenation. In one scenario, a 1064 nm laser equipped with a 5:7 mm spot size is deployed in a rapid back-and-forth fashion at 5 Hz and 12–15 J/cm^2. The device is moved from region to region based on either the surface temperature or when the heat becomes too uncomfortable to the unanesthetized patient. Typically, one achieves a surface temperature of about 39–42°C and then moves to an adjacent region. The lack of anesthetic is imperative in this approach, as excessive pain must be reported by the patient and should alert the operator to

Pearl 4

Good contact between the handpiece and the skin along with taut pressure may maximize the depth of the laser penetration, evenly treat the skin within the spot size, and will decrease the risk of postinflammatory hyperpigmentation. When using IPL devices to treat the face, this becomes very important, especially in darker-pigmented skin, as the face is full of many crevices and contours and most IPL devices utilize a rectangular handpiece, which makes good contact difficult in the perinasal and periocular regions.

Finally, although the utility of IPL devices allows for treatment of a wide variety of conditions, the addition of radiofrequency has been utilized to supplement and improve outcomes with use of IPL devices (Elos, Syneron). Bipolar radiofrequency exhibits a preference for warmer tissue. This technology takes this property into consideration by utilizing the IPL system to heat the target chromophore and then using the radiofrequency technology to target the now 'warmer' tissue target. Contact cooling helps avoid epidermal damage and keep the tissue heat in the dermis. This synergistic technology has proven efficacy in treatment of photoaging, helping reduce wrinkles, lentigenes, and telangiectasias.

Light-emitting diodes

LEDs for photoaging consist of a panel(s) of numerous small lamps that emit low-intensity light. Some companies have miniaturized these devices to handheld units that are used at home, while most professionals are using panels that can treat the entire face in one treatment session. One advantage of LED devices is that they are well tolerated by patients. With no pain, large surface areas of skin can be treated simultaneously.

Typically, LED devices emit a range of wavelengths. These devices are available in various wavelengths from blue to infrared. Depending on the wavelength and treatment parameters, LEDs emit milliwatt light in a small range around a peak wavelength. Thus, for example, if one were to select a LED with a dominant wavelength of 500 nm, the device will likely emit light from approximately 480 to 520 nm.

The interaction of LED devices with the skin are unclear, though most believe that photomodulation of cell receptors, cell organelles, or existing protein products is partially responsible. Unlike many of the devices discussed above, non-thermal interactions with the extracellular matrix and fibroblasts remodel existing collagen, increase collagen production by fibroblasts, inhibit collagenase activity, and result in rhytid reduction.

One of the most popular LED systems is the Gentle Waves® device (Light BioScience, LLC, Virginia Beach, VA). The system generates 588 nm yellow light pulses with an on-time of 250 ms and off-times of 10 ms for a total of 100 pulses resulting in a total light dose of 0.1 J/cm^2. Although some trials showed significant improvement in pore size, skin tone, and texture, the most comprehensive controlled clinical trial showed no significant skin changes in objective outcomes after a series of treatments. Boulos found that there was a strong placebo effect with the 588 nm Gentle Waves® system, and that little objective improvement was observed by blinded raters. Despite the subjective improvement in two trials, objective improvement in blinded studies is unproven.

In a study of 633 nm and 830 nm LED biostimulation, two treatments per week over 4 weeks showed increases in collagen production and mild wrinkle improvement. In a study using a reconstructed skin substitute irradiated with 633 nm LED panels, increases in collagen production were also observed. Additionally, in the clinical arm of the study, patients receiving treatment 3 times a week for 4 weeks (12 treatments) were found to get mild to moderate wrinkle improvement compared with sham treatment.

Photodynamic therapy

Over the past 20 years, photosensitizing agents have enjoyed an increasing role in medical and cosmetic dermatology. Twenty percent 5-aminolevulenic acid (5-ALA, a 'prodrug') is absorbed by rapidly proliferating epidermal and dermal cells and converted into photoreactive products of the hemoglobin pathway, most notably protoporphyrin IX (see Fig. 5.1). Protoporphyrin IX is subsequently activated by certain wavelengths of light, as highlighted by the absorption peaks in Figure 5.1, resulting in singlet oxygen production and resultant cellular destruction.

Many light sources have been used for PDT (Box 5.3). This variety is possible owing to multiple absorption peaks by protoporphyrin IX. The largest peaks are at 417, 540, 570, and 630 nm. The PDL, IPL, and LED devices have all been used to activate protoporphyrin IX. There are many variables that affect the immediate PDT response, among them the ALA incubation time, pre-ALA skin preparation regimen, degree of skin photodamage, anatomical region, light dose, wavelength range, and power density. Overall, lower power densities (i.e. continuous wave light sources) create more singlet oxygen than pulsed light. Also, we have found that applying numbing creams simultaneously with the ALA solution can accelerate ALA absorption and thereby accelerate protoporphyrin formation, leading to a much more robust response.

Pearl 5

Microdermabrasion, chemical peels, acetone, alcohol, retinoids, and thorough cleansing of the treatment area have all been advocated for making the stratum corneum more uniform, increasing the likelihood that the PDT will penetrate deeper and more evenly.

Many studies have shown the improvement of actinic keratoses and acne with PDT. Some studies have shown evidence of increased collagen formation. Gold et al have reported improvement in crow's feet, skin texture,

Non-ablative fractional laser rejuvenation

6

Chung-Yin Stanley Chan, Andrei Metelitsa, Jeffrey S. Dover

Summary and Key Features

- Non-ablative fractional resurfacing is a safe and effective treatment that has become the cornerstone for facial rejuvenation and acne scarring
- It is effective in treating a variety of conditions including acne scarring, mild to moderate photoaging, and some forms of dyspigmentation
- Non-ablative fractional photothermolysis (NAFR) has minimal downtime with almost no restrictions on activity immediately following treatment
- Common areas treated include the face, neck, chest, and hands
- All Fitzpatrick skin phototypes can be treated provided settings are adjusted accordingly
- The preoperative consultation is a vital component of the treatment regimen to ensure optimal outcomes
- Erythema and edema are common sequelae after treatment and resolve within a few days
- Long-term complications are exceedingly rare
- Technology in the field is changing rapidly and the selection of equipment is based on individual preference
- Home-based devices are a new frontier for lasers but will not replace office-based systems

Introduction

Treatment approaches are constantly being developed and refined in the field of skin rejuvenation. Since its original introduction in 2004, fractional photothermolysis has provided rejuvenation treatment approaches that are both effective and safe. Developed by Anderson & Manstein, fractional photothermolysis generates targeted microthermal treatment zones (MTZs), columns of thermally denatured skin of controlled width and depth, in the dermis. Their original device utilizing this technology induced necrosis within the epidermis and dermis while leaving the stratum corneum histologically intact and was thus termed non-ablative fractional photothermolysis (NAFR).

One of the main advantages of NAFR is limited discomfort and the minimal recovery that is required after the procedure. In contrast to conventional resurfacing devices, fractional photothermolysis treats only a fraction of this skin, allowing for rapid epidermal repair from undamaged areas. Although multiple treatment sessions are required to achieve the desired outcome, downtime is limited to an average of 3 days of redness and swelling as opposed to an average of 7–10 days of an open wound after aggressive non-fractional ablative resurfacing. Combined with an excellent safety profile, NAFR has become the cornerstone of laser skin rejuvenation for the treatment of photoaging and acne scarring and a variety of other clinical applications.

Pathophysiology

In fractional photothermolysis, a regular array of pixelated light energy creates focal areas of epidermal and dermal tissue damage or microthermal treatment zones (MTZ) (Fig. 6.1). Since its inception, several different lasers have been developed to take advantage of this technological advance. Each laser has parameters that can modify the density, depth, and size of the vertical columns of MTZs. The individual wounds created by FP are surrounded by healthy tissue resulting in a much quicker healing process when compared with traditional ablative skin resurfacing. This targeted damage with MTZ is hypothesized to stimulate neocollagenesis and collagen remodeling leading to the clinical improvements seen in scarring and photoaging. In the original study by Manstein et al., the histologic changes seen after NAFR were elegantly described. Immediately following treatment, lactate dehydrogenase (LDH) viability staining showed both epidermal and dermal cell necrosis within a sharply defined column correlating with the MTZ. There was continued loss of dermal cell viability 24 hours after treatment, but via a mechanism of keratinocyte migration, the epidermal defect had been repaired. One week after treatment, individual MTZs were still evident by LDH staining, but after 3 months there was no histologic evidence of loss of cell viability. Water serves as the target chromophore allowing for thermal damage to epidermal keratinocytes and collagen.

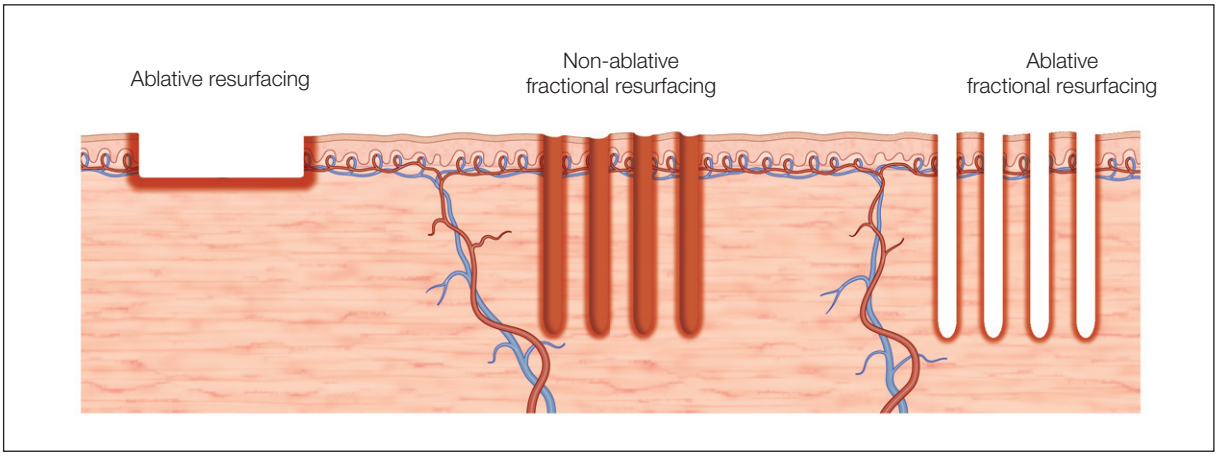


Figure 6.1 Diagram showing the differences between traditional ablative, non-ablative fractional, and ablative fractional resurfacing. With the fractional laser technology, microthermal treatment zones are created with intervening islands of unaffected tissue. Healing time is significantly less, and the energy can safely reach deeper into the dermis.

Hantash and colleagues demonstrated a unique mechanism of tissue repair with fractional photothermolysis. In 2006, they demonstrated, using an elastin antibody, that damaged dermal content was incorporated into columns of microscopic epidermal necrotic debris (MEND) and shuttled up through the epidermis and extruded in a process of transepidermal elimination. This mechanism, which had not been described with previous laser technologies, explains the elimination of altered collagen in photoaging and scars and was also hypothesized to provide novel treatment strategies for pigmentary disorders like melasma as well as depositional diseases like amyloid and mucinoses.

Epidemiology

According to the American Society for Plastic Surgery statistics, which provides a comprehensive estimate on the total number of cosmetic procedures performed in the United States, minimally invasive cosmetic procedures have increased by more than 100% since 2000. In 2010, over 300 000 non-ablative laser skin resurfacing procedures were performed with the majority done on females.

Equipment

As the technology of fractional photothermolysis continues to evolve, new devices continually come to market. A list of currently available NAFR systems is given in Table 6.1. The table is not comprehensive and, as one can imagine, the devices will change constantly. This section will provide a brief description of a few of the more commonly used devices.

The original non-ablative fractional resurfacing system described by Manstein featured a scanning handpiece with a 1500 nm wavelength. The updated, currently available model, the Fraxel re:store (Solta Medical, Hayward, CA), employs a 1550 nm erbium glass laser. The device has tunable settings to adjust the density of the MTZs and energy depending on the treatment. Density can be varied to treat anywhere from 5 to 48% while energy settings can be adjusted to control depth of penetration from 300 to 1400 μm. Most of the studies available on non-ablative fractionated lasers are based on this device.

Solta Medical's newest addition, the Fraxel Dual, couples the 1550 nm erbium laser with a 1927 nm thulium fiber laser in one platform. The thulium laser provides a more superficial treatment option and better addresses dyspigmentation while the 1550 nm penetrates deeper to stimulate collagen remodeling. The system increases flexibility, allowing the practitioner to switch between the two lasers to tailor treatment accordingly. Parameters can be adjusted similarly to the Fraxel re:store. Cooling is also built in with the Fraxel Dual.

Palomar Medical Technologies (Burlington, MA) offers an intense pulsed light platform with individual handpieces that attach to a single unit to cover a wide range of uses. The Lux1440 and Lux1540 handpieces provide two wavelength options (1440 and 1550 nm) for fractional non-ablative photothermolysis. In addition, the company has developed a new XD Microlens for their non-ablative laser handpieces. In their study, the company claims that, as the dermis is compressed by the optical pins on the handpiece, the pins are brought closer to deeper targets and the interstitial water is displaced from the dermal–epidermal junction into the surrounding spaces. With less water to absorb, scattering of the laser light is reduced enabling increased absorption of the light by deeper targets.

The Affirm (Cynosure, Inc., Westford, MA) is a 1440 nm Nd:YAG laser device that utilizes a proprietary Combined Apex Pulse (CAP) technology. The technology creates columns of coagulated tissue surrounded by uncoagulated tissue columns, which purportedly improves

Table 6.1 Non-ablative fractional lasers

Device	Manufacturer	Type	Wavelength (nm)
Affirm	Cynosure (Westford, MA)	Nd:YAG	1440 +/– 1320
Clear+ Brilliant	Solta Medical (Hayward, CA)	Diode	1440
Fraxel re:fine	Solta Medical (Hayward, CA)	Erbium	1410
Fraxel re:store (former SR 1550)	Solta Medical (Hayward, CA)	Erbium	1550
Fraxel dual	Solta Medical (Hayward, CA)	Erbium + thulium	1550 + 1927
Lux 1440	Palomar Medical Technologies Inc. (Burlington, MA)	Nd:YAG	1440
Lux 1540	Palomar Medical Technologies Inc. (Burlington, MA)	Erbium	1540
Matrix RF	Syneron (Irvine, CA)	Diode + bipolar RF	915 + RF
Mosaic	Lutronic (San Jose, CA)	Erbium	1550
Sellas 1550	Enhanced Image Technologies (Charlotte, NC)	Erbium	1550

Box 6.1
Clinical indications for non-ablative fractional resurfacing

- Photoaging
- Scarring (atrophic, hypertrophic, hypopigmented)
- Disorders of pigmentation (melasma, nevus of Ota, drug-induced pigmentation)
- Poikiloderma of Civatte
- Premalignant conditions (actinic keratoses, disseminated superficial actinic porokeratosis)
- Striae distensae
- Vascular disorders (telangiectatic matting, residual hemangioma)

treatment efficacy. The Affirm uses a stamping handpiece with two spot sizes and energies that penetrate up to 300 μm in depth. A recent advance has been the addition of their multiplex technology, which stacks a 1320 nm wavelength with the 1440 nm system, allowing for penetration down to 1000–3000 μm.

Applications

While NAFR is currently approved by the US Food and Drug Administration for the treatment of benign epidermal pigmented lesions, periorbital rhytides, skin resurfacing, melasma, acne and surgical scars, actinic keratoses, and striae, it has been reported to be used in many other clinical settings (Box 6.1).

Photoaging

With their seminal study in 2004 using a prototype non-ablative fractional resurfacing device, Manstein and colleagues first demonstrated the clinical effectiveness of fractional photothermolysis by showing improvement in periorbital rhytides. Three months after four treatments with the fractionated device, 34% of patients had moderate to significant improvements and 47% had improvement in texture as rated by blinded investigators. Overall, 96% were noted to be 'better' post-treatment. The skin tightening seen after non-ablative fractional resurfacing is similar to ablative resurfacing with tightening within the first week after treatment, apparent relaxation at 1 month, and retightening at 3 months (Case study 1).

CASE STUDY 1
The right patient

A 58-year-old Caucasian male with mild rhytides and mild to moderate photodamage with scattered facial lentigines presents for consultation. You recommend a series of non-ablative fractional resurfacing laser procedures. Six months after the sixth laser procedure, you see the patient back in follow-up. He is delighted with his improvement in both texture and skin tone and subsequently refers a couple of his friends to see you.

The above patient is the ideal patient for non-ablative fractional resurfacing. These results are typical of the improvement we see in our patients when selected appropriately.

Subsequent reports have confirmed the efficacy of NAFR beyond just periorbital lines. Wanner and colleagues showed statistically significant improvement in photodamage of both facial and non-facial sites with 73% of patients improving at least 50%. In 2006, Geronemus also reported his experience with fractional photothermolysis, finding it to be effective in treating mild to moderate rhytides. Figures 6.2 and 6.3 show typical improvement in rhytides and pigmentation after treatment with non-ablative fractional resurfacing. For deeper rhytides, such as the vertical lines of the upper lip,

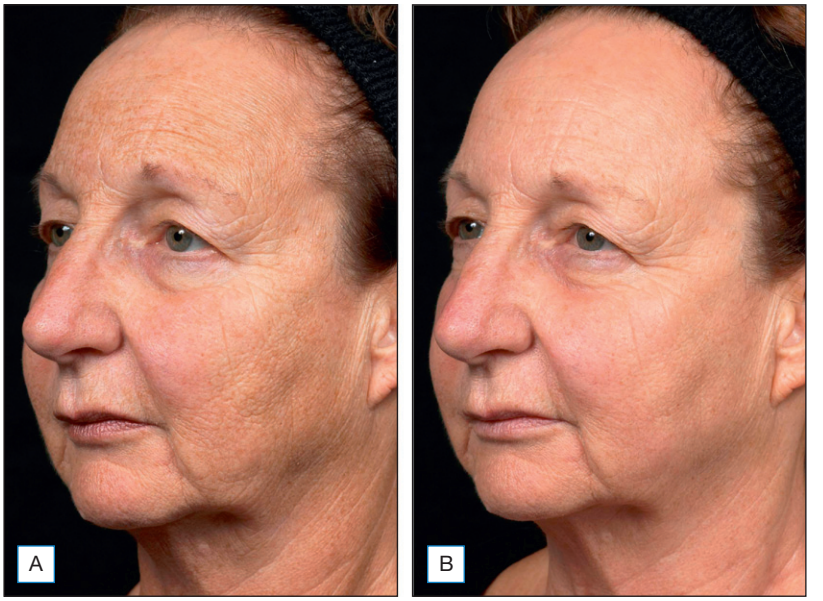


Figure 6.2 Improvement in moderate rhytides 1 month after two treatments with Fraxel 1927 nm. *(Photo courtesy of Solta Medical.)*

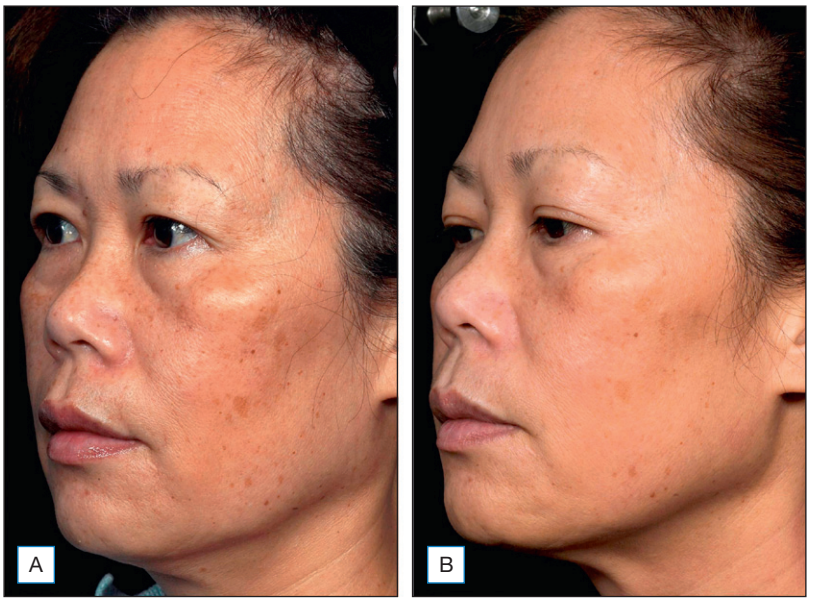


Figure 6.3 Improvement in rhytides and dyspigmentation 1 month after three treatments with Fraxel re:store. *(Photo courtesy of Solta Medical.)*

improvement is also seen but not nearly to the same degree as in ablative approaches.

NAFR is also considered to be an effective and safe treatment modality for photoaging off the face including the neck, chest, arms, hands (Fig. 6.4), legs, and feet. These body sites are typically very challenging to treat with other treatment modalities given either increased risks of complications (e.g. scarring) associated with ablative technologies or lack of efficacy that has been previously observed with other non-ablative devices. Jih et al reported statistically significant improvement in pigmentation, roughness, and wrinkling of the hands in ten patients treated with non-ablative fractional resurfacing. In our experience, we have found NAFR to be very safe when settings are adjusted accordingly.

Scarring

Scarring can induce a tremendous psychological, physical, and cosmetic impact on individuals. Previous therapeutic modalities in scar treatment include surgical punch grafting, subcision, dermabrasion, chemical peeling, dermal fillers, as well as laser resurfacing with ablative and non-ablative devices. Published studies have demonstrated

Pearl 6

Large treatment areas (>400 cm^2) should be avoided to reduce the risk of lidocaine toxicity.

Pearl 7

In darker-pigmented patients, treatment densities should be decreased; consider doing less passes in an effort to reduce the risk of hyperpigmentation.

General technique

We find the supine position most comfortable for the patient and practitioner. In this position, the practitioner can be seated comfortably with elbows close to 90° to alleviate fatigue and repetitive stress injury. During treatment, patient positioning is crucial to ensure perpendicular application of the laser handpiece. For example, when treating the neck, especially in the submandibular area, it is often helpful to have the chin tilted upward to allow for better exposure.

With the scanning handpiece of the Fraxel systems (Solta Medical, Hayward, CA), we deliver eight passes when treating acne scars, rhytides, and photoaging of the face. We use a double-pass, 50% overlap technique. One linear pass is delivered, the handpiece is brought to a complete stop, lifted, repositioned, and then returned along the same path for a second pass. The handpiece is then moved laterally by 50% and the technique is repeated until the treatment area is completed. As a result, each area is treated with four passes. For the next four passes, we direct the passes perpendicular to the first treatment to ensure complete and even laser coverage. Dividing the face into four quadrants also helps manage the treatment area and reduce the risk of overlap or missing a section.

For facial resurfacing, our settings are individualized according to patients' needs and tolerability. We often start with energy levels between 40–50 mJ and a treatment level of 6–8 (Table 6.2). The settings are often increased during subsequent visits if tolerated.

For stamping handpieces, the fractionated energy is delivered according to the tip size. For example with the StarLux system (Palomar Medical Technologies Inc., Burlington, MA) and the 15 mm Lux1540 handpiece, three to four passes are generally delivered with a 50% overlap in both directions. The handpiece should be lifted off the skin between each pulse, and pulse-stacking is not recommended. For facial resurfacing with the Lux1540 15 mm tip, we recommend using 10–15 mJ per microbeam with a pulse width of 10–15 ms. With the Affirm (Cynosure, Westford, MA) 1440 nm device, we use 3–5 mJ, depending on the tip size, and perform two passes for facial resurfacing, The number of passes and treatment parameters vary with the different machines and is beyond the scope of this chapter.

Cooling

A cooling device used in conjunction with the NAFR laser device should be standard for all treatments. A popular forced-air cooling device, the Zimmer Cryo (Zimmer Medizin Systems, Irvine, CA) increases patient comfort significantly. Some laser systems now also come with a built-in cooling device. In a study of 20 patients, 19 noted reduced pain with the addition of a cooling device.

Post-treatment

Upon completion of the treatment, patients are advised to ice their skin for several minutes and then periodically over the next few hours. Not only does this help with patient comfort, but it also reduces post-procedure swelling. Erythema develops immediately afterwards in all treated patients (Fig. 6.8) and typically resolves in 3 days. Use of non-comedogenic moisturizers is also recommended. Patients are advised to wear sun protection for several weeks after their treatment to reduce the risk of hyperpigmentation. In those with an increased risk of hyperpigmentation, hydroquinone may be started immediately after the procedure. We routinely wait to start lightening agents until we see the first signs of post-inflammatory pigmentation, which is usually around day 21 post-treatment. In a recent prospective study by Alster et al, a light emitting-diode device (Gentlewaves, Light BioSciences, Virginia Beach, VA) has been shown to decrease erythema intensity and duration following treatment, although the precise mechanism of action is unclear.

Safety and complications

NAFR is a well-tolerated procedure with an excellent safety profile. Fisher and Geronemus studied the immediate and short-term side effects showing a favorable side effect profile. In their study of 60 patients with skin types I–IV, all patients expectedly developed erythema immediately post-treatment, which in most patients resolved in 3 days. Xerosis occurred in 86.6% of patients, usually presenting 2 days after treatment and resolving by day 5 or 6. This was minimally bothersome and responded well to moisturization. Other frequently reported post-treatment side effects were transient and included facial edema (82%) and flaking (60%). Small, superficial scratches were also reported in 46.6% of patients. These scratches, which all resolve without sequelae, are thought to be related to tangential application of the hand piece or pulse stacking by inexperienced users. Pruritus (37%) and bronzing (26.6%) are also common side effects of treatment.

Perhaps the most valuable finding from this short-term study was the impact on the patient's quality of life; 72% reported limiting social activities by an average time of only 2.1 days, which is in stark contrast to the downtime seen with the conventional resurfacing laser. The most commonly attributed reasons were erythema and edema.

Intense Pulsed Light Therapy

Barbara Soltes, MD

KEYWORDS

• IPL • Hirsutism • Acne • Phototherapy

The property of light has long been used as a tool for the restoration of health. Hippocrates wrote for decades about the elements of nature as essential components in the balance of sickness and wellness. The healing powers of sunlight became one of the earliest recorded treatments in modern medicine.[1,2] In the early centuries, light treatments were used to correct a wide variety of medical conditions, such as smallpox and tuberculosis.[2] With the advent of the twentieth century, the traditional light treatment was altered and laser emerged as an aesthetic tool. In 1963, Goldman and colleagues[3] first described ruby laser injury to pigmented hair follicles. In the following years, the ruby laser was used to treat other conditions, with little regard for absorption of light energy by various tissues. A historical case reported in 1983 was that of a young boy treated for a vascular nevi with a high-intensity laser, which resulted in severe epidermal damage. In the same year, Anderson and Parrish[4] developed the theory of photothermolysis. This theory was based on pulsed light of a specific wavelength and duration directed at a particular chromophore (melanin, hemoglobin, and water) within the skin layer. The chromophore within a designated tissue could be destroyed selectively, while leaving surrounding tissue unaffected.[4,5] With this concept came an explosion in the number of new light sources in the twenty-first century. These light sources had different wavelengths to accommodate a spectrum of aesthetic procedures with minimal pain.[6–8] In 2008, nearly 75 million aesthetic light procedures were performed, and the number is expected to double because of a growing and demanding young consumer market.

Intense pulsed light (IPL) therapy is an example of an aesthetic light treatment. IPL therapy was initially approved by the US Food and Drug Administration (FDA) in 1998 for photorejuvenation of the pigmented lesions of aging. Shortly thereafter, it was approved for photoepilation and acne photoclearance. IPL therapy has a reputation of being a safe, fast, and effective treatment with a reasonable cost. At present, there are more than 300 registered IPL manufacturers in countries all over the world.[6]

IPL

IPL technology involves parallel xenon flash lamps and capacitors contained within a handheld wand or an articulated arm, which is applied directly to the surface of

Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology, Rush-Presbyterian-St Luke's Medical Center, Chicago, IL 60612, USA
E-mail address: basmd@aol.com

Obstet Gynecol Clin N Am 37 (2010) 489–499
doi:10.1016/j.ogc.2010.09.005 **obgyn.theclinics.com**
0889-8545/10/$ – see front matter

the skin. Single or multiple pulses of high-intensity light are rapidly discharged to the skin surface. The light travels through the skin at a selected wavelength until it strikes the desired chromophore (**Fig. 1**). The pulsed light is converted to heat energy, which coagulates the desired target, such as a hair bulb or capillary within the dermis of the skin. It does not penetrate deep enough to cause thermal damage to the epidermis. This technique is known as selective photothermolysis. In addition, the IPL wand possesses a filter to remove any ultraviolet (UV) components that lead to UV damage. The pulses of light produced are of very short duration, which minimizes skin discomfort and discoloration.[9]

IPL machinery range from large freestanding units to compact mobile units (**Fig. 2**). The standard properties of an IPL machine provide a wide spectrum of optimal wavelengths, power, and pulse durations. These properties allow for selective photothermolysis for a variety of skin conditions. The usual specifications are as follows:

- Light source delivering a full spectrum of filtered IPL
- Optical adapters or crystal filters with wavelengths of 410 to 1400 nm
- Variable power (energy) range from 26 to 40 J/cm^2
- Variable pulse duration from 5 to 30 milliseconds
- Two pulse modes, single and multidose.

The variability of wavelengths achieved with a simple change of a crystal filter allows for several aesthetic procedures to be done at one visit (**Fig. 3**).[7,10,11]

PATIENT PREPARATION

A complete written medical history is the first requirement of IPL treatment. Absolute contraindications to IPL therapy include seizure disorder, skin cancer, systemic lupus erythematosus, pregnancy, shingles, vitiligo, skin grafts, and open skin lesions. Medications that are associated with photosensitivity (tetracyclines, sulfonylureas, isotretinoin, thiazide diuretics, nonsteroidal antiinflammatory drugs, St John's wort) should not be used while undergoing photo treatments. A relative contraindication to IPL therapy is tanning or sun exposure within 30 days of the procedure. It is important to set expectations and estimate the number of treatments required for a desired

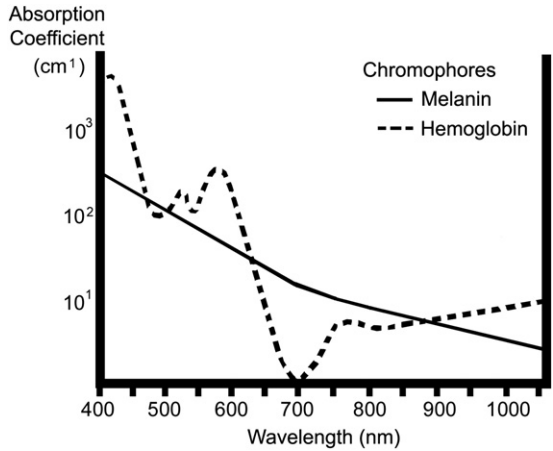


Fig. 1. Chromophore absorption in human skin.

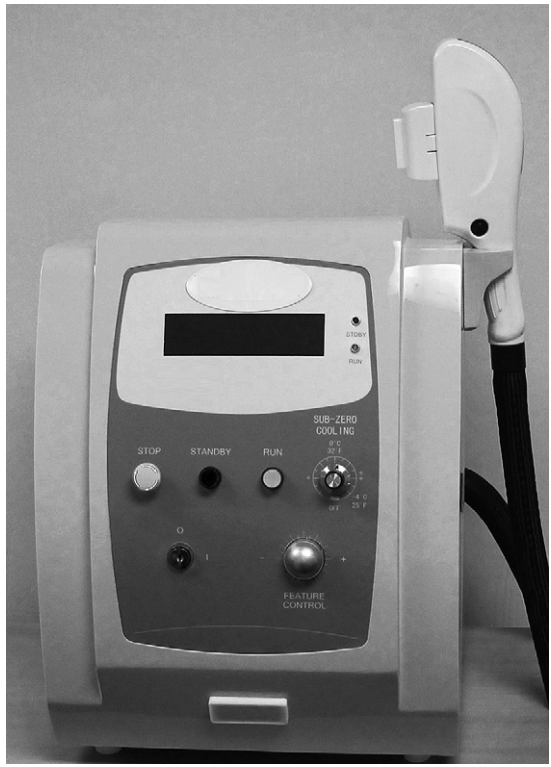


Fig. 2. IPL system.

outcome. Generally, a plan consists of 4 to 6 treatments at monthly intervals. A consent form that explains the potential risks should be obtained before any treatment.[11] The risks include alterations in skin pigmentation and, rarely, scarring at the treatment site.[12]

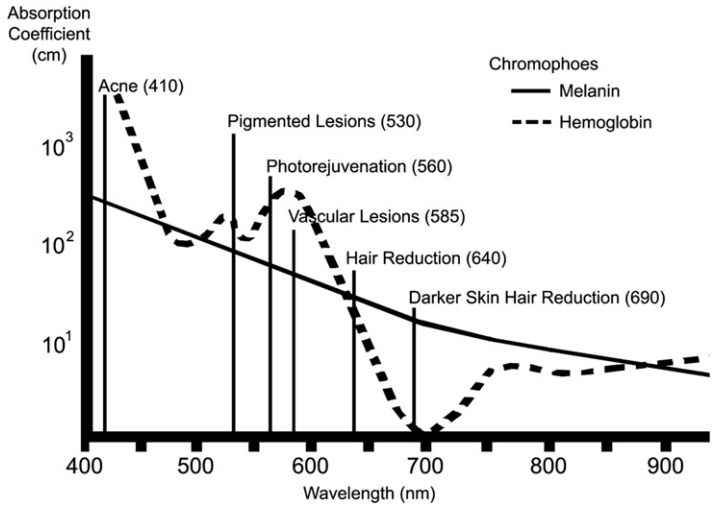


Fig. 3. Wavelength spectrum for clinical indications.

Skin assessment is essential for any phototherapy. The determination of a skin type is made by a self-administered questionnaire. Points are assigned based on genetic composition, reaction to sun exposure, and tanning habits. The final score designates a Fitzpatrick skin type, which correlates well with one of 6 skin types, from very fair (type 1) to very dark (type 6) (**Table 1**). This classification system has been used since 1975 as a proven diagnostic and therapeutic tool in all dermatologic conditions. It was adopted by the FDA for the evaluation of sun protection factor values of current sunscreens.[11,13,14]

Based on the skin type and the photo procedure to be performed, a filter is selected. Filters are wavelength specific; that is, for acne photoclearance, a wavelength of 410 nm is needed, whereas for photoepilation, a wavelength of 640 to 690 nm is selected. Adjustable energy or fluences (26–40 J/cm^2), along with a variable pulse duration (5–30 milliseconds), that is the safest and most efficacious for the desired procedure must be selected. A single pulsed mode is used when higher energy is required, such as photoepilation in a woman with a light skin tone. Multipulsed mode delivers a minipulse, followed by a millisecond delay, and then a final minipulse. The advantage of the multidose mode is that it allows for the epidermis to cool while thermal energy accumulates in a larger chromophore, such as a blood vessel. The skin to be treated must be clean and dry immediately before the photo treatment. No acetone or alcohol should be used. A spot test may be done initially to determine the most effective power level for a particular skin type and condition.[11,14,15] Protective eyewear should be used to avoid retinal damage.

The FDA has approved 8 indications for IPL treatments. The 2 indications that would be a suitable addition to any gynecologic practice are photoepilation (hair removal) and acne photoclearance. Only these 2 indications are discussed in further detail. Other indications include photorejuvenation, photoclearance of pigmented lesions and vascular lesions, rosacea, telangiectasias (spider veins), and solar lentigo (brown spots).[7]

Table 1
Fitzpatrick skin classification system

Skin Type	Response to Sun Exposure	Examples	Susceptibility
I	Always sunburn, never tan	White, very fair and freckled Red or blond hair Blue-eyed Celts	Very high
II	Usually sunburn, tan with difficulty	White, fair Red or blond hair Blue, hazel, or green eyes Scandinavians	High
III	Sometimes sunburn, tan gradually	Beige, fair Any hair color Any eye color Very common	Average
IV	Rarely sunburn, tan easily	Brown Dark hair Brown-eyed Mediterranean Caucasian	Low
V	Very rarely sunburn, tan very easily	Dark brown Mideastern Latin American	Very low
VI	Never sunburn, tan very easily	Black	Minimal

Fig. 8. IPL photo epilation. (*Courtesy of* Sybaritic, Inc, MN; with permission.)

directed to the site of desired hair removal. The duration of pulse frequency correlates positively with the length of the hair to be removed. The longer the hair the greater the pulse frequency. The focused light travels through the skin until it strikes the bulb of the hair. The bulb contains the highest concentration of melanin compared with the rest of the hair shaft. As the light is converted to heat energy, the bulb and most of the hair shaft are coagulated. The intense heat also destroys the hair-producing papilla or the entire hair follicle. To be effective, an adequate amount of heat energy must reach both structures to coagulate them and stop the hair growth. Effective hair reduction is best achieved with hair follicles in the anagen phase. In general, 4-week intervals are required between treatments to yield the best hair removal results (**Fig. 8**).[24–27]

SUMMARY

Light therapy remains an important aspect of medicine. IPL therapy is based on selective photothermolysis, which allows for a rapid treatment with great results and minimal discomfort. It has been proved to be a safe and efficacious phototherapy

ELSEVIER

Seminars in Cutaneous Medicine and Surgery

Light-Emitting Diodes (LEDs) in Dermatology

Daniel Barolet, MD*,†

Light-emitting diode photobiomodulation is the newest category of nonthermal light therapies to find its way to the dermatologic armamentarium. In this article, we briefly review the literature on the development of this technology, its evolution within esthetic and medical dermatology, and provide practical and technical considerations for use in various conditions. This article also focuses on the specific cell-signaling pathways involved and how the mechanisms at play can be put to use to treat a variety of cutaneous problems as a stand-alone application and/or complementary treatment modality or as one of the best photodynamic therapy light source.
Semin Cutan Med Surg 27:227-238

Light therapy is one of the oldest therapeutic modalities used to treat various health conditions. Sunlight benefits in treating skin diseases have been exploited for more than thousands of years in ancient Egypt, India, and China. Solar therapy was later rediscovered by Niels Ryberg Finsen (Fig. 1, Fig. 2), a Danish physician and scientist who won in 1903 the Nobel Prize in Physiology or Medicine in recognition of his contribution to the treatment of diseases, notably lupus vulgaris. Phototherapy involving the use of an artificial irradiation source was born.[1]

It was only many years later that light therapeutic benefits were uncovered again using other segments of the electromagnetic spectrum (EMS) with visible and near-infrared wavelengths. In the late 1960s, Endre Mester, a Hungarian physician, began a series of experiments on the carcinogenic potential of lasers by using a low-powered ruby laser (694 nm) on mice. To his surprise, the laser did not cause cancer but improved hair growth that was shaved off the animal's back for the purpose of the experiment. This was the first demonstration of "photobiostimulation" with low-level laser therapy (LLLT), thereby opening a new avenue for medical science. This casual observation prompted him to conduct other studies provided support for the efficacy of red light on wound healing. Since then, medical treatment with coherent-light sources (lasers) and noncoherent light (light-emitting diodes, LEDs) has expanded. The use of LLLT and LEDs is now applied to many thousands of people worldwide each day for various medical conditions.

*RoseLab Skin Optics Research Laboratory, Montreal, Canada.
†Professor of Dermatology, McGill University School of Medicine, Montreal, Canada.
Address reprint requests to Daniel Barolet, MD, RoseLab Skin Optics Laboratory, 3333 Graham Blvd., Suite 206, Montreal, Quebec, H3R 3L5, Canada. E-mail: daniel.barolet@mcgill.ca

LED photobiomodulation is the newest category of nonthermal light therapies to find its way to the dermatologic armamentarium and will be the focus of this review. Initial work in this area was mainly developed by National Aeronautics and Space Administration (NASA). NASA research came about as a result of the effects noted when light of a specific wavelength was shown to accelerate plant growth. Because of the deficient level of wound healing experienced by astronauts in zero-gravity space conditions and Navy Seals in submarines under high atmospheric pressure, NASA investigated the use of LED therapy in wound healing and obtained positive results. This research has continued and innovative and powerful LEDs are now used for a variety of conditions ranging from cosmetic indications to skin cancer treatment (as a photodynamic therapy light source).

LED Technology

LEDs are complex semiconductors that convert electrical current into incoherent narrow spectrum light. LEDs have been around since the 1960s but have mostly been relegated to showing the time on an alarm clock or the battery level of a video camera. They have not until recently been used as sources of illumination because, for a long time, they could not produce white light—only red, green, and yellow. Nichia Chemical of Japan changed that in 1993 when it started producing blue LEDs which, combined with red and green, produce white light, opening up a whole new field for the technology. The industry has been quick to exploit it. LEDs are based on semiconductor technology, just like computer processors, and are increasing in brightness, energy efficiency, and longevity at a pace reminiscent of the evolution of computer processors. Emitted light are now available at wavelengths ranging from ultraviolet (UV) to visible to near infrared (NIR) bandwidth (247 to 1300 nm).

1085-5629/08/$-see front matter
doi:10.1016/j.sder.2008.08.003

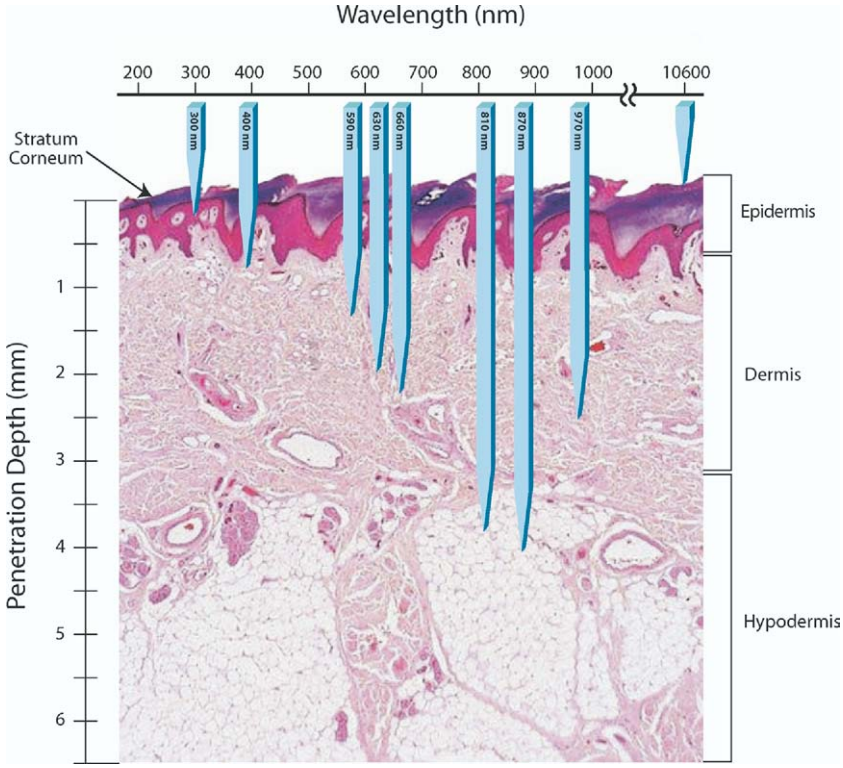


Figure 6 Optical penetration depth.

The various cell and tissue types in the body have their own unique light absorption characteristics, each absorbing light at specific wavelengths. For best effects, the wavelength used should allow for optimal penetration of light in the targeted cells or tissue. Red light can be used successfully for deeper localized target (eg, sebaceous glands), and blue light may be useful for the treatment of skin conditions located within the epidermis in photodynamic therapy (PDT) (eg, actinic keratoses). To reach as many fibroblasts as possible, which is often the aim of LED therapy, a deeply penetrating wavelength is desirable. At 660 nm, for instance, light can achieve such a goal reaching a depth of 2.3 mm in the dermis, therefore covering fibroblasts up to the reticular dermis. The wavelength used should also be within the absorption spectrum of the chromophore or photoacceptor molecule and will often determine for which applications LEDs will be used. Because cytochrome *c* oxidase is the most likely chromophore in LLLT, 2 absorption peaks are considered in the red (~660 nm) and NIR (~850 nm) spectra.[6]

Two major wavelength boundaries exist for LED applications: at wavelengths <600 nm, blood hemoglobin (Hb)

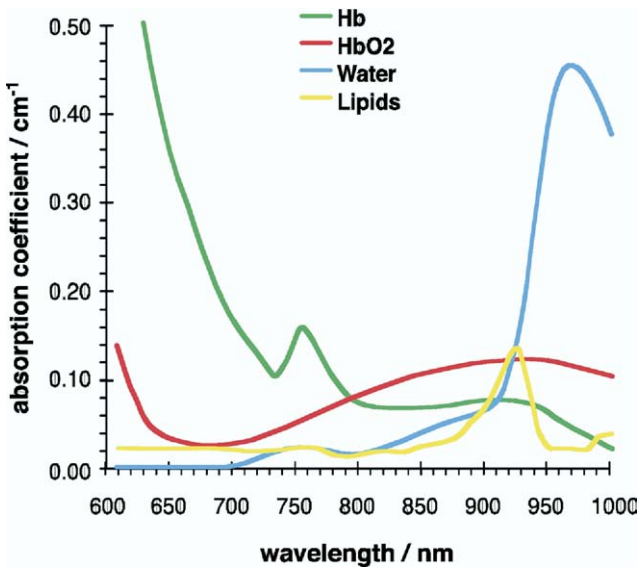


Figure 7 Main tissue constituents absorbing in the 600–1000 nm spectral range. Adapted with permission from Taroni P, Pifferi A, Torricelli A, et al: In vivo absorption and scattering spectroscopy of biological tissues. Photochem Photobio Sci 2:124-129, 2003.

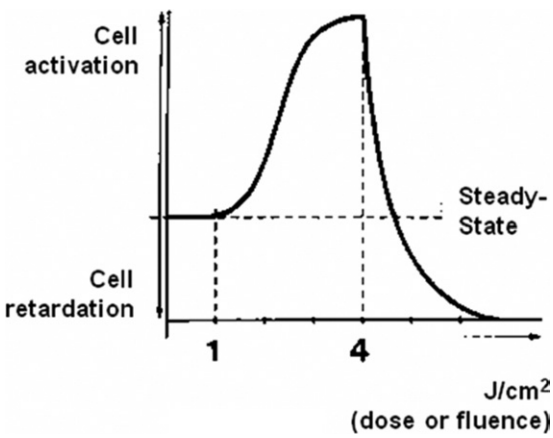


Figure 8 Schematic representation of Arndt-Schulz curve.

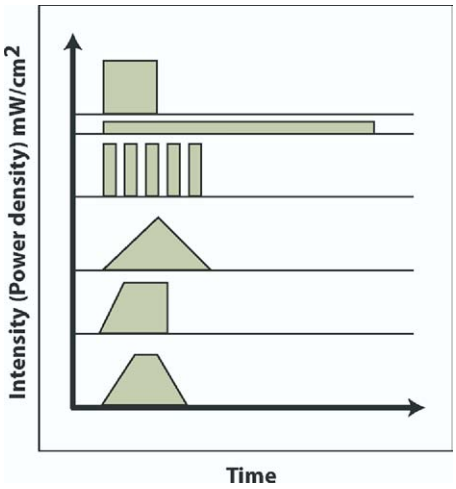


Figure 9 Different light delivery patterns with similar fluence.

is a major obstacle to photon absorption because blood vessels are not compressed during treatment. Futhermore, at wavelengths >1000 nm, water is also absorbing many photons, reducing their availability for specific chromophores located, for instance, in dermal fibroblasts. Between these 2 boundaries, there is a valley of LED possible applications (see Fig. 7).

Fluence and Irradiance

The Arndt-Schulz law states that there is only a narrow window of opportunity where you can actually activate a cellular response using precise sets of parameters, i.e. the fluence or dose (see Fig. 8). The challenge remains to find the appropriate combinations of LED treatment time and irradiance to achieve optimal target tissue effects. Fluence or dose is, indicated in joules per cm^2 (J/cm^2). The law of reciprocity states that the dose is equal to the intensity × time. Therefore, the same exposure should result from reducing duration and increasing light intensity, and vice versa. Reciprocity is assumed and routinely used in LED and LLLT experiments. However, the scientific evidence supporting reciprocity in LED therapy is unclear.[11]

Dose reciprocity effects were examined in a wound healing model and showed that varying irradiance and exposure time to achieve a constant specified energy density affects LED therapy outcomes.[12] In practice, if light intensity (irradiance) is lower than the physiological threshold value for a given target, it does not produce photostimulatory effects even when irradiation time is extended. Moreover, photoinhibitory effects may occur at higher fluences.

In Fig. 9, different light delivery patterns are shown. Interestingly, they are all of the same fluence but over time, the energy of photons does not reach the biological targets in the same way. This may alter the LED biological response significantly. The importance of pulsing will be discussed in the next section.

Certainly a minimal exposure time per treatment is necessary—in the order of several minutes rather than only a few seconds—to allow activation of the cell machinery; otherwise, tissue response is evanescent and no clinical outcome is expected. The ideal treatment time has to be tailored according to the skin condition or degree of inflammation present at the time of treatment.

Pulsing and Continuous Modes

Both pulsed wave and continuous wave (CW) modes are available in LED devices, which add to the medical applicability. The influence of CW versus pulsing mode, as well as precise pulsing parameters (eg, duration, interval, pulse per train, pulse train interval), on cellular response has not been fully studied. To date, comparative studies have shown conflicting results.[13] In our own experience, sequentially pulsed optical energy (proprietary pulsing mode with repeated sequences of short pulse trains followed by longer intervals) has been shown to stimulate more collagen production than CW mode.[14]

Under certain conditions, ultra-short pulses can travel deeper into tissues than CW radiation.[15,16] This is because the first part of a powerful pulse may contain enough photons to take all chromophore molecules in the upper tissue layer to excited states, thus literally opening a road for itself into tissue. Moreover, too long a pulse may produce cellular exhaustion whereas too short a pulse may deliver insufficient energy for a biologic effect to occur. Targeted molecules and cells may-on a smaller scale than selective photothermolysis-have their own thermal relaxation times.[14]

The NO photodissociation theory could also be part of the answer, especially the need for pulsing characteristics during LED therapy. Interestingly, fireflies use such pulsing phenomenon. There, oxygen reacts with the luciferyl intermediate to produce a flash of light. The glory is that the flash switches itself off. Light dissociates NO from cytochrome oxidase, allowing oxygen to bind again. Then, the mitochondria consume oxygen once more, allowing the luciferyl intermediate to build up until another wave of NO arrives.[17]

Precise Positioning of Treatment Head

Very precise positioning or working distance is mandatory to ensure optimal beam delivery intensity covering the treatment area so as to achieve maximum physiological effects. Accurate positioning ensures that the proper amount of photons is delivered to the treated skin to avoid hot or cold spots in the treatment field. This is especially important in photobiology as a required amount of energy must be delivered to the target to trigger the expected cell response. If insufficient photons reach the target, no cell response will result. Some LED devices even provide optical positioning systems to allow reproducible treatment distance within precise limits (±3 mm).

Timing of Treatments Outcomes

There are some indications that cellular responses after light irradiation are time dependent. A recent study suggests that responses such as ATP viability can be observed directly (1 hour) after the irradiation, whereas other responses such as cell proliferation require at least 24 hours before the true

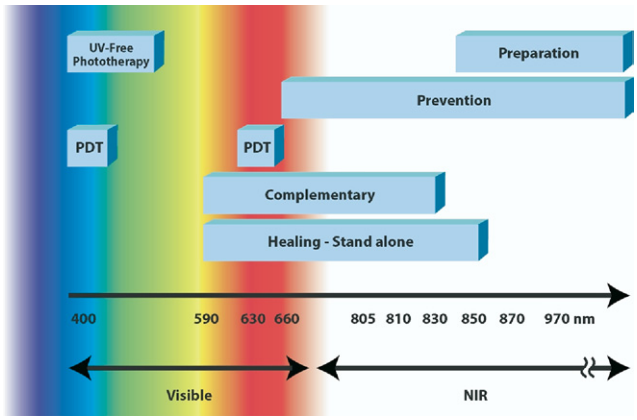


Figure 10 Current and promising LED applications as a function of wavelengths.

effect can be observed.[18] It is thus important to establish time-dependent responses to adequately assess photomodulatory effects. Fibroblasts in culture show physiological cyclical patterns of procollagen type I up-regulation and metalloproteinase-1 (MMP-1) down-regulation that can be emphasized by LED treatments every 48 hours.[19]

State of Cells and Tissues

The magnitude of the biostimulation effect depends on the physiological condition of the cells and tissues at the moment of irradiation.[20] Compromised cells and tissues respond more readily than healthy cells or tissues to energy transfers that occur between LED-emitted photons and the receptive chromophores. For instance, light would only stimulate cell proliferation if the cells are growing poorly at the time of the irradiation. Cell conditions are to be considered because light exposures would restore and stimulate procollagen production, energizing the cell to its own maximal biological potential. This may explain the variability in results in different studies.

Effects of LED

LED therapy is known for its healing and antiinflammatory properties and is mostly used in clinical practice as a supplement to other treatments such as nonablative thermal technologies. Different LED applications can now be subdivided according to the wavelength or combination of wavelengths used (see Fig. 10). LED therapy can be used as a standalone procedure for many indications, as described herein. A summary of recommended LED parameters for various clinical applications are presented in Table 1.

When reviewing the literature, one needs to keep in mind that results from different studies may be difficult to compare because the potential effects of variation of treatment parameters (eg, wavelength, fluence, power density, pulse/continuous mode and treatment timing) may vary from one study to the next. Moreover, there is the possibility that the photobiomodulatory effects are dissimilar across different cell lines, species and patient types. We will now discuss current LED applications.

Wound Healing

Early work involving LED mainly focused on the wound healing properties on skin lesions. Visible/NIR-LED light treatments at various wavelengths have been shown to increase significantly cell growth in a diversity of cell lines, including murine fibroblasts, rat osteoblasts, rat skeletal muscle cells, and normal human epithelial cells.[21] Decrease in wound size and acceleration of wound closure also has been demonstrated in various in vivo models, including toads, mice, rats, guinea pigs, and swine.[22,23] Accelerated healing and greater amounts of epithelialization for wound closure of skin grafts have been demonstrated in human studies.[24,25] The literature also shows that LED therapy is known to positively support and speed up healing of chronic leg ulcers: diabetic, venous, arterial, pressure.[26]

According to our experience, LED treatments are also very useful after CO_2 ablative resurfacing in reducing the signs of the acute healing phase resulting in less swelling, oozing, crusting, pain, and prolonged erythema thereby accelerating wound healing (see Fig. 11). It is important to keep in mind that to optimize healing of necrotic wounded skin, it may be useful to work closer to the near infrared spectrum as an increase in metalloproteinases (ie, MMP-1, debridment-like effect) production accelerates wound remodeling.

Inflammation

Free radicals are known to cause subclinical inflammation. Inflammation can happen in a number of ways. It can be the result of the oxidation of enzymes produced by the body's defense mechanism in response to exposure to trauma such as sunlight (photodamage) or chemicals. LED therapy brings a new treatment alternative for such lesions possibly by counteracting inflammatory mediators.

A series of recent studies have demonstrated the antiinflammatory potential of LED. A study conducted in arachidonic acid-treated human gingival fibroblast suggests that 635 nm irradiation inhibits PGE 2 synthesis like COX inhibitor and thus may be a useful antiinflammatory tool.[27] LED photobiomodulation treatment has also been shown to accelerate the resolution of erythema and reduce posttreatment discomfort in pulsed dye laser (IPL)-treated patients with photodamage and to prevent radiation-induced dermatitis in breast cancer patients.[28,29] Patients with diffuse type rosacea (unstable) (see Fig. 12), keratosis pilaris rubra, as well as postintervention erythema (eg, IPL, CO_2) (Fig. 11) can benefit from a quicker recovery with complementary LED therapy. (See also section on wound healing).

Because LED is known to reduce MMPs, it might be useful in conditions in which MMPs are implicated. One such case is lupus erythematosus (LE). LE is a heterogeneous autoimmune disease associated with aberrant immune responses including production of autoantibodies and immune complexes and specific MMPs have been implicated in its etiol-

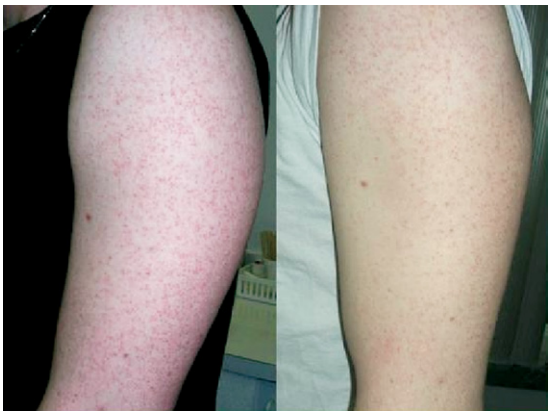


Figure 16 A 24-year-old patient with KPR after 2 months of daily treatments with 660/805 nm home use LED device.

decreased the number of cystic lesions in comparison with the non IR-heated side (Fig. 15).[44]

Photoregulation

Photoregulation involves an exciting new 2-level (importance of dermal–epidermal communication via cytokines) approach that we have evaluated with success to enhance the biological effects of a given topical. The main goal of this application would be to synergistically optimize any bioactive compound trajectory/route to ultimately up-regulate specific gene expression with simultaneous down-regulation of undesired ones via cell signaling pathways. In the esthetics industry, we believe such a method—even though still in its infancy—will become applicable in such applications as home-use skin rejuvenation and the treatment of inflammatory acne, hyperpigmentation disorders, oily skin, hyperhidrosis, eczema, etc.

UV-Free Phototherapy

UV radiation phototherapy has been used for decades in the management of common skin diseases.[45] However, there are side effects associated with UV deleterious effects as well as several contra-indications, including the long-term management of children and young adults and patients receiving topical or systemic immunosuppressive drugs. The primary effectors of UV phototherapy in the treatment of various skin conditions bear similarities with some of those associated with blue LEDs and IR phototherapy with LEDs, including singlet oxygen production and modulation of interleukins.[46,47] This provides a unique opportunity to explore the use of LED in skin conditions where UV therapy is used without the downside of inherent side effects. This approach has been termed UV-free therapy.

For instance, the mode of action of UVA phototherapy for atopic dermatitis was found to involve the induction of apoptosis in skin-infiltrating T-helper cells through a mechanism that requires the generation of singlet oxygen.[48] A recent study demonstrated that visible light (400-500 nm) can be successfully used for the treatment of patients with atopic eczema.[49] In our hands, even resistant KPR (keratosis pilaris rubra) may respond to LED therapy in the visible-NIR spectrum (Fig. 16). These promising results introduce a wide range of new potential application for LED.

Photodynamic Therapy (PDT)

PDT can best be defined as the use of light to activate a photosensitive medication that is applied to the skin prior to treatment. The PDT light source has a direct influence on treatment efficacy. Nowadays, the importance of treatment parameters of this light source is unfortunately greatly underestimated. High-end LED devices meet this challenge and can be used as the light source of choice for PDT (Table 3). Thus, PDT can serve as a treatment that complements other skin rejuvenation therapies or topical agents used to enhance collagen production. The use of a dual wavelength (red and blue) LED light source enhances PDT results for acne and other sebaceous disorders.[50] Red wavelength (630 nm) can reach the sebaceous glands and blue (405 nm) light photobleaches any residual protoporphyrin IX (PpIX) in the epidermis, thereby reducing posttreatment photosensitivity (Fig. 17). The way light photons are delivered seems to hold part of the answer for more effective PDT. Hence, dose rate is becoming one of the important criteria as opposed to total dose (fluence). Also, it is now suggested to avoid peak power effects on the photosensitizer—so-called thermal effects—that are usually encountered with light sources (thermal technologies) such as IPLs and lasers (ie, PDL). PDT frequent indications, both cosmetic and medical, are described in Table 4. LED technology clearly brings several advantages to

Table 3 Fluorescent and High end LED Systems for PDT

	Model		
Device Parameters	**Blu-U**	**LumiPhase-R/B**	**Omnilux Revive**
Wavelength (nm)	Fluorescent tubes 417	LED 405/630 (R/B)	LED 633
Power density (mW/cm²)	10	150/60 (R/B)	105
Working distance gauge	No	Optical Positioning System on both R & R/B Models	No
Treatment time (sec)	1000	160-1000	1200-1800
PDT light source	Yes	Yes	Yes