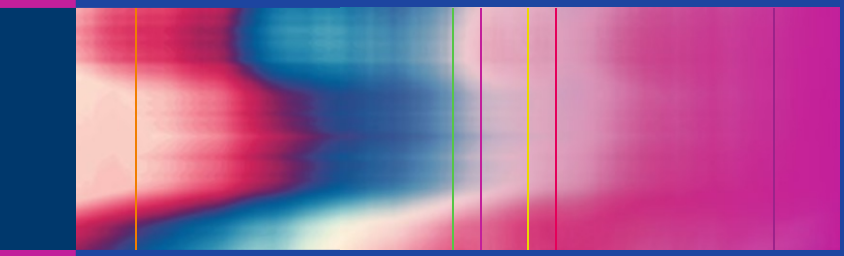
Keyvan Nouri
Editor



Handbook of Lasers in Dermatology

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Keyvan Nouri
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Editor
Keyvan Nouri, MD
Miami
FL
USA

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This book is dedicated to my dear family and friends who have been there for me throughout my life.
I love you all.

Keyvan Nouri, MD

Preface

The use of lasers in dermatology continues to grow and evolve. Over the last five decades, dramatic improvement in laser technology has yielded new indications and applications for lasers in cutaneous disorders.

Existing texts that highlight the use of lasers in dermatology are complete and well-written; however, they are often bulky and not easily transportable. Hence, it has been hard for the dermatologist to find a complete and concise reference that highlights only the specific use of lasers in cutaneous medicine.

This handbook is different. Unlike other texts that highlight the use of lasers in cutaneous disorders, this handbook has been designed to provide a basic structural framework of the use of lasers in dermatology. It clearly outlines laser techniques for each specific dermatologic disorder. It is comprehensive, yet concise and handy—and can be easily transported and taken to the wards or various clinics.

The authors of *Handbook of Lasers in Dermatology* are experts, and have attempted to comprehensively cover each topic in a concise manner that can be easily read by beginners and experts alike. It is my hope that this handbook will provide dermatologists with a handy and reliable reference guide that comprehensively reviews all of the major indications for use of lasers in dermatology—with the ultimate goal of improving patient care and treatment outcomes.

We are extremely grateful to the contributing authors. Without them, this handbook would not exist. We anticipate this handbook will be of interest to all dermatologists who

use lasers in their clinical practice. Enjoy reading. Hopefully, you will find this to be as valuable a resource as we have found it to be.

Miami, FL, USA Keyvan Nouri, MD

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I would like to acknowledge and thank all of the authors and contributors that have made this handbook come to fruition. Their time, energy, and unwavering commitment to this project have made this a concise, up-to-date, and reliable handbook on lasers for dermatologic use. I sincerely appreciate all of their hard work and dedication, and thank them for their contributions. Without them, this text would not have been possible.

Throughout my career, my family has always supported me in my many endeavors. I cannot thank them enough for their kind encouragement and endless love.

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Keyvan Nouri, MD

Contents

Contributors

Harleen Arora Department of Dermatology and Cutaneous Surgery, University of Miami—Miller School of Medicine, Miami, FL, USA

Maryam Afshar, MD Division of Dermatology, UC San Diego, San Diego, CA, USA

Annelyse C. Ballin, MD Department of ENT, Facial Plastic Surgeon, Pontifical Catholic University of Parana, Santa Casa de Curitiba Hospital, Curitiba, Parana, Brazil

R. Glen Calderhead, MS, MSc, PhD, DrMedSci, FRSM Clinical Research Facility, Clinique L, Goyang City, Goyang-shi, Gyeonggi-do, South Korea

Anna H. Chacon, MD Department of Dermatology and Cutaneous Surgery, University of Miami—Miller School of Medicine, Miami, FL, USA

Jesús Cuevas, MD, PhD Pathology Department, Guadalajara University Hospital, University of Alcalá, Alcalá de Henares (Madrid), Spain

Maya G. Debbaneh, BA Department of Dermatology, University of California, Irvine, San Francisco, CA, USA

Leyre A. Falto-Aizpurua, MD Department of Dermatology and Cutaneous Surgery, University of Miami—Miller School of Medicine, Miami, FL, USA

Katlein Franca, MD, MS Department of Dermatology and Cutaneous Surgery, University of Miami—Miller School of Medicine, Miami, FL, USA

David J. Goldberg, MD, JD Skin Laser & Surgery Specialists of New York and New Jersey, Hackensack University Medical Center, New York, NY, USA

Department of Dermatology, Mount Sinai School of Medicine, UMDNJ- New Jersey Medical School, New York, NY, USA

Fordham Law School, New York, NY, USA

Boncehol Lee Goo, MD Clinique L Dermatology, Goyang City, Gyeonggi, South Korea

Salvador González, MD, PhD Dermatology Service, Ramon y Cajal Hospital (Consultant), Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Christian R. Halvorson, MD Department of Dermatology, University of Maryland School of Medicine, Baltimore, MD, USA

Chad Hivnor, MD Dermatology Department, San Antonio Uniformed Health Education Consortium, Lackland, TX, USA

Judith Hong, MD Department of Dermatology, San Francisco Veteran Affairs Medical Center, Santa Rosa, CA, USA

Omar A. Ibrahimi, MD, PhD Wellman Center for Photomedicine, Massachusetts General Hospital, Stamford, CT, USA

Connecticut Skin Institute, Stamford, CT, USA

Martin Kassir, MD, FAAD Department of Dermatology and Lasers, Worldwide Laser Institute, Dallas, TX, USA

Laiqua Khalid, MD Laboratory on Sex and Gender Differences in Health and Disease, Department of Surgery, University of Miami Miller School of Medicine, Miami, FL, USA

Department of Medicine, Jackson Memorial Hospital, Miami, FL, USA

Suzanne L. Kilmer, MD Department of Dermatology, Laser and Skin Surgery Center of Northern California, University of California Davis, School of Medicine, Sacramento, CA, USA

John Koo, MD Department of Dermatology, University of California, San Francisco Psoriasis Center, San Francisco, CA, USA

Jennifer A. Ledon, MD Department of Dermatology and Cutaneous Surgery, University of Miami—Miller School of Medicine, Miami, FL, USA

Eric S. Lee, MD Department of Dermatology and Cutaneous Surgery, University of Miami—Miller School of Medicine, Miami, FL, USA

Vishal Madan, MBBS (Hons), MD, FRCP Department of Dermatology, Salford Royal NHS Foundation Trust, Manchester, Lancashire, England, UK

Andrew A. Nelson, MD Department of Dermatology, Tufts University, Private Practice Nelson Dermatology, St. Petersburg, FL, USA

Tanya Nino, MD Department of Dermatology, Loma Linda University Medical Center, Loma Linda, CA, USA

Keyvan Nouri, MD Department of Dermatology and Cutaneous Surgery, University of Miami—Miller School of Medicine, Miami, FL, USA

Tokuya Omi, MD, PhD Department of Dermatology, Queen's Square Medical Center, Yokohama, Japan

Neh Onumah, MD Skin of All Color, LLC, East Windsor, NJ, USA

Concepción Parrado, MD, PhD Department of Histology and Pathology, University of Málaga, Campus de Teatinos, Malaga, Spain

Maria Valéria Bussamara Pinheiro, MD Department of Dermatology, Federal University of São Paulo – UNIFESP, São Paulo, SP, Brazil

Salma Pothiawala, MD, MPH Department of Dermatology and Cutaneous Surgery, University of South Florida, Tampa, FL, USA

Rachel N. Pritzker, MD Department of Dermatology, Chicago Cosmetic Surgery and Dermatology, Chicago, IL, USA

Thomas E. Rohrer, MD Procedural Dermatology Program, SkinCare Physicians, Chestnut Hill, MA, USA

Nicole E. Rogers, MD, FAAD Department of Dermatology, Tulane University School of Medicine, Metairie, LA, USA

Jessica A. Savas, MD Department of Dermatology and Cutaneous Surgery, University of Miami—Miller School of Medicine, Miami, FL, USA

Andrea Smith, MD Department of Dermatology, Loma Linda University Medical Center, Loma Linda, CA, USA

Olivera Stojadinovic, MD Department of Dermatology and Cutaneous Surgery, University of Miami—Miller School of Medicine, Miami, FL, USA

Davina Tolbert, MPH Skin of All Color, LLC, East Windsor, NJ, USA

Marjana Tomic-Canic, PhD Department of Dermatology and Cutaneous Surgery, University of Miami—Miller School of Medicine, Miami, FL, USA

Abel Torres, MD, JD Department of Dermatology, Loma Linda University Medical Center, Loma Linda, CA, USA

Jill S. Waibel, MD Miami Dermatology and Laser Institute, Miami, FL, USA

Department of Dermatology and Cutaneous Surgery, University of Miami, Miller School of Medicine, Miami, FL, USA

Department of Internal Medicine, Baptist Hospital, Miami, FL, USA

Robert A. Weiss, MD, FAAD, FACPh Department of Dermatology, University of Maryland, Hunt Valley (Baltimore), MD, USA

Laser Skin & Vein Institute, Hunt Valley (Baltimore), MD, USA

Heather Woolery-Lloyd, MD Department of Dermatology and Cutaneous Surgery, University of Miami, Miller School of Medicine, Miami, FL, USA

Julia Wu, MD Division of Dermatology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA

Jane Yoo, MD, MPP Department of Dermatology, Albert Einstein College of Medicine, New York, NY, USA

Chapter 1
Basic Principles of Lasers: Interactions Between Lasers and Tissue

Salma Pothiawala, Suzanne L. Kilmer, and Omar A. Ibrahimi

Abstract Lasers have become extremely important treatment devices in the field of dermatology. They have a variety of applications, ranging from the treatment of vitiligo, cutaneous T-cell lymphoma, hair removal, and skin resurfacing, among others. It is therefore fundamental for the clinician to have an understanding of laser-tissue interactions.

S. Pothiawala, MD, MPH
Department of Dermatology and Cutaneous Surgery, University of South Florida, 13330 USF Laurel Drive, Tampa, FL 33612, USA
e-mail: salma.pothiawala@post.harvard.edu

S.L. Kilmer, MD
Department of Dermatology, Laser and Skin Surgery Center of Northern California, University of California Davis, School of Medicine, 3835J Street, Sacramento, CA 95816, USA
e-mail: skilmer@skinlasers.com

O.A. Ibrahimi, MD, PhD (✉)
Wellman Center for Photomedicine, Massachusetts General Hospital, 999 Summer Street, Suite 205, Stamford, CT 06905, USA

Connecticut Skin Institute, 999 Summer Street, Suite 205, Stamford, CT 06905, USA
e-mail: omar.ibrahimi@gmail.com

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Keywords Dermatology • Lasers • Physical properties • Tissues • Thermal properties • Optical properties

Introduction

- Lasers have become extremely important treatment devices in the field of dermatology. They have a variety of applications, ranging from the treatment of vitiligo, cutaneous T-cell lymphoma, hair removal, and skin resurfacing, among others. It is therefore fundamental for the clinician to have an understanding of laser-tissue interactions.

Spontaneous and Stimulated Emission

- LASER is an acronym for *l*ight *a*mplification by *s*timulated *e*mission of *r*adiation [1].
- Spontaneous emission is the process by which an excited atom spontaneously emits a photon. Electrons go from excited to a resting state when a photon of energy is released [2]. Photon emission can be stimulated by an external source of energy that will increase the population of excited electrons, a process known as pumping [2–8].
- A laser contains a laser chamber, a lasing medium (solid, liquid, or gas) and an external source of energy. Stimulated emission occurs when the external source of energy causes electrons to be excited in the lasing medium. A cascade reaction is generated when these excited electrons release photons, which then collide with other excited electrons in the lasing medium and cause a release of many identical photons at the same time. Laser light continues to be generated as long as the above cascade perpetuates [2–8].

Laser Light Properties

- Laser light has several unique properties including monochromicity, coherence, and collimation [9].

Monochromacity

- As opposed to light from the sun, laser light is monochromatic and emits a well-defined wavelength of light (Table 1.1) [1]. The liquid, solid, or gas contained in the laser medium dictates the wavelength of light that is emitted [2].
- In terms of clinical significance, this monochromatic property of laser light allows it to target specific chromophores, such as water, hemoglobin, and melanin, and allows for specific clinical applications [3]. Further, the depth of penetration into tissue of laser light is in general inversely proportional to its wavelength between 280 and 1,300 nm, a factor that must be taken into account when selecting a particular laser for clinical use. Above 1,300 nm, light is absorbed by water and therefore penetration is decreased [9].

Coherence

- Laser beams are both temporally and spatially coherent, and akin to a column of soldiers marching in step [3]. This phenomenon results from stimulated emission, and allows laser beams to have a high power density [2].

Collimation

- Laser beams are parallel to each other, and therefore exhibit collimation. A collimated beam is created in the laser chamber when light is reflected between two mirrors and only the exit of parallel waves is allowed [2, 6]. Collimation allows laser light to travel long distance without loss of intensity [2].
- In practice, a lens on a laser focuses the parallel light beam down to the smallest possible spot size, or the diffraction-limited spot, to allow the light to focus on the clinical target [7].

Radiometry

- The four main concepts in understanding laser light and skin interactions are energy, power, fluence, and irradiance [1].
- The amount of light emitted from a laser can be quantified by both energy and power. Energy represents work (measured in joules), while power (measured in watts or joules per second) is the rate at which energy is expended [1].
- The intensity of the laser beam on the skin is a function of the area of skin over which it is spread (i.e., the spot size) [2].

  Spot size = cross-sectional area of laser beam

- Fluence (measured in joules per square centimeter) is the energy density of a laser beam.

TABLE 1.1 Lasers used in dermatology [1]

Laser — wavelength (nm)	**Chromophore**
Excimer — 308	DNA/RNA
KTP — 532	Hemoglobin
Pulsed dye — 585–595	Hemoglobin
Q-switched ruby — 694	Blue, black tattoo pigment
Long-pulsed ruby — 694	Melanin
Q-switched Alexandrite — 755	Blue, black, green tattoo pigment
Long-pulsed Alexandrite — 755	Melanin
Diode — 810	Melanin
Q-switched Nd:YAG — 1,064	Tattoo pigment
Long-pulsed Nd:YAG — 1,064	Melanin
Long-pulsed Nd:YAG — 1,320	Water
Diode — 1,450	Water
Er:glass — 1,540	Water
Er:YAG — 2,940	Water
Carbon dioxide — 10,600	Water

- Fluence = watts × seconds/cm^2 = joules/cm^2 = laser output × pulse duration/spot size
- Irradiance (measured in watts per square centimeter) refers to the power density of a continuous wave laser beam, and it is inversely proportional to the square root of the radius of the spot size [1, 2, 4].

  Irradiance = watts/cm^2 = laser output/spot size

- Exposure time, fluence, and irradiance of a laser can be altered depending on the particular clinical use desired by the clinician [1].

Tissue Interactions

Skin Optics

- Laser interacts with skin in four possible ways: reflection, absorption, scattering, or transmission [2, 9].
- Transmission is the passage of light through a tissue without altering either the tissue or the light itself [1, 9].
- Reflection occurs when light "bounces off" the surface of this tissue without entry into tissue. Four percent to seven percent of light is reflected off the skin secondary to the difference in the refractive index between stratum corneum and air [9]. Increasing the angle incidence increases the amount of light reflected. Injury to structures such as the cornea and retina can occur with particular lasers if adequate reflection of laser beams occurs and eye protection is not employed [1].
- Scattering refers to the fragmentation of light after it has entered the skin, and it results from the interaction of light with varied elements that makeup tissue. It mainly results from interaction of light with dermal collagen [1, 9]. When scattering occurs, light is dispersed over a larger area within the tissue, and the depth of penetration of the light beam is reduced at the same time [1]. In general, longer wavelengths of light depict less scattering. However, laser

light in the infrared region with a wavelength above 1,300 nm penetrates superficially due to its chromophore being water [6].
- Effects on tissue are only achieved if light is absorbed as this results in the release of photons [2]. Based on the wavelength of light, a particular chromophore will be targeted and absorb that light, releasing thermal energy. The three major chromophores in the skin are melanin, hemoglobin, water [9]. Table 1.1 shows types of lasers and the chromophores they target [9].

Thermal Interactions and Selective Photothermolysis

- Thermal energy is generated when laser light is absorbed by tissue and then converted to heat, which diffuses into surrounding tissue [1, 5].
- The clinical goal when using lasers is to selectively target a specific chromophore without causing damage to surrounding tissue. This is achieved via using a laser with a wavelength in the absorption spectrum of the target chromophore [9]. The fluence must also be sufficient to deliver adequate thermal energy, and the exposure time must be less than the thermal relaxation time to ensure the least amount to thermal damage via heat diffusion to adjacent tissue [2].
- Thermal relaxation time refers to the time necessary for a target to cool to half of its peak temperature after irradiation, and it is proportional to the square of the size of the target [6].

Photomechanical Effects

- Occurs with nanosecond and picosecond pulsed lasers. Sudden heating can cause thermal expansion with resulting acoustic and shock waves that can cause tissue damage [9].

Laser Parameters

Laser Beam

- The highest beam intensity with the majority of cutaneous lasers occurs at the center of the beam, with diminution at the periphery. This results in the clinically the operator having to overlap treatment areas in order to administer a constant amount of energy to all areas of the treatment field [1].

Spot Size

- Irradiance and fluence are inversely proportional to the square root of the radius of the spot size (Table 1.1) [1].
- Scattering increases with smaller spot sizes, which results in less energy fluence in target tissue. Spot sizes of 7–10 mm results in maximal penetration into tissue to the level of the reticular dermis. Further depth of penetration is not achieved with spot sizes above 10–12 mm.

Pulse Duration

- Laser beams may be pulsed or continuous. A short laser pulse can emit higher peak power compared to a continuous laser and allows for more selective tissue damage [1].
- The rate of energy transfer from a laser is dependent on the duration of time of exposure to the laser beam. Q-switched lasers, for example, produce short pulses of 10–100 ns at high peak power [9].
- The thermal relaxation time of the target chromophore is proportional to the size of the target structure, and it determines the pulse duration used [1].
- Q-switched lasers used for the removal of pigmented lesions and tattoos have short thermal relaxation times as the structures being targeted, melanosomes [10–12] and ink [13], respectively, are small.

Surface Cooling

- Surface cooling is employed to prevent the inadvertent targeting of chromophores that may lie more superficial to the actual target chromophore, such as the case of a laser for hair removal targeting epidermal melanin in addition to dermal melanin in hair follicles.
- All cooling methods remove heat at the surface of the skin through a cooling agent, which is a gas, liquid, or solid.
- Three main methods of surface cooling are precooling, parallel cooling, and postcooling [1, 14].
- Precooling involves the use to a gel or cryogen spray on the skin prior to laser treatment [1, 14]. Cryogen spray cooling is the most effective and aggressive method of precooling for short pulsed lasers [9].
- Parallel cooling is optimal for lasers with longer pulse durations, and it occurs concomitantly with the laser tip and generally involves the use of water-cooled sapphire tip (solid) [1, 14].
- Post-cooling involves the cooling after laser therapy, such as with an ice pack, and minimizes pain, edema, and erythema but does not prevent thermal injury [1, 9, 14].

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Chapter 2
Laser Safety: Standards and Guidelines

Rachel N. Pritzker and Thomas E. Rohrer

Abstract As new laser technologies for various applications within the field of dermatology continue to emerge, the number of laser procedures continues to rise. With the increase in use, the associated injuries to healthcare personnel and patients may also be more prevalent. Although laser related incidents in healthcare settings are greatly underreported, a majority represents avoidable injury with proper safety measures [1]. Therefore, a thorough understanding of safety precautions is imperative. The American National Standards Institute (ANSI) publishes safety standards pertaining to medical laser use and is the basis of all safety guidelines and recommendations. Knowledge of these standards is crucial for a successful safety program in any healthcare facility.

R.N. Pritzker, MD (✉)
Department of Dermatology, Chicago Cosmetic Surgery and Dermatology,
20 W. Kinzie, #1130, Chicago, IL 60654, USA
e-mail: pritzker.rachel@gmail.com

T.E. Rohrer, MD
Procedural Dermatology Program, SkinCare Physicians,
1244 Boylston Street, Chestnut Hill, MA 02467, USA
e-mail: trohrer@skincarephysicians.net

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Keywords Laser Safety • ANSI • Laser-Beam Related Hazards • Personal Protective Equipment • Control of Laser Hazards • Laser Generated Airborne Contaminants (LGAC)

Introduction

As new laser technologies for various applications within the field of dermatology continue to emerge, the number of laser procedures continues to rise. With the increase in use, the associated injuries to healthcare personnel and patients may also be more prevalent. Although laser related incidents in healthcare settings are greatly underreported, a majority represents avoidable injury with proper safety measures [1]. Therefore, a thorough understanding of safety precautions is imperative. The American National Standards Institute (ANSI) publishes safety standards pertaining to medical laser use and is the basis of all safety guidelines and recommendations. Knowledge of these standards is crucial for a successful safety program in any healthcare facility.

Regulatory Organizations of Laser Safety

American National Standards Institute (ANSI)

- ANSI is a non-profit, consensus group that develops and maintains the national sets of standards.
- Laser experts from manufacturers, professional societies, government agencies, educational institutes, and consumer and labor interests represent the group.
- The published series of ANSI-Z136 standards pertains to the safe use of lasers. In particular, the ANSI Z136.1 (Safe Use of Lasers) and the ANSI Z136.3 (Safe Use of Lasers in Health Care) detail the expected standards for laser use in the dermatologic setting.
- The latest revision of the Z136.3 standard was published in 2011. Changes from the previous documents include

definition revisions, new terms, and enhanced appendices with additional information for specific medical specialties [2].
- Adherence to these recommended standards is voluntary but they are generally the basis for other organizations' standards and often referenced in litigation for malpractice.

Occupational Health and Safety Administration (OSHA)

- OSHA is the agency of the United States Department of Labor that regulates workplace safety and health conditions.
- There are no OSHA specific standards for medical laser safety, but there are general guidelines that reference the ANSI Z136 series.
- If investigated by OSHA under the General Duty Clause, compliance with ANSI Z136 is emphasized [3].

Center for Devices and Radiological Health (CDRH)/Food and Drug Administration (FDA)

- A regulatory board that ensures manufactures of lasers adhere to the performance requirements of the Federal Laser Product Performance Standard (FLPPS).
- The FLPPS assigns lasers into hazard categories similar to the ANSI classes, discussed below, and are required to be affixed to the laser during manufacturing.

The Joint Commission (TJC)

- Formally named the Joint Commission for Accreditation of Healthcare Organizations (JCAHO), and is a non-for-profit organization that accredits health care programs.
- It evaluates adherence to ANSI standards in the hospital and clinic settings.

Other Professional Societies

- The American Society for Laser Medicine and Surgery (ASLMS), American Academy of Dermatology (AAD), and the American Society of Dermatologic Surgery (ASDS) encourage the safe use of lasers without specific stated standards, but have published recommended procedural skills and training for laser operation.

Hazard Classification of Lasers

- ANSI classifies lasers into four categories based on their capability to cause injury to eyes or skin. They are based on factors including power of laser beam, wavelength, duration of exposure, and the maximal permissible exposure (MPE) (Table 2.1).
- The MPE is the level of exposure over which adverse biologic changes occur [4].
- The most recent ANSI classification system was accepted in 2007 and implements Arabic numerals to designate the four categories; the prior classification used Roman numerals. Changes to the 2007 classification reflected new knowledge of low risk lasers, not altering the classification of Class 4 lasers used in the medical field.
- The FLPPS requires that all manufactures label lasers by their hazard category [4, 5].

Laser-Beam-Related and Non-beam Hazards

Ocular Hazards

- The eye is uniquely susceptible to laser light and poses the most dangerous risk of permanent damage. Ocular incidents represent a majority of reported injuries [1]. Varying laser wavelengths affect different anatomical structures of the eye (Figs. 2.1, 2.2, and 2.3).

TABLE 2.1 2007 ANSI classification

Class	Hazard risk	Protection measures
1	No risk as they are incapable of producing damaging levels of laser emission. The MPE cannot be reached when viewing the laser directly. Examples: laser printer, CD and DVD players	Exempt from any control measures or surveillance
1M	Class 1 may pose an increased risk if viewed directly through certain optical instruments such as an eye-loupe or telescope	Exempt from protective measures except when used with optical instruments
2	Low power lasers in the visible light spectrum (0.4–0.7 μm) that can be directly viewed for less than the ART. Examples: most laser pointers, bar code scanners	Exempt from any control measures or surveillance
2M	Class 2 may pose an increased if viewed directly through certain optical instruments	Exempt from protective measures except when used with optical instruments
3R	Medium-powered lasers that may be hazardous under direct and specular reflection viewing conditions. Considered lower risk than 3B Examples: high power laser pointers	Protective measures not required, but recommended
3B	Higher risk than 3R. May produce ocular damage without optical instrumentation Examples: laser light show projectors, lower power industrial/ research lasers	Required administrative controls, protective equipment, training, and appointment of LSO

(continued)

Table 2.1 (continued)

Class	Hazard risk	Protection measures
4	High-powered, >0.5 W, lasers that present significant risk in regards to direct beam exposure to the eye or skin. May pose a diffuse reflection or fire hazard risk, and may produce laser generated air contaminant. Examples: medical, industrial, and research lasers	Required administrative controls, protective equipment, training, and appointment of LSO

MPE maximal permissible exposure, *ART* aversion response time, 0.25 s, in which the movement of the head or eye blink in response to bright light, *LSO* laser safety officer [4, 5]

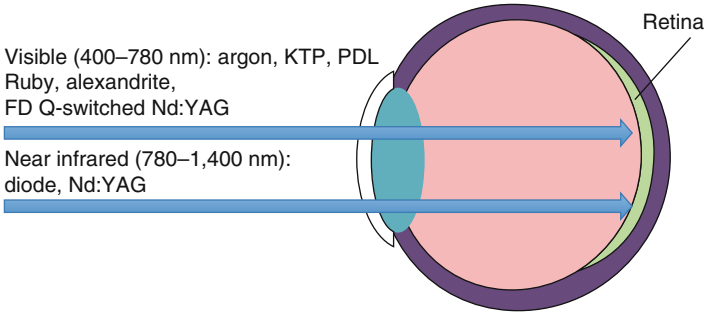

Figure 2.1 Retina. The wavelengths that affect the retina and associated dermatologic lasers. If injured, the effects are painless and may result in substantial loss of vision or a blind spot, retinal burn, and/or loss of visual acuity. *KTP* potassium titanyl phosphate, *PDL* pulsed dye laser, *FD* frequency doubled, *Nd:YAG* neodymium-doped yttrium aluminum garnet

Retina

- The focusing ability of the eye can concentrate a collimated laser beam by a factor of 100,000 onto the retina, making it distinctly susceptible to damage [6].
- Due to this increased potential for permanent injury, the spectrum from 400 to 1,400 nm is known as the retinal hazard region.

- Wavelengths which affect the retina and associated dermatologic lasers include:
  - Visible (400–780 nm) — Argon, KTP, PDL, Ruby, Alexandrite
  - Near Infrared (780–1,400 nm) — Diode, Nd:YAG
- The potential effects include painless injury as the retina lacks pain receptors, substantial loss of vision, retinal burn, and/or foveal injury; a loss of visual acuity or blind spot.

Cornea

- The cornea is the outermost layer of the eye used for barrier protection and focusing.
- Wavelengths which affect the cornea and associated dermatologic lasers include:
  - UV-C (200–280 nm)/UV-B (280–315 nm) — Excimer
  - Mid-Infrared (1,400–3,000 nm) — Erbium:YAG
  - Far-Infrared (3,000–1,000,000 nm) — CO_2
- The potential effects include painful injury as the cornea contains pain receptors, photokeratitis, and/or a superficial or deep corneal burn. Deeper burns can cause opacification and scarring.

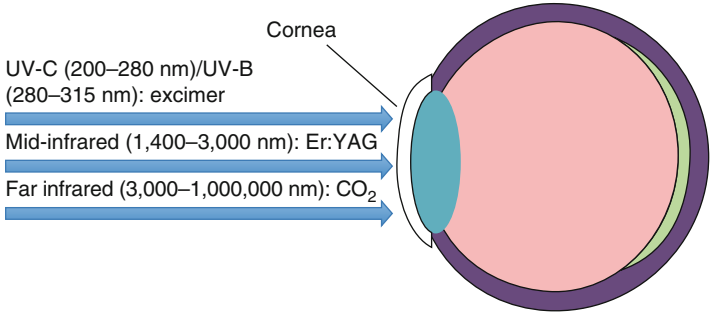

FIGURE 2.2 Cornea. The wavelengths which affect the cornea and associated dermatologic lasers. If injured, the effects are painless and may result in photokeratitis, deep or superficial corneal burn, opacification, and/or scarring. *Er: YAG* erbium-doped yttrium aluminum garnet, *CO_2* carbon dioxide

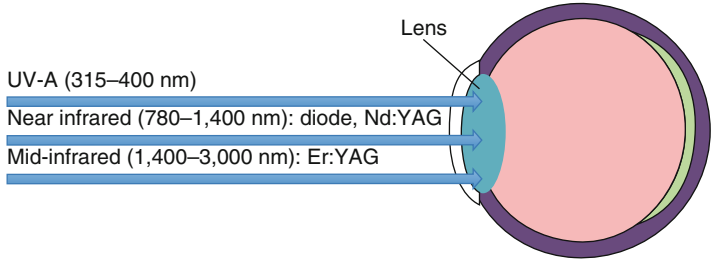

FIGURE 2.3 Lens. The wavelengths that affect the lens and associated dermatologic lasers. If injured, the effects may result in an acute exposure lentricular burn or chronic exposure cataract formation. *Nd:YAG* neodymium-doped yttrium aluminum garnet, *Er: YAG* erbium-doped yttrium aluminum garnet

Lens

- The lens, along with the cornea, is in the anterior segment of the eye and focuses light onto the retina.
- Wavelengths which affect the lens and associated dermatologic lasers include:
  - UV-A (315–400 nm)
  - Near-Infrared (780–1,400 nm) — Diode, Nd:YAG
  - Mid-Infrared (1,400–3,000 nm) — Erbium:YAG
- The potential effect of an acute exposure is a lenticular burn, while chronic exposure can cause cataracts [6].

Laser Generated Airborne Contaminants (LGAC) Hazards

- LGAC or smoke is an ongoing conversation within the medical field.
- ANSI recognizes that electrosurgical devices produce the same type of smoke as lasers.

- There are over 30 known chemicals contained within surgical smoke. It is known that mutagenic/carcinogenic chemicals including carbon monoxide, acrylonitrile, hydrocyanide, and benzene are found within surgical smoke [7].
- These are the same cardiotoxic and carcinogenic chemicals found in cigarette smoke, although in much lower levels, and their chronic exposure hazard cannot be determined [7].
- It is also postulated that viruses and bacteria can be transmitted through plume [8]. Viable bacteria HPV DNA has been demonstrated in laser plume [9] but not found in other studies [10]. A comparative study showed that carbon dioxide (CO_2) laser operators treating verruca had increased incidence of nasopharyngeal HPV infection than the control population [11].
- Although proviral HIV DNA was recovered in suction tubing of smoke evacuators, other studies exploring transmission of HIV and hepatitis have been inconclusive [8].
- The ASLMS statement on surgical plume (2007), postulates a potential hazard from vaporized tissue plume. Although studies are inclusive about the consequences of laser plume, it should be considered potentially hazardous and evacuator systems should be used at all times [12].

Fire Hazards

- Class 4 lasers can cause electrical or flash fires.
- Electrical fires occur within the laser from faulty electrical wiring; flash fires occur when the laser beam hits various flammable materials.
- Potential flash fire hazards in the laser room include hair, hair products, make-up, fabrics (especially rayon and nylon), drapes, alcohol, chlorhexidine (contains isopropyl alcohol), elastic strap on safety eyewear, plastic, and gauze.

- Greatest risk is with the CO_2 and erbium:YAG lasers. A recent study demonstrated that even one pulse of the CO_2 laser created overt flames to a dry underpad drape and cotton balls. It produced smoke and char to dry gauze and a dry drape [13].

Skin Hazards

- Similar to the eye, injury to the skin can be photochemical or thermal in nature; however, the skin is much less sensitive to laser radiation than the eye.
- Damage to the skin depends on duration of exposure, wavelength and pulse repetition.
- Sunburn-like reactions are most common in the UV range, especially UV-B, while thermal burns occur in the infrared spectrum [6].

Control and Management of Laser Hazards

Laser Safety Officer (LSO)

- ANSI requires appointment of an LSO to each facility or organization operating a Class 4 laser, and is the main focus of the laser safety program.
- The LSO can be the laser operator, laser user, or other trained person with the training and experience to administer the laser safety program of the site.
- In the new ANSI Z136.3-2011, expansions of the safety management team were made. Some changes were controversial [2] for adding more administrative duties. These include, for larger health care facilities, a Deputy Laser Safety Officer (DLSO) must be appointed if the LSO is unavailable during laser operation. And if multiple facility sites exist, a Laser Safety Site Contact

(LSSC) is recommended at each location. In general, the LSSC is responsible for the supervision of laser use in a specific area and is a liaison between staff and the LSO. These new roles are noted to be advised and not mandatory.

- The LSO has numerous responsibilities outlined in ANSI Z136.3 including but not limited to the creation and maintenance of policies and procedures (P&P). These document the operation, maintenance, and safety program in detail of the healthcare facility. For examples of P&P, one can refer to ANSI Z136.3 Appendix H [4].

Health Care Facility and Equipment Safety Audits

- Audits of the facility and safety features are to be conducted and documented by the LSO. The frequencies of such audits are per the LSO, but not less than yearly [4].

Perioperative Checks

- It is important to adhere and document a detailed perioperative checklist pertinent to the laser in use. Examples of complete safety checklists are provided in ANSI Z136.3 Appendix B [4].

Signs and the Laser Treatment Control Area (LTCA) (Fig. 2.4)

- The Laser Treatment Control Area (LTCA) contains the Nominal Hazard Zone (NHZ), and is established by the LSO as the location in which the laser is used.
- The Nominal Hazard Zone (NHZ) is the space around the laser within which the level of the radiation (direct,

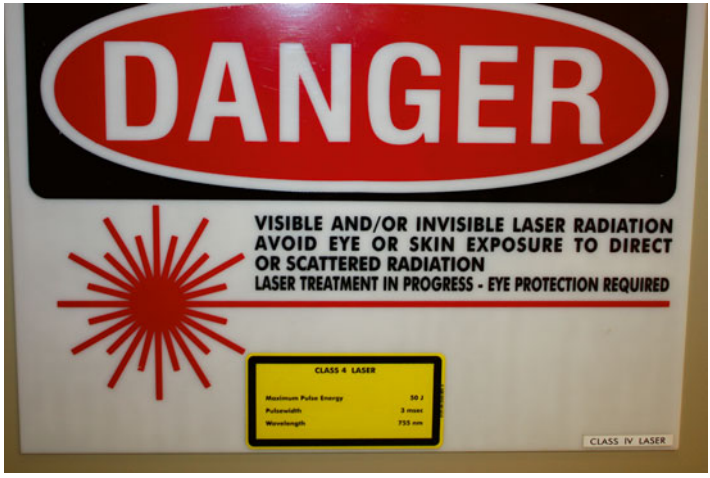

FIGURE 2.4 An example of a Class 4 laser sign

reflected, or scattered) exceeds the MPE. Calculations for NHZ can be found in the ANSI Z136.1, but usually the NHZ involves the entire LTCA for Class 4 lasers.

- Warning signs with the wavelength of laser contained listed are required on all doors entering the LTCA when the laser is in use and removed when not in use.
- The symbols and text on the sign varies depending on the class and wavelength of the laser, but standardized for each laser class.
- All facility windows with access to the LTCA must be covered with an appropriate barrier when the laser is in use, especially for visible and infrared wavelengths that are transmitted by glass.
- All mirrors should be covered when the laser is in use.
- To minimize the risk of a collimated beam hitting a flat, specular surface, special instruments and room furnishings should have specialized surfaces with either mechanically textural changes and/or a specialized coating [6].

Equipment Controls

- The switch that controls the laser activation must be guarded to avoid accidental activation.
- An emergency shut off switch should be accessible easily at all times and reachable by the laser operator.
- Safety audits of the equipment must be documented under the guidance of the LSO, at least annually [4].

Personal Protective Equipment (PPE)

Ocular Protective Equipment (Figs. 2.5 and 2.6)

- Important key terms to define include [4].
  - **Maximal Permissible Exposure (MPE)** — the level of exposure over which adverse biologic changes occur. It is calculated based on the wavelength, energy, and duration of exposure.
  - **Nominal Hazard Zone (NHZ)** — the calculated space around the laser within which the level of the radiation (direct, reflected, or scattered) exceeds the MPE.
  - **Optical Density (OD)** — the filter factor of protective eyewear. It is the attenuation factor by which the particular lens decreases the specific wavelength's beam upon hitting the surface, calculated based on laser power and the MPE. For example, an OD of 4 allows 0.0001 % of the laser energy to be transmitted through the eyewear.
- ANSI and OSHA mandate protective eyewear within the NHZ for all Class 3 and 4 lasers.
- The OD of various lasers are calculated and seen in ANSI Z136.1 or provided by the laser manufacturer.
- Eyewear must be permanently labeled with the wavelength range it covers and the degree of protection (OD) and should be checked to match the laser in use.

FIGURE 2.5 Examples of various types of protective eyewear. Including intense pulsed light (IPL) shutter goggles in the middle, right position

FIGURE 2.6 The optical density (*OD*) and wavelength are clearly marked on these Alexandrite laser goggles. This information must be permanently displayed on all protective eyewear

- Intense pulsed light (IPL) is a polychromatic light over a broad wavelength spectrum, therefore specialized goggles with protection over these wavelengths or goggles with shutter speed technology triggered by the light are needed.

- Optical glass filters the light from the CO_2 laser, but eyewear must still have peripheral shields.
- Reflective filters include glass protective eyewear which have better visibility, but are heavy in weight, can cause hazardous reflections, and can scratch easily.
- Absorbent filters include eyewear made from polymeric materials which are light in weight, but can be easily cracked and may make it more difficult to see the treatment field.
- All goggles, glasses or prescription eyewear with special filter materials must have peripheral shields.
- For patient protective eyewear, the same appropriate measures within the NHZ must be upheld.
- The same eyewear as the laser operator or fitted opaque or metallic mini-goggles can be used. Caution is warranted, as the strap may be flammable.
- Treatment in the periocular area may require corneal shields, especially when treating the eyelids.
  - Ophthalmic anesthetic drops to the eyes and a lubricant in the inside surface of the shield must be used prior to placement.
  - Metallic shields with a non-reflective treated surface have been shown to be superior in comparison to other eye shields [14].

Control of Laser Generated Airborne Contaminants (LGAC)

- ANSI, OSHA, NIOSH (National Institute for Occupational Safety and Health) state the need to control LGAC from laser procedures through the use of ventilation and respiratory protection, but do not provide exact recommendations for equipment to be used.
- The particle size of smoke generated from lasers is approximately 0.30 μm, but ranges from 0.10 to 0.80 μm. The viral particles measure approximately 0.1 μm [7].
- Local exhaust systems are the first line defense to control LGAC. They include the wall suction system or a smoke evacuator; many believe the latter is the most important protective measure [7].

- In smoke evacuators, the ultra-low penetration air (ULPA) filters particles over 0.12 μm, whereas the high efficiency particulate air (HEPA) filters above 0.3 μm.
- The placement of the suction tip is paramount, as it has shown to be 98.6 % effective at 1 cm from site of tissue damage and less than 50 % at a 2 cm distance [7]. Many lasers now include a suction device on the handpiece to emphasize this point. The tip should be cleaned after each use.
- General surgical masks do not filter particles under 5 μm, therefore specialized high-filtration masks (laser masks) capturing particles as small as 0.1 μm should be used.
- It is important to keep the mask dry, as moisture will inhibit the electrostatic based filtration.
- Masks, gloves, and clothing should be worn to protect against spatter to adhere to universal precautions.

Fire Controls

- Safety equipment such as a fire extinguisher, water basin, and fire resistant drape should be readily available.
- All potential flammable materials should be removed from the treatment field, for example make-up removed and hair covered with a water-soluble lubricating ointment or a wet towel.
- Special care should be taken with the use of gauze and drapes; they should be wet or non-flammable.

Medical Examination of Health Care Personnel (HCP) and Incident Reporting

- Any accidental exposure to laser radiation which exceeds the MPE for the specific laser in use constitutes an exposure incident.
- A medical examination of an HCP suspected to have endured a laser related injury should be examined in a timely manner, within 48 h.
- If the injury resulted in ocular exposure within the retinal hazard region (400–1,400 nm), then an ophthalmologist should perform the examination [6].

- The LSO must document all exposure incidents.
- Only incidents that cause serious injury or death are required to be reported to the FDA by the manufacturer or facility under the Medical Device Reporting (MDR) regulation.

Training in Laser Safety

- The LSO is responsible for the training of all laser operators and support staff, emphasizing the use of each particular laser and the understanding of ANSI standards.
- This safety training is distinct from the technical training of laser medicine.
- Examples of laser safety education program criteria are shown in ANSI Z136.3 Appendix F [4].
- The Laser Institute of America (LIA) and Rockwell Laser Industries (RLI) offer a variety of courses online and on-site for all personnel.

Conclusion

As there are cases reports of permanent ocular damage [1] and other associated risks from the application of lasers in the healthcare field, it is imperative for all personnel to understand the potential hazards and take the appropriate control measures to avoid these possible, dangerous risks. Continuous education and training about laser safety at each laser healthcare site is of upmost importance and should keep laser safety at the forefront of laser use.

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Chapter 3
Overview of Lasers Used in Dermatology

Jessica A. Savas, Jennifer A. Ledon, Kaitlein Franca, and Keyvan Nouri

Abstract Before one can efficiently utilize laser technology, one must first have a basic understanding of laser-tissue interactions. This chapter aims to provide a quick reference outlining the currently available laser devices and their associated indications. A brief overview of the physical properties of the major cutaneous chromophores including thermal relaxation times and absorption spectra are also discussed. It is important to note that as laser technology evolves, new laser devices are being developed and indications for use are constantly expanding; therefore, this chapter may serve as a guide to the currently used devices and common indications, but should not be considered comprehensive.

Keywords Laser • Chromophore • Thermal relaxation time • Absorption spectra • Overview • Cutaneous • Dermatology

J.A. Savas, MD (✉) • J.A. Ledon, MD
K. Franca, MD, MS • K. Nouri, MD
Department of Dermatology and Cutaneous Surgery,
University of Miami—Miller School of Medicine,
1475 NW 12th Avenue, 2nd Floor, Miami, FL 33136, USA
e-mail: jsavas@med.miami.edu; jledon1@med.miami.edu;
k.franca@med.miami.edu;
knouri@med.miami.edu, knourimd@gmail.com

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Table 3.1 Overview of dermatologic lasers and associated indications [1, 2]

Source	Wavelength	Primary chromophore	Modes	Indications	Depth of penetration
Xenon-chloride excimer	308 nm	Non-specific	Pulsed	Vitiligo (hypopigmentation in general)	Epidermis
				Psoriasis	
				Atopic dermatitis	
				Mycosis fungoides	
				Morphea	
Argon	488/514 nm	Hemoglobin	Continuous	Vascular lesions	Epidermis
Copper vapor/ bromide	510 nm	Hemoglobin	Pseudo-continuous	Epidermal pigmented lesions	Epidermis
	578 nm			Vascular lesions	
Potassium-Titanyl-Phosphate (KTP) crystal filter on Nd:YAG laser	532 nm	Hemoglobin, melanin, tattoo ink	Long-pulsed	Vascular lesions, facial telangiectasia, pigmented lesions	Epidermis
			Q-switched	Red/orange/yellow tattoos	

Dye (PDL)	577 nm 585 nm 590 nm 595 nm 600 nm	Hemoglobin, tattoo ink	Pulsed	Vascular lesions (facial telangiectasia, hemangiomas, port-wine stains, pyogenic granulomas, Kaposi's sarconoma, Poikiloderma of Civatte) scars, striae. Verrucae, red/yellow/ orange tattos	Mid-dermis
Ruby	694 nm	Melanin	Long-pulsed	Hair removal	Mid-dermis
			Q-switched	Pigmented lesions	Mid-dermis
				Tattoo removal (black, blue)	

(continued)

TABLE 3.1 (continued)

Source	Wavelength	Primary chromophore	Modes	Indications	Depth of penetration
Alexandrite	755 nm	Melanin Hemoglobin (deoxyhemoglobin > oxyhemoglobin) Carbon ink particles	Long-pulsed	Hair removal	Deep dermis
				Lentigines	
				Lower extremity telangiectasia removal	
			Q-switched	Pigmented lesions	Deep dermis
				Tattoo removal (green)	
Diode	800–810 nm	Follicular melanin	Long-pulsed	Hair removal	Deep dermis
	940 nm				
	1,350–1,450 nm			Nonablative skin resurfacing	
Neodymium-doped: Yttrium-Aluminum-Garnet (Nd:YAG)	1,064 nm	Melanin	Long-pulsed	Hair removal, vascular lesions, leg veins	Deep dermis/ subcutaneous tissue
			Continuous	Deep coagulation of tissue	
	1,320 nm		Pulsed	Skin rejuvenation, acne scars	

Erbium:glass	1,520 nm	Cellular water	Fractionated, non-ablative	Photorejuvination, scars, striae	Upper/mid-dermis
Erbium:Yttrium-Aluminum-Garnet (Er:YAG)	2,940 nm	Cellular water	Pulsed	Ablative skin resurfacing, removal of epidermal lesions	Epidermis/ superficial dermis
Carbon dioxide (CO_2)	10,600 nm	Cellular water	Continuous wave	Actinic cheilitis, verrucae, rhinophyma	Epidermis/ superficial dermis
			Fractionated	Resurfacing	
			Pulsed	Ablative skin resurfacing, removal of epidermal/dermal lesions	
Intense pulsed light (IPL)	400–1,200 nm	Variable		Superficial pigmented lesions, vascular lesions, hair removal, nonablative dermal remodeling	Variable

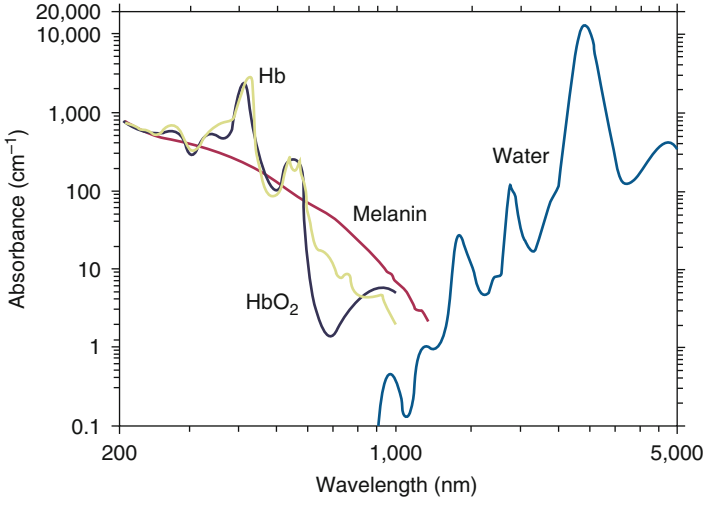

FIGURE 3.1 Absorption spectra of cutaneous chromophores [2]

TABLE 3.2 Properties of cutaneous chromophores [2]

Chromophore	Thermal relaxation time (TrT)
200 μm hair follicle	20 ms
50–100 μm blood vessel	1–5 ms
7 μm erythrocyte	20 μs
1 μm melanosome	1 μs
0.1 μm tattoo particle	10 ns

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Chapter 4
Anesthesia for Lasers

Annelyse C. Ballin, Katlein França, and Keyvan Nouri

Abstract Among the most frequent procedures performed by dermatologists, patients consider that treatments involving laser and lights cause moderate to severe pain. One of the patient's main concerns about laser procedures is pain and discomfort, especially for the first time patient. In order to reduce the sensation of pain, distress, and patient's anxiety level, anesthesia can be applied before laser treatments. Local anesthesia (topical anesthesia or local anesthetic injection), nerve blocks, oral sedation with a benzodiazepine and/or intravenous anesthesia can be applied prior to the procedure. The most widely used type of anesthesia for laser procedures is topical anesthesia, associated or not with ice. Topical anesthetics available on the market and approved by

A.C. Ballin, MD (✉)
Department of ENT, Facial Plastic Surgeon,
Pontifical Catholic University of Parana, Santa Casa de Curitiba Hospital, Bruno Filgueira Street, 369 10th floor, Curitiba, Parana 80240-220, Brazil
e-mail: annelysecb@gmail.com

K. França, MD, MS • K. Nouri, MD
Department of Dermatology and Cutaneous Surgery,
University of Miami—Miller School of Medicine,
1475 NW 12th Avenue, 2nd Floor, Miami, FL 33136, USA
e-mail: k.franca@med.miami.edu; knouri@med.miami.edu, knourimd@gmail.com

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the FDA have been proven to be safe and effective for the majority of the laser procedures, even for infants and young kids where extra caution is required.

Keywords Laser • Anesthesia • Topical anesthesia • Local anesthesia • Lidocaine • Dermatology • Pain • Clinical procedures

Introduction

Among the most frequent procedures performed by dermatologists, patients consider that treatments involving laser and lights cause moderate to severe pain [1]. One of the patient's main concerns about laser procedures is pain and discomfort, especially for the first time patient.

- Patients can forgo any sort of anesthesia, or have only topical cooling, cryospray or ice before and/or during laser procedures.
- In order to reduce the sensation of pain, distress, and patient's anxiety level, anesthesia can be applied before laser treatments.
- The determining factors for deciding whether or not to use anesthesia, and which type of anesthesia to use include:
  - Laser treatment device and settings
    - Deeper penetration of the laser into the skin: more painful
    - Higher treatment level setting: more painful
  - Size and location of the area to be treated
    - Larger areas: more painful
    - Sensitive areas (such as perioral, inguinal): more painful
  - Patient's pain thresholds
    - It appears that males have lower thresholds than females [2]

  - Age of the patient [3]
    - Anesthesia is an important issue when infants and children are treated with a laser [4]

- Local anesthesia (topical anesthesia or local anesthetic injection), nerve blocks, oral sedation with a benzodiazepine and/or intravenous anesthesia can be applied prior to the procedure.
- Since the most widely used type of anesthesia for laser procedures is topical anesthesia, associated or not with ice, this chapter will focus on topical anesthesia.

Topical Anesthesia

- Cocaine was the first topical anesthetic discovered and is the only naturally occurring local anesthetic in medical use today [5]. However, its uses as a local anesthetic is no longer supported by the literature because of general concern about toxicity and federal regulatory issues [6].
- Several topical local anesthetics are currently available for use in dermatologic procedures (See Table 4.1)

Table 4.1 Some topical anesthetics currently available for use

Product	**Active topical anesthetics**
EMLA cream	2.5 % lidocaine and 2.5 % prilocaine
LMX 4	4 % lidocaine
LMX 5	5 % lidocaine
Synera® (S-Caine Patch)	lidocaine 70 mg and tetracaine 70 mg
Topicaine	4 or 5 % lidocaine
Topex, HurriCaine	20 % benzocaine
Greencaine	4 % lidocaine
LidoCream	4 % lidocaine
Zcaine	4 % lidocaine

- Topical anesthesia allows a variety of laser procedures to be performed on the skin without anatomic distortion from local anesthetic injection and without an increase in the risk of procedural complications from general anesthesia.
- Topical anesthetics act by:
  - Targeting free nerve endings in the dermis
    - Providing cutaneous analgesia
  - Blocking the ability of the sodium channels to open
    - Preventing the initiation and transmission of nerve impulses
- The ideal topical anesthetic agent would [5, 7]:
  - Be able to penetrate the stratum corneum without producing local or systematic side effects
  - Produce effective anesthesia within minutes when applied to intact skin
  - Has prolonged duration of action
  - Easy to use
- The molecular structure of local anesthetics consists of three components [8]:
  - Tertiary amine
  - Aromatic ring
    - It is lipophilic
    - The lipid solubility allows diffusion across the lipophilic nerve cell membrane
    - Affects the intrinsic potency of the anesthetic
  - Intermediate ester or amide linkage:
    - Amide anesthetics:
      - For example: lidocaine and prilocaine
      - Allergic contact reactions are rare [9]
      - Metabolized in the liver via the microsomal enzymes

- Ester group [9, 10]:
  - For example: procaine, tetracaine, and benzocaine
  - Allergic contact reactions are common
  - Contraindicated in patients with allergies to hair dyes, PABA, and sulfonamides
  - Metabolized by plasma cholinesterase and other nonspecific esterases

- Topical anesthetics available on the market typically contain lidocaine
  - Products containing lidocaine may be found as a cream, gel, liquid or patch
  - Lidocaine is classified as pregnancy category B
  - Epinephrine may be added to induce vasoconstriction and consequently:
    - Increase the duration of the analgesia and
    - Slow the rate of systemic absorption of lidocaine [6, 11]
- The most widely used lidocaine preparations are EMLA (Astra Pharmaceuticals, Westborough, MA) and LMX (Ferndale Laboratories, Ferndale, MI) [11].
- Benzocaine is also used as a topical anesthetic
  - It is found in many over-the-counter sunburn products, oral ulcer ointments and eardrops.
  - Lidocaine is more potent than benzocaine and for that reason it is more often used in cutaneous procedures.
- The most common laser procedure for which topical agents are used is laser-assisted hair removal and fractional lasers [10].

Application of Topical Anesthetic

First wash the area to be treated:

- With a mild cleanser and water
  - To remove contaminants that could decrease the absorption and/or efficacy of the anesthetic agent, such as makeup and dirt

- Avoid benzoyl peroxide products
  - They may reduce efficacy of topical anesthetic products by decreasing their absorption [12]

To apply the cream:

- Use a gloved finger or a tongue depressor
- Apply a uniform layer of the product: approximately 1/8″ thick [10]
- If the product is applied with a bare finger (not recommended), wash the finger right after the application

Application of topical anesthetic can be performed:

- In the doctor's office or
- Patients can apply it at home, before they arrive at the office
  - They must receive adequate instructions on its safe application (described above) since inadequate application can cause adverse events [13–19].

Topical Application Time

- Topical anesthetic is left on skin for at least 30 min, depending upon the choice of product
- Usually, the agent is left on skin for 30–60 min [10]
- Guardiano and Norwood showed that a 30-min application of EMLA and LMX-5 were effective in reducing pain in Nd:YAG 1,064 nm laser hair removal. Neither anesthetic was used under occlusion [2].
- For procedures that have the target in deeper dermal depths, such as ablative skin resurfacing treatments, lidocaine products should be left on skin for at least 60 min [10].
- Usually the longer the agent is left in the area increases its absorption and enhances the anesthetic effect. However, the increased time on the skin also augments the risk of complications
  - Sherling et al recommended that in order to prevent complications topical lidocaine application time should not surpass 1 h [20].

- If desired, a quicker onset of analgesia may occur by occluding with plastic wrap, massaging the cream into the skin, or using iontophoresis [10, 21].

Removal of Topical Anesthetic

- Immediately preceding the treatment:
  - Remove topical anesthetic with dry gauze
  - Clean the skin by wiping it with a water-moistened gauze
- Alcohol-containing topical anesthetics:
  - Have fire potential
  - Remove any residual cream before laser procedures [22]

Precaution

- Although topic anesthetics are usually safe, complications can occur, such as: allergic reactions, cardiotoxicity, central nervous system toxicity, even death [13–19]. Patients suffering from anesthetic toxicity experience first tinnitus, lightheadedness, circumoral numbness, diplopia, and metallic taste in the mouth
- Whenever there are no guidelines for optimal use and safety of all topical products, reading the package inserts of each product seems reasonable
- Physicians must be aware of the factors that govern undesirable systemic absorption [10]:
  - Size and location of the area to be treated
  - Age of the patient
  - Weight of the patient
  - The amount (in grams) of anesthetic to be used
- A large number of pharmaceutically compounded anesthetics, not approved by the FDA, are available on the market. The issues with said products are:

  - Some of them use high concentrations of active anesthetics (higher than the products approved by the FDA)
  - Others do not disclose the strength of active anesthetics
  - Others mix various active anesthetics
  - Have variability in product quality
- The majority of complications reported with the use of topical anesthetics involves:
  - Use of non-approved FDA products
  - Use of doses higher than recommended
  - Application in a larger area than recommended
  - Use in infants
- Consequently, in order to minimize the potential risks of anesthetic-induced toxicity, physicians should [20]:
  - Read the product package inserts
  - Use the lowest possible dosage capable of producing anesthesia
  - Use the anesthesia on an area that does not surpass 300–400 cm^2
  - Evaluate the patient periodically to monitor for any complication to the anesthesia
  - Topical anesthetic application time should not surpass 1 h
    - Remove the product completely before treatment
    - Use products approved by the FDA (Table 4.2)

FDA Approved Topical Anesthetics

Table 4.2 FDA approved topical anesthetics

EMLA cream®
LMX®
Pliagis Cream® (S-Caine Peel)
Synera® (S-Caine Patch)

EMLA

- EMLA (Astra Pharmaceuticals, Westborough, MA) is the most commonly used topical anesthetics for anesthetizing intact skin [11].
- Released in the US in 1993, EMLA is approved by the FDA for use only on normal intact skin [5] and represents the first major breakthrough for dermal anesthesia on intact skin [6].
- It is a eutectic mixture of local anesthetics (EMLA). Most pure anesthetic agents exist as solids. Eutectic mixtures are liquids and melt at lower temperatures than any of their components, permitting higher concentrations of anesthetics.
- It is a composition of two local anesthetics:
  - 25 mg per mL of lidocaine (2.5 %) and 25 mg per mL of prilocaine (2.5 %), in an oil-in-water emulsion
  - The emulsifiers allow for an increase in the concentration of lidocaine and prilocaine in the oil droplet (80 %) while keeping the concentration of both low (5 %) in the mixture, avoiding systemic toxicity [5]
- The onset of anesthesia depends on:
  - Contact time with EMLA
  - Anatomic location
    - On face and thighs the onset is less than 25 min [23]
    - For procedures on mucous membranes involving oral and genitalia, the onset is in 5–15 min without occlusion [24]
    - EMLA is ineffective on thickened stratum corneum on glabrous skin like palms and soles. Consequently, it is not recommended for procedures in these areas [5]
- The depth of anesthesia depends on:
  - Duration of application of EMLA:
    - A study applied EMLA on the dorsal side of the forearms and showed that the anesthetic effect reached a maximal depth of 3 mm after a 60-min application, and 5 mm after a 120-min application [25]

- The duration of analgesia:
  - Analgesia continues and may even increase for 30–60 min after the cream is removed [25, 26]
- Adverse effects of EMLA are typically transient and localized. The most common adverse effects are:
  - Edema and redness or
  - Blanching of the skin at the application site
    - It occurs due to the vasoconstrictive effect of the prilocaine [10]
    - It is maximal at 90 min after application
    - It is followed by a rebound vasodilation between 2 and 3 h after application [27]
    - Although blanching effect may be problematic during treatment of vascular lesions, Ashinoff and Geronemus showed that a 60-min EMLA application was safe and effective in the treatment of port-wine stains with the pulsed-dye laser [28]
- The most serious complication is methemoglobinemia
  - It is a rare complication of prilocaine and other local anesthetics [10]
  - It involves the oxidation of iron from the ferrous to the ferric state in hemoglobin. Methemoglobin has a reduced oxygen binding capacity, which affects the transport of oxygen
  - The signs of methemoglobinemia vary according to the level of methemoglobin [10, 14, 16]:
    - Methemoglobin levels of 15–30 %: cyanosis
    - Methemoglobin levels of 30–50 %: headache, dyspnea, and tachycardia
    - Methemoglobin levels greater than 50 %: lethargy and coma
  - There have been reports of significant methemoglobinemia (20–30 %) in infants and children following applications of EMLA. These cases involved the use of

larger doses than recommended of application, or infants under the age of 3 months who did not have fully mature enzyme systems, or infants receiving concomitantly methemoglobin-inducing agents [14].
  - EMLA cream therefore should not be applied in patients with congenital or idiopathic methemoglobinemia. (EMLA, AstraZeneca insert)
  - EMLA should not be applied in patients under 12 months of age who are concomitantly receiving a medication known to exacerbate methemoglobinemia, such as phenazopyridine, sulfonamides, phenobarbital dapsone, acetaminophen, nitrates, and nitrites (EMLA, AstraZeneca insert)
  - Patients with glucose-6-phosphate dehydrogenase deficiency or hemoglobinopathies may also be at risk of methemoglobinemia [4]

- Care must be taken when using EMLA in the periocular region
  - One strategy to permit a drug to penetrate the stratum corneum is alkalinizating the pH of the product.
  - EMLA cream achieves a pH of 9 by having sodium hydroxide in its composition
  - The side effect of this alkalinity is that it can also cause chemical eye injury in the form of corneal abrasions and ulcerations [17–19]

LMX-4 and LMX-5

- Other commercially available topical anesthetics approved by the FDA include LMX-4 and LMX-5 (Ferndale Laboratories, Ferndale, MI)
- LMX-4 was previously called ELA-MAX, and contains 4 % lidocaine
- LMX-5 contains 5 % lidocaine, is marketed for anorectal use, but it is often used as a skin anesthetic
- Both are creams and use liposomes as drug carriers

- Liposomes have several lipid bilayers which:
  - Resemble the lipid bilayers of the cell membrane, facilitating dermal penetration of anesthetic [6]
  - One might believe that by facilitating dermal penetration, the onset of the anesthetic effect is faster
    - One study showed that a 30-min application of LMX (with occlusion) is as effective as a 60-min application of EMLA (with occlusion) for achieving topical analgesia [29]
    - Another study demonstrated that LMX (without occlusion) produced the same topical anesthesia as EMLA (with occlusion) in a shorter period of time [30]
    - However, Guardiano and Norwood demonstrated there was no statistically significant difference in discomfort reduction between EMLA and LMX-5 after a 30-min unoccluded application time [2]
  - Also, liposomes protect the drug from metabolic degradation
- LMX does not contain prilocaine and therefore there is no risk of methemoglobinemia associated with LMX [2]

Pliagis Cream

- Pliaglis® (Galderma Laboratories, Fort Worth, TX) is a eutectic mixture of local anesthetics developed under the name of S-Caine Peel and is approved by the FDA for use only on intact skin in adults (18–65 years old)
- It is the first and only FDA-approved topical anesthetic that combines the highest concentrations of lidocaine (7 %) plus tetracaine (7 %)
- It is applied as a cream, dries on exposure to air, and forms a flexible membrane, which can be easily peeled off
- It was discontinued in 2008 eventually because of an inability to obtain consistent product viscosity [10]
- In October 2012, the FDA approved the manufacturing site change for Pliaglis [31]. Galderma relaunched Pliagis in the USA in March 2013.

- Since Pliagis has an ester anesthetic in its formulation (tetracaine):
  - Allergic contact reactions may be more common than other topical anesthetics without an ester group [9, 10]
  - It is contraindicated in patients with allergies to hair dyes, PABA, and sulfonamides [9, 10]
- Methemoglobinemia has been associated with use of tetracaine
- Onset of action:
  - As early as 20–30 min [32]
  - Administration for 60 min prior to laser-assisted tattoo removal and leg vein ablation have been proven to be effective in significantly reducing pain [7, 32].

Synera

- Marked as Synera (Zars, Inc, Salt Lake City, UT), the S-Caine Patch is a topical patch that combines a small amount of topical anesthetic (lidocaine 70 mg and tetracaine 70 mg) and heat, using proprietary "Controlled Heat Assisted Drug Delivery" technology
- Synera is FDA cleared for local dermal analgesia for superficial venous access and superficial dermatological procedures, such as excision, electrodessication and shave biopsy of skin lesions

When Other Types of Anesthesia May Be Necessary for Laser Treatments

Dermatologic Surgery Procedures

- Nowadays, local anesthetic injection (with or without intravenous sedation) is mainly used for dermatologic surgery procedures using a laser device, such as blepharoplasty [33] or rhinophyma treated with the CO_2 laser [34]

Skin Resurfacing Treatments

Ablative CO_2 or Er:YAG Laser Resurfacing

- Individual cosmetic units (periorbital, perioral) can be treated:
  - Only with topical anesthetic agents. For example: EMLA cream applied under occlusion for 90 min [35]
  - Or with topical anesthesia combined with local or regional injection anesthesia [36]
- Full face:
  - Topical anesthesia in combination with infiltrative (local or regional nerve blockade) or other types of systemic anesthesia is usually needed [35]

Nonablative Resurfacing Treatment

- Topical anesthesia is sufficient for pain control during nonablative resurfacing [10, 35]
- Patient comfort can also be amplified by the additional use of a cooling device applied to the skin.
- After the treatment, ice packs may be applied

Fractional Resurfacing

- Some authors consider that lower fluencies are tolerated well without any sort of anesthesia [36]
- Other authors use topical anesthesia before the procedure for:
  - 60 min [20]
  - At least 60 min or [10, 36, 37]
  - 90 min (EMLA cream under occlusion) [35]
- Air cooling in combination with topical anesthesia has been shown to enhance tolerability of ablative and nonablative fractionated laser resurfacing [38, 39]

- A round table discussion among experienced physicians and a review of recent literature findings suggested that if patients are still uncomfortable with topical anesthesia, it is better to associate regional nerve blocks instead of raising the dose of topical anesthesia and have complications due to the use of a large amount of topical product. Some doctors of the round table also give ibuprofen 800 mg orally 45 min before the procedure [20]

Pediatric Population

Grevelink et al showed that the use of general anesthesia to treat pediatric port wine stain with laser [3]:

- Did not increase risk of procedural complications
- On the contrary, treatments were faster and able to cover a larger area because patients did not move
- Consequently, the authors suggested the use of general anesthesia in younger children with larger lesions, and topical or local anesthesia in children with smaller lesions
- Although this study was done in 1997, recent literature agrees with that suggestion [4]

Pediatric population with increased risk of methemoglobinemia with the use of EMLA should have alternative forms of anesthesia, such as injectable lidocaine for small areas of the face and neck, or general anesthesia for larger areas [40].

Conclusions

Topical anesthetics available on the market and approved by the FDA have been proven to be safe and effective for the majority of the laser procedures, even for infants and young kids where extra caution is required. More effective newer anesthetics are being introduced constantly.

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Chapter 5
Psychological Considerations Prior to Laser Procedures

Katlein Franca, Jennifer A. Ledon, Jessica A. Savas, and Keyvan Nouri

Abstract The use of lasers in dermatology had increased significantly in the past decade. The psychological estate of the patients, the concerns and possible side effects that laser therapy may cause should be carefully learned, presented and discussed previously. This chapter will present some concepts of basic psychology, advice about patients expectations, and tips for the establishment of a good doctor-patient relationship.

Keywords Psychology • Lasers • Psychodermatology • Dermatologic procedures • Patients expectations

K. Franca, MD, MS (✉) • J.A. Ledon, MD
J.A. Savas, MD • K. Nouri, MD
Department of Dermatology and Cutaneous Surgery,
University of Miami—Miller School of Medicine,
1475 NW 12th Avenue, 2nd Floor, Miami, FL 33136, USA
e-mail: k.franca@med.miami.edu; jledon1@med.miami.edu;
jsavas@med.miami.edu; knouri@med.miami.edu,
knourimd@gmail.com

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Introduction

The use of lasers in dermatology had increased significantly in the past decade. More and more, new devices become available in the market and several dermatological diseases are now possible to be effectively treated [1]. Because it is a relatively new therapy, misconceptions and false expectations are common and physicians should be aware and prepared to deal with these facts [2]. The psychological estate of the patients, the concerns and possible side effects that laser therapy may cause should be carefully learned, presented and discussed previously.

This chapter will present some concepts of basic psychology, advices about patients' expectations and tips for the establishment of a good doctor-patient relationship.

Knowing the Patient: Basic Psychology to Physicians

Psychology refers to the scientific study of the human mind and its functions, especially those affecting behavior in a given context [3]. It relies on scientific methods to investigate questions and make conclusions. Several techniques are used to understand the humans' behavior and mind and this includes questionnaires [4], naturalistic observation [5], experiments [6], case studies [7], etc. The study of psychological and behavioral process related to health, healthcare and illness is the goal of the Health Psychology, a branch of the science of psychology [8].

The physician that will perform a laser procedure must understand the patients' expectations, previous experiences and recognize any psychological problem that may interfere with the procedure [9]. Patient's beliefs and behaviors must be learned during the medical interview and all the questions and concerns should be clarified before the procedure (Table 5.1).

Table 5.1 Medical interview and exam prior to laser procedures: tools for success

Detailed medical interview	Systematic physical exam
Systematic interview	Make the patient comfortable
Adequate language	Perform a detailed exam
Time necessary	Attempt to establish:
Consider:	Patients skin type, presence of discolorations, deformities, asymmetries
Patients previous medical and life experiences, comorbidities, expectations, concerns and doubts about the procedure	

Patients Expectations

Patients that will be submitted to a laser procedure certainly present expectations [10]. Laser technology is popularly known to be effective, precise and low time recovering. In this information era, patients learn from different sources, sometimes with doubtful validity [11]. Lasers in dermatology can be used to treat medical conditions, such as skin cancers, vascular lesions, onychomycosis, wound healing, acne and others. Or can be used for aesthetic purposes like for example to remove a tattoo, hair removal or skin rejuvenation [12]. For this group of patients, specially, there is a higher expectation regarding the results and extra attention should be provided in order to clarify the false expectations and possible side effects of the therapy.

Usually patients learn about the procedure from family members, friends and other sources such as television, magazines and Internet. Patients' previous experiences with other and similar procedures will also determine the future expectations [9]. In this scenario is important to understand the patient's individual and cultural beliefs and consider how much information they will assimilate. The physician must be trained to provide the appropriate information about the

realistic results of the procedure and clarify the doubts and concerns that the patient may have and explain the patient why his or her expectations are unrealistic [13].

Common Psychological/Psychiatric Disorders

A psychiatric disorder is a psychological pattern or anomaly behavior not considered part of normal personal development or culture [14]. It usually causes distress or disability and can be associated with particular brain functions or regions of the nervous system [15]. These mental disorders are defined by a combination of four factors: how the patient acts, feels, thinks or perceives [14]. Mental disorders are common in entire world and affect people of all ages, cultures, educational and income levels. A study showed that an estimate of 26.2 % of Americans ages 18 and older suffers from a mental disorder in a given year [16]. Physicians in all medical specialties, including the one's that perform laser procedures will most likely at some point, have patients presenting mental disorders and other psychological problems that may interfere with the comprehension and expectations of the procedure [17].

There are currently, two established systems to classifying mental disorders:

- The International Classification of Diseases, produced by the World Health Organization: http://www.who.int/classifications/icd/en/ [18]
- The Diagnostic and Statistical Manual of Mental Disorders, fourth edition and fourth edition text revision (DSM IV-TR) created by the American Psychiatry Association: Available at http://www.psychiatry.org/practice/dsm [19]

  The Diagnostic and Statistical Manual of Mental Disorders fifth edition is due for publication in May 2013 and will supersede the DSM-IV, which was last revised in 2000.

The most common mental disorders, according to the DSM-IV and DSM-IV-TR are listed in Tables 5.2 and 5.3.

Table 5.2 Depressive disorders and bipolar disorders

Depressive disorders	Bipolar disorders
Dysthymic disorder	Bipolar disorders
Major depressive disorder	Cyclothymic disorder
Depressive disorder NOS[a]	Mood disorder due to (several medical conditions)
	Mood disorder NOS[a]

[a]Not otherwise specified

Anxiety Disorders

It is a medical condition characterized by excessive and persistent worry. Anxiety is considered a natural response in humans, but it can become a pathologic disorder when it is excessive and interferes in the quality of life, causes physical and affective symptoms and changes the cognition and social behavior [20, 21]. It includes:

- Generalized anxiety disorder
- Panic disorder
- Agoraphobia without history of panic disorder
- Specific phobia
- Social phobia
- Obsessive-compulsive disorder
- Posttraumatic stress disorder
- Acute stress disorder
- Anxiety disorder due to a general medical condition
- Anxiety disorder NOS[1]

Mood Disorders

Mood disorders are a group of mental disorders characterized by depression, sometimes alternate with periods of

[1]Not otherwise specified.

elevated mood. This classification includes depressive disorders and bipolar disorders [22].

Psychotic Disorders

Several mental disorders cause abnormal thinking and perceptions [23]. Patients with psychotic disorders may present delusions and hallucinations. Delusions can be defined as beliefs held with strong conviction despite superior evidence to the contrary [24, 25]. While hallucinations are false or distorted, sensory experiences appear to be real perceptions. The most common type of psychotic disorder is schizophrenia and its variables [25].

- Schizophrenia
- Schizophreniform disorder
- Schizoaffective disorder
- Delusional disorder
- Brief psychotic disorder
- Shared psychotic disorder
- Psychotic disorder due to… [other general medical conditions]
- Psychotic disorder NOS[2]

Impulse Control and Substance Related Disorders

Impulse control disorders refer to the failure to resist an impulsive act or behavior that may be harmful to self or others. They are thought to have both environmental and neurological causes and can be exacerbated by stressful situations [26]. While the substance related disorders are disorders of dependence, abuse, intoxication and substance withdrawal caused by illegal or legal substances [27].

[2]See footnote 1.

Table 5.3 Impulse control and substance related disorders

Impulse control disorders	Substance related disorders
Intermittent explosive disorder	Substance dependence:
Kleptomania	Alcohol, opioids, cocaine, inhalant, polysubstance, etc.
Pathological gambling	
Pyromania	
Trichotillomania	
Impulse-control disorder NOS[a]	

[a]Not otherwise specified

Eating Disorders

This group of mental illness refers to behaviors, attitudes and emotions involving food and weight [28].

- Anorexia nervosa
- Bulimia nervosa
- Eating disorder NOS[3]

Doctor Patient Relationship

Doctor-patient relationship is the keystone of the medical practice and healthcare. This relationship should be based on trust, respect and ethics and should follow the bioethical principals of autonomy, justice, beneficence and non-maleficence [29]. Good communication skills can lead doctors to experience fewer difficult consultations [30].

Tips for a good doctor patient relationship:

- Show empathy and compassion during the interview process

[3]See footnote 1.

- Keep eye contact and don't cross the arms, be friendly and respectful
- Let the patient talk and feel that someone is listening carefully.
- Note the verbal and non-verbal signs showed by patients
- Touch the patient skin while examining
- Share with the patient the decision making process

Difficult Patients

Health care providers will often have patients with serious quirks. These patients may be more difficult to deal with and can compromise the quality of the treatment [31]. Below you will find a list of characteristics of patients that may be more difficult and will require more attention and work from the doctors.

- Patients that don't follow doctor's instructions
- Takes poor care of themselves
- Patients impolite, mean and belligerent
- Angry patients
- Defensive Patients
- Complainant Patients
- Patients with previous bad experiences
- Somatizing patients
- Patients with mental disorders

How to Manage Difficult Patients

Managing difficult patients can be challenging for many doctors. It can cause frustration, stress and may lead to professional burnout [32]. It is important to remind that physicians are expected and required to act in their patient's interests, even when those interests may conflict with their own [33].

Some advices are given in this section.

- Don't get drawn into a conflict
- Always apologize for any inconvenience caused

- Modulate your response when the patients says something inappropriate
- Always offer help to solve the problem in order to continue discussing the conflicting situation
- Listen and consider all the patients complaints before any pre judgment
- Try your best to satisfy the patients requirements, if they are not realistic explain to the patient carefully why
- Always thank the patient

Conclusions

Psychological aspects of patients have become a topic of research and interest of healthcare practitioners in general. With those that perform laser procedures is not different and understanding the psychology of patients and the establishment of a good doctor-patient relationship is certainly of the keys to success. This chapter presented some psychology concepts, a comprehensive overview of the most prevalent mental disorders and important tips for the doctor-patient relationship.

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Chapter 6
Vascular Lasers

Vishal Madan

Abstract Lasers and flashlamps are the mainstay of treatment of vascular malformations of the skin. A thorough understanding of the principles of selective photothermolysis will allow the laser practitioner to use the right device with appropriate wavelength and pulse duration at right fluence to effectively and safely treat the vascular lesion in their patients. In this chapter we will focus on use of such lasers in the treatment of vascular indications.

Keywords Alexandrite laser • Flash lamps • Intense pulsed light • KTP laser • Pulsed dye lasers • Nd:YAG laser • Vascular lasers

Vascular Lasers

- Several laser and light systems are available for the treatment of vascular lesions. Those in use currently include:
  - Pulsed dye laser (PDL) 585, 595 nm
  - Potassium-titanyl-phosphate (KTP) laser 532 nm

V. Madan, MBBS (Hons), MD, FRCP
Department of Dermatology, Salford Royal NHS Foundation Trust, Stott Lane, Salford, Manchester, Lancashire M6 8HD, England, UK
e-mail: vishal.madan@srft.nhs.uk

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- Long-pulsed Alexandrite laser 755 nm
- Long-pulsed neodymium-doped:yttrium aluminum garnet (Nd:YAG) laser 1,064 nm
- Copper vapour laser 578 nm
- Intense Pulsed Light (IPL) Sources 515–1,200 nm
- Photodynamic therapy

The aim of laser treatment of vascular lesions is selective vessel destruction with minimal perivascular thermal injury. To achieve this, the operator must choose a device emitting appropriate wavelength that will reach the chromophore (e.g. oxyhemoglobin) and be selectively absorbed. The operator will choose pulse duration with the aim of confining the laser energy to the target. Limiting the fluence to the chromophore will allow destruction of the target without damage to perivascular tissues, thus limiting adverse effects. Cooling the epidermis allows the use of high fluence to achieve better lesional clearance and more comfortable and safer treatments.

Vascular Laser Indications

- Port wine stains
- Hemangiomas
- Facial telangiectasias and erythema
- Leg veins and telangiectasias
- Scars
- Verrucae
- Psoriasis and other inflammatory skin conditions, e.g. granuloma faciale
- Others
  - Spider nevi/angiomas
  - Angiofibromas
  - Cherry angiomas
  - Venous lakes
  - Angiokeratomas
  - Striae rubra
  - Poikiloderma of Civatte

Port Wine Stains (PWS)

- The yellow beam of pulsed-dye laser (PDL) at 577–595 nm allows selective targeting of this capillary malformation.
- Most patients achieve improvement, but few achieve clearance of their PWS.
- Early treatment may be beneficial.
- Red or pink PWS typically respond better than purple lesions.
- Site of PWS may affect degree of clearance attained.
- PWS on the face and neck respond better than those on the leg and hand.
- Proximal PWS respond better than distal PWS.
- Forehead and lateral face PWS respond better than those over the middle of the face [1].
- Compared with conventional flashlamp PDL, new generation long-pulsed, tunable PDL at 595 nm, with 1.5 ms pulse duration, high fluence and with surface cooling achieves better clearance of PWS [2].
- Despite this, most patients never achieve complete clearance of PWS.
- Some PWS may recur after initial improvement.
- Methods to achieve improvement in such resistant PWS are detailed in Chap. 28
- KTP (frequency-doubled Nd:YAG) at 532 nm, long-pulsed Alexandrite laser at 755 nm and long-pulsed Nd:YAG laser at 1,064 nm have been used to treat resistant PWS. Risk of epidermal injury resulting in scarring or dyspigmentation may be higher with these lasers than second generation long-pulsed PDL.
- Long-pulsed Nd:YAG laser is appropriate for bulky PWS or PWS varicosities as these do not usually respond to conventional PDL treatments.
- Role of intense pulsed light (IPL) in the treatment of resistant PWS is becoming established [3].

Capillary Hemangiomas (CH)

- Proliferative CH especially complicated lesions on the face, near the eye or those with the potential of causing respiratory compromise are best treated with oral propranol [4].
- Role of PDL in the treatment of uncomplicated CH is unclear and controversial [5, 6].
- Ulcerated CM respond to PDL and this can improve the pain associated with ulceration.

Facial Telangiectasia and Erythema

- PDL and KTP are the most frequently used lasers for facial telangiectasia.
- Purpura induced by PDL treatments lasts for 7–10 days.
- Non purpuric treatments can be achieved with long-pulsed PDL, at the expense of reduced efficacy.
- KTP laser is very effective in the treatment of facial telangiectasias but carries a higher risk of scarring than the PDL.
- Telangiectasia associated with systemic sclerosis, which can be challenging to treat with the PDL, may respond to IPL [7, 8].
- Nasal ala telangiectasia can be particularly difficult to treat. Using an elliptical spot on the PDL at high fluence with 40 ms pulses may improve these telangiectasia [9].
- Diffuse facial erythema of rosacea can be treated using a larger spot size with PDL, long-pulsed Nd:YAD or IPL [10, 11].

Leg Veins and Telangiectasia

- Sclerotherapy remains the mainstay of treatment for leg telangiectasias.
- Veins too small to be injected may be treated with lasers.
- KTP, Alexandrite, Diode and long-pulsed PDL and Nd:YAG lasers can all be used to treat leg vein telangiectasia up to 1 mm in size.

- Based on the depth of penetration, KTP will only treat the most superficial telangiectasias.
- Long-pulsed Nd:YAG penetrates deepest but has a relatively poor hemoglobin absorption.

Scars and Keloids

- PDL treatments can improve clinical appearance, surface texture, skin pliability and pruritus of hypertrophic scars.
- Scars less than 1 year old respond better than scars of longer duration.
- Laser treatments can be combined with other modalities such as intralesional corticosteroid injections, steroid impregnated tapes and 5-fluorouracil.
- Treating keloids with lasers is challenging.
- Some patients with keloids may benefit from sequential intralesional corticosteroids and PDL treatments [12].

Verrucae

- There is little evidence that laser treatment of verrucae is more successful than conventional treatments. Thus, lasers are generally reserved for patients with verrucae that have been refractory to other treatment [13].
- High fluence PDL may lead to resolution of verrucae in more than 50 % patients [14].
- The mechanism of PDL in the treatment of verrucae is selective obliteration of vasculature within the verrucae.
- Debridement is important prior to laser treatment to enhance the penetration of laser beam.

Psoriasis and Other Inflammatory Disorders

- Besides excimer laser at 308 nm, the PDL is also shown to be effective in the treatment of psoriasis [15].
- Unlike the excimer laser, which targets cell proliferation, PDL targets the enlarged dermal papillaries in psoriatic plaques.

- The need for repeated treatments and impracticality of treating large psoriatic plaques makes this modality less appealing in routine management of psoriasis.
- Granuloma faciale – some patients with this inflammatory skin condition will respond to PDL [16].
- Similarly, response to PDL in other inflammatory skin conditions such as acne vulgaris, lupus erythematosus, sarcoidosis, eczematous lesions, papulopustular rosacea, lichen sclerosis, granuloma annulare, Jessner lymphocytic infiltration of the skin, and reticular erythematous mucinosis is variable [17]. There are reports of success of PDL in lupus telangiectasia, but in the author's experience they are more resistant to treatment than idiopathic or rosacea telangiectasia.

Other Indications

- **Spider nevi/angiomas** – These are easy to treat vascular lesions which clear in one to two sessions of PDL or KTP laser may be very effective.
- **Angiofibromas** – the macular lesions without significant fibrous component respond well to PDL. Papular lesions respond better to ablative lasers.
- **Cherry angiomas** – both PDL and long-pulsed Nd:YAG laser can lead to complete resolution of these lesions.
- **Venous lakes** – if thick, these may not respond to the PDL and long-pulsed Nd:YAG laser may be considered.
- **Angiokeratomas** – like cherry angiomas, these also respond satisfactorily to the PDL or long-pulsed Nd:YAG laser.
- **Striae rubra** – the PDL may bring about a modest improvement in the erythema associated with these red stretch marks. These, and their white counterparts (striae alba), remain challenging to treat and new non-ablative technologies are being explored for these indications [18, 19].
- **Poikiloderma of Civatte** – manifesting as pigmentation and erythema on the lateral neck has been treated with the PDL with varying effects. Using high fluence on the PDL can result in late depigmentation which may be as distressing

as the original condition [20]. Some authors have reported very high efficacy and low incidence of side effects after treating poikiloderma of Civatte with IPL [21].

Contraindications

- Active infection e.g. Herpes simplex
- Recent tan
- Pregnancy
- Dysmorphophobia
- Isotretinoin treatment
- Cryoglobulinemia
- Cold urticaria
- Skin fragility disorders
- Unrealistic expectations
- Antiplatelet and anticoagulant medications (risk of prolonged purpura)

Complications

- Blistering in the immediate post-operative period
- Edema
- Crusting
- Post-inflammatory hyperpigmentation
- Post-inflammatory hypopigmentation
- Scarring

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Chapter 7
Laser Treatment for Spider Veins

Leyre A. Falto-Aizpurua, Harleen Arora, and Robert A. Weiss

Abstract Increased venous pressure causes dilation of normal leg veins creating varicose or spider veins. This can be a consequence of loss of smooth muscle tone causing valvular insufficiency or more rarely deep vein thrombosis. The treatment of choice for eliminating spider veins of the leg is sclerotherapy, although the use of laser technology as a safe and relatively painless alternative has been long anticipated. We will discuss in this chapter some lasers and light therapies that have been used, including the argon, copper bromide, Nd:YAG, diode, long-pulse infrared Alexandrite and pulsed dye lasers, as well as the intense pulsed light. These are

L.A. Falto-Aizpurua, MD • H. Arora
Department of Dermatology and Cutaneous Surgery,
University of Miami—Miller School of Medicine,
1475 NW 12th Avenue, Suite 2175, Miami, FL 33136, USA
e-mail: lafalto@gmail.com; haroramed@gmail.com

R.A. Weiss, MD, FAAD, FACPh (✉)
Department of Dermatology, University of Maryland,
54 Scott Adam Road, Hunt Valley (Baltimore), MD 21030, USA

American Society for Laser Medicine and Surgery,
Laser Skin and Vein Institute, 54 Scott Adam Road,
Hunt Valley (Baltimore), MD 21030, USA
e-mail: rweiss@mdlsv.com

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indicated for vessels of different sizes and depths and have different clearance rates. Unfortunately, laser therapy has not been found to be as effective, but it can be used as a supplementary form of therapy. Development of new technologies or the significant improvement of present technologies, as well as adjuvant therapies should be further explored.

Keywords Laser • Leg Veins • Spider Veins • Varicose Veins • Argon • Pdl • Copper Bromide • Ipl • Nd:Yag • Diode • Long-pulse Alexandrite • Laser Therapy • Sclerotherapy

Introduction

- Dilation of veins is due to increased venous pressure primarily which can be related to apoptosis of vein smooth muscle cells and loss of venous tone resulting in the creation of varicose veins [1]. Formation of varicose veins can stem from other causes such as valvular insufficiency, deep vein thrombosis, and congenital venous malformations [2].
- Sclerotherapy is the treatment of choice for eliminating varicose and spider veins of the leg.
- Laser technology as a safe and relatively painless alternative has been long anticipated [3]. Unfortunately, it has not been found to be as effective, but it can be used as a supplementary form of therapy.
- Recent research and advances in technology have allowed lasers and intense pulsed light (IPL) to be used to treat telangiectatic vessels of the leg with greater effectiveness and fewer adverse effects [4, 5]. These advances include:
  - Epidermal protection using methods such as dynamic cooling (spray) instead of contact cooling [6].
  - Deeper penetration and decreased interaction with melanin due to the use of longer wavelengths.
  - More thorough heating of large vessels by use of longer pulse durations.
  - Increased spot sizes to allow the target to be accessed by a greater number of photons.

- Lasers for vascular indications should be classified based on their respective light colors (green, yellow, red, or infrared). Physicians should determine the appropriate laser to use through analysis of the location, size, and oxygenation of the target vessel.

Background

- The basis of laser therapy for vascular presentations is "selective photothermolysis," a concept which requires the selective destruction of a target with minimal damage to the surrounding structures. For instance, selective photothermolysis has been widely studied through the use of pulsed dye lasers for treating port wine stains [7].
- First explained by Anderson and Parrish in 1981, the theory of selective photothermolysis necessitates the selection of a chromophore, which is directed with a light at a wavelength that is maximally absorbed by that target to induce selective thermal destruction. The pulse duration of the light must be less than the target's thermal relaxation time [8].
- Laser involves the conversion of light to heat energy, which produces destruction and leads to denaturing of proteins. The main target of the heat is collagen in the vein walls, but proteins in the blood and surrounding muscular layers can also be denatured.
- The targeted chromophore in superficial red vessels however is oxyhemoglobin, which has several absorption peaks. Its primary absorption peaks fall at 418, 542, and 577 nm, which are in the blue/green/yellow section of the visible light spectrum, although there is also a broad absorption band from 800–1,100 nm. The absorption peak at 418 nm cannot be utilized because it is at a wavelength that melanin also strongly absorbs. Wavelengths near 542 nm still too heavily absorbed by melanin and would also likely cause epidermal damage, needing some sort of cooling mechanism. The higher wavelength absorption band is useful for deeper vessels, usually over 3 mm into the dermis.

- Absorption characteristics depend on the depth and size of the target vessel [9]. Deeper penetration and more uniform delivery of energy are reached with the usage of longer wavelengths. Therefore, leg venulectases and telangiectasias, which are over 1 mm deep require longer wavelengths. In terms of size, vessels with large diameters will need more time for heat to be evenly diffused throughout lumen, requiring longer pulse durations [10].
- Telangiectasias of the leg are difficult to treat with lasers because they are present at deeper depths of subcutaneous tissue [11]. Leg veins are generally treated with a wavelength between 600 and 1,064 nm because of their depth [12, 13]. Pulse duration is required enough to provide an even energy delivery and thermocoagulation throughout the entire diameter of the vessel.
- Optimal wavelength absorption also varies with respect to the color of the telangiectasia. Leg veins tend to have a reduced oxygenation state, leading to a violaceous rather than a red color. This adds an additional complication because blue telangiectasias, with an oxygen concentration of about 69 %, may have a slightly different optimal wavelength absorption than red telangiectasias, which have an oxygen concentration of 76 % [14].

Indications

- Although sclerotherapy is the preferred treatment for small telangiectasia, several clinical states call for IPL or lasers as a primary treatment.
- Lasers may be used as primary treatment in the following instances:
  - arteriovenous malformations
  - vessels <1–2 mm in diameter resistant to sclerotherapy and telangiectatic matting which can occur post-sclerotherapy
  - non-cannulizable microtelangiectasias
  - telangiectasias arising from arteriovenous anastomosis or a terminal arteriole, which can be treated without considering underlying hydrostatic pressure [15]

- patients prone to post-procedural hyperpigmentation due to chemical irritation of vessel wall caused by sclerotherapy
- patients who are apprehensive about allergies to sclerosant, needle punctures, or the competence of novice practitioners
- areas such as the feet or ankles
- superficial vascular ectasias (deep purple venous lakes and cherry angiomas)

Contraindications

Absolute

- Active local infection.
- Photo-aggravated skin disease and medical conditions.

Relative

- If patient has psoriasis, unstable vitiligo, keloid, or is taking isotretinoin.
- High-pressure reticular veins: telangiectasias of the legs are often associated with reticular veins and their resulting high reverse pressure. IPL and lasers, with the exception 1,064 nm lasers, should not be used to treat reticular veins as they are incompletely treated.
- Patients with venous flow obstruction: these patients should not have their varicosities ablated because they work as bypass pathways allowing blood flow around the obstruction.

Procedural Technique

Preoperative and Operative Considerations

- Determine if laser, sclerotherapy, a combination of both or any other modality is adequate based on the type and size of leg veins that are to be treated, your expertise and the

patients expectations. Discuss estimated number of treatments and frequency of sessions needed to achieve maximal results.
- Choose appropriate laser parameters (wavelength, fluence, pulse duration, spot size).
- Always use protective glasses and laser safety measures.
- Minimal pressure should be used to avoid compressing targeted area.
- Epidermal cooling techniques including dynamic, contract or air cooling should be chosen for every device in order to protect the surrounding perivascular tissue and epidermis [16].
- For certain devices, particularly IPL, the delivery crystal is held 1–3 cm off the skin and applying a small layer of gel to the skin, visualization of the area to be treated is increased. Larger spot sizes and infrared wavelengths such as 1,064 nm leads to lateral spread of thermal energy, in which thermal coagulation is more easily visualized.
- Immediate visual end point is darkening of the treated vessel. Within the following 10 min, urtication and loss of the visual vessel margins should be observed.
- Specific lasers:
  - 1,064 nm lasers: (1) pulses should be spaced out laterally by at least 2 mm, (2) stacked pulsing should never be utilized since thermal dispersion takes 15–20 s.
  - IPL: a layer of gel and epidermal cooling should be used.
  - Visible light lasers such as PDL and 532 nm: up to three passes may be performed over the treated area.

Postoperative Considerations

- Follow up visits may be determined based on the device being used, but typically are at 1 month intervals.
- Patient should be aware of post-treatment instructions, as well as expected and possible side effects:
  - Pain may be experienced but usually does not require pain medications.

- Compression stockings and leg elevation might be recommended for edema depending on the treated area. If larger vessels, use compression stockings for 2 weeks [17].
- If larger vessels were treated, patients are recommended to walk 10–15 min right after procedure.
- Post-treatment hyperpigmentation is seen in up to 75 % [13]. The incidence increases with the size of the vessel treated.
- Patients are recommended to stay out of the sun.

Choosing the Right Laser

Argon Laser

- Ionized argon produces a beam in the blue and green visible light spectrum.
- The argon laser produces 488 and 511 nm wavelengths, which are absorbed by hemoglobin.
- A small but significant quantity is absorbed by epidermal melanin, preventing further penetration into skin, resulting in thermal injury.
- Due to its small spot size, poor specificity and adverse side effects is not recommended for the treatment of leg veins.

KTP Crystal Frequency Doubled Neodymium-Doped Yttrium Aluminum Garnet (Nd:YAG) Laser

- An Nd:YAG laser is directed through a potassium titanyl phosphate (KTP) crystal producing a beam in the green visible light spectrum.
- It produces a 532 nm wavelength and has a skin depth penetration of 0.75 mm [2, 18].
- It is effective for superficial (<1 mm depth) and small (<1 mm diameter) vessels because epidermal melanin interferes with laser absorption [18].
- Several studies have reported complete clearance but up to four treatment sessions might be needed to achieve maximal improvement [18–22].

- This laser can also be used in conjunction with sclerotherapy of the larger or "feeding" veins to optimize results and with an epidermal cooling system to reduce side effects [19, 21].
- Important side effects are moderate pain, immediate edema and erythema, and reversible hyper- or hypo- pigmentation due to a significant absorption by melanin [2, 21].

Pulsed Dye Laser (PDL)

- This laser uses various dyes at wavelengths at the longer oxygenated hemoglobin absorption peaks to overcome interference from overlying melanin.
- PDL technology has significantly evolved to overcome original limitations to treat leg veins, such as purpura that can lead to long-standing hyperpigmentation [2]. Improvements include longer pulse durations of 10–40 ms, optics which allow for treatment of 10 mm segments with a single pulse and laser pulse synchronized cooling.
- Current technology can deliver stacked pulses, permitting additive effects without excessive fluence per pulse, minimizing unwanted side effects and complications.
- Complete or moderate clearance has been achieved for vessels <1 mm in diameter [23–26].
- Integrated cooling systems improves efficacy of this technology [27].
- Common side effects are transient purpura, hyperpigmentation, edema and erythema [2, 28].

Copper Bromide Laser

- Copper bromide lasers produce a yellow beam at a wavelength of 578 nm [29].
- Some units treat small bright red superficial telangiectasias on the leg, especially when combined with epidermal cooling, which also reduces the risk of pigmentation changes.
- This laser never gained wide acceptance because of technical limitations; diode lasers in this wavelength may soon be available but generally has been replaced by PDL.

Long-Pulse Infrared Alexandrite Laser

- This laser emits light in the mid-infrared spectrum (755 nm) and penetrates 2–3 mm in depth into the skin.
- It can be used for deep violaceous vascular lesions because the absorbance peak of deoxygenated hemoglobin that is also 755 nm [2].
- The Alexandrite laser was proven to be the most effective therapy for 0.4–3.0 mm leg telangiectasias with up to a 63 % reduction after three treatment sessions but this result significantly improved when sclerotherapy was added to treatment [30].
- Another study determined the optimal pulse duration for patients with Skin Types I-III achieving 65 % clearance, 12 weeks after a single treatment for superficial leg veins [31].
- It has not gained widespread acceptance for treatment of leg telangiectasias <0.5 mm, due to pain and technical limitations [24].
- When treating small red telangiectasias, newer higher-fluence devices combined with dynamic spray cooling showed greater efficacy with fewer treatments [32].
- To prevent some of the side effects such as dyspigmentation disorders, this laser works best on Fitzpatrick's Skin Types I-III due to its high absorbance by melanin [33].

Diode Lasers

- These emit infrared light at different wavelengths including 800, 810, 900, 940 and 980 nm, which are absorbed by hemoglobin's tertiary peak and work for the treatment of leg telangectesias [18].
- Longer wavelengths penetrate the skin deeper, being able to treat larger telangectasias of the leg; it has limited use for small spider veins [18].
- Garden et al. demonstrated a mean of 60 % clearance after 2.2 treatments, using an 810 nm diode laser [34].
- Another study demonstrated over 75 % clearance after 4 weeks of treatment in 12 out of 26 patients using a 940 nm diode laser [35].

- When combining the 900 nm diode with bipolar radiofrequency, Trelles et al. demonstrated a vessel clearance rate greater than 75 % at 6 months in 50 % of the patients [36].
- In order to protect the epidermis and to diminish side effects, epidermal cooling is advisable, as is the avoidance of tanned legs given that there exists some absorption by melanin.

Nd:YAG Laser

- With a wavelength of 1,064 nm, this laser has deep penetration (5–6 mm) and is considered the laser of choice for leg vein treatment [37].
- Although the light absorption of hemoglobin at 1,064 nm is low, it is still approximately ten times as high as the light absorption of water, which is the major absorber in the dermis at this wavelength [38].
- When vessels reach a temperature of 70 °C, methemoglobin (Met-Hb) forms. Met-Hb absorption coefficient is roughly three times as high as that of oxyhemoglobin at 1,064 nm. At a high fluence, difference in temperature between the vessel and the dermis is similar for large and small vessels, but a larger vessel needs more time to cool compared to a smaller one. Therefore, effectiveness of leg vein coagulation increases with vessel size [38].
- The advantage of this laser over the alexandrite and diode lasers is that it allows for deeper penetration and decreased absorption interference by melanin [39].
- Because this laser already penetrates deeply, there is no reason for the beam diameter to exceed the vessel diameter by more than 0.5 mm. A spot size approximately 25 % larger than the maximum vessel size that is being treated is recommended [38].
- Long pulse duration with a low fluence is more effective for large vessels (0.1–1.6 mm) [40].
- Shorter pulse durations and higher fluences are more effective for small vessels (<0.5 mm) [41].

- A study of 20 patients with 1–3 mm reticular veins showed over a 75 % clearance in two thirds of the treated vessels with a single treatment [42].
- A common side effect is hyperpigmentation for treatment of greater than 1 mm diameter targets but this normally resolves with time, whereas hypopigmentation and scars are uncommon [37]. Longer pulse durations minimize purpura, edema, and hyperpigmentation [43].
- Given that this might be a painful procedure, cooling or topical anesthesia is essential.

High Intensity Pulsed Light (IPL)

- Produces non-coherent wavelengths of 515–1,200 nm but commonly 550–570 nm filters are used, emitting primarily yellow and red light with some infrared [18, 44].
- Each wavelength can be delivered at different intensities and filters can select for desired wavelength to be emitted [18].
- To treat vessels 0.6–1.5 mm in diameter, shorter wavelengths can be used while larger wavelengths should be used for larger vessels (3–5 mm) [18, 45].
- Efficacy has been proved for 0.1–3 mm diameter vessel and when combining wavelengths smaller vessels respond better to treatment, with a reported 90 % clearance rate in vessels 0.2–1 mm in diameter [46, 47].
- An advantage of the IPL is that it provides larger spot sizes and causes minimal purpura [46].
- Common side effects are erythema, edema, and a mild burning sensation. When higher fluences are used, they can result in a burning discomfort, purpura, dyspigmentation and scarring [18].
- Our experience is 30–40 % clearance with two to three treatments of the legs. In the technical method described, the incidence of adverse sequelae is minimal with hypopigmentation occurring in 1–3 % of patients resolving within 4–6 months. Tanned or darkly pigmented

Fitzpatrick Type III patients were likely to develop hypo- and hyperpigmentation in addition to blistering and superficial erosions. Treatment of Fitzpatrick Skin Types IV–VI is to be avoided [1].

Complications

- Vessel rupture is possible, leading to purpura, which is typically associated with long-term (months) hyperpigmentation.
- Post-operative pigment changes may occur. In patients with darker skin types, it might take 4–6 months to resolve [2].
- Caution is advised in the malleolar region due to the presence of a thin, stretched dermis and reflection from underlying periosteum [2].
- Some patients experience severe inflammation.
- Ulceration or breaking of the skin may occur.
- Possible dyspigmentation or scarring.

Prevention and Management of Complications

- If purpura is observed, the pulse duration of the laser should be extended.
- Blanching of the skin is possible and should be avoided with the use of all lasers. Graying of the skin, urtication, and erythema in the shape of the laser crystal with IPL indicates the wrong treatment parameters and should be avoided during treatment.
- The lowest effective fluence and minimal necessary laser treatment should be used to prevent long term pigmentation changes.
- If severe inflammation is encountered, a fluticasone proprionate cream 0.05 % can be applied topically twice a day for 1 week [2].
- Conservative daily wound care is necessary if ulceration or breaking of the skin occurs. Ulcers usually take about 6–10

weeks to resolve and are likely to leave hypopigmented scars. The use of occlusive hydrocolloid dressings and gentle debridement of necrotic tissue of the ulcer will aid re-epithelialization [2].

Future Directions

- Laser therapy will hopefully live up to expectations and be a valuable addition for treatment for leg veins. Although sclerotherapy remains the treatment of choice, further research may improve laser therapy.
- A device which combines 585 nm long-pulsed dye laser and 1,064 nm Nd:YAG was used to treat 60 female patients with leg vein varicosities [48]. Overall patient satisfaction was 47, and an objective assessment of 40 and 49 based on photography and computer assessments, respectively.
- Recently a newer version of IPL, called Optimized Pulse Light (OPL), was introduced that includes double filtration and changes in delivered spectrum based on pulse duration. Further testing on leg telangiectasia is being conducted.
- Development of new technologies or the significant improvement of present technologies, as well as adjuvant therapies should be further explored.

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Chapter 8
Laser Therapy for Pigmented Lesions

Julia Wu, Jane Yoo, and David J. Goldberg

Abstract Laser therapy of pigmented lesions is a very efficacious way of removing cosmetically unappealing lesions on the skin. It is generally very safe and case reports of using lasers on pigmented lesions date back nearly half a century ago. However, as with any treatment, there are important considerations both to ensure maximal effectiveness of treatment and also to prevent potentially damaging adverse

J. Wu, MD
Division of Dermatology, Montefiore Medical Center,
Albert Einstein College of Medicine, 3411 Wayne Avenue,
2nd Floor, Bronx, NY 10467, USA
e-mail: julia.wu@med.einstein.yu.edu

J. Yoo, MD, MPP
Department of Dermatology, Albert Einstein College of Medicine,
1 Columbus Place, #N9J, New York, NY 10019, USA
e-mail: jane.yoo.md@gmail.com

D.J. Goldberg, MD, JD (✉)
Skin Laser & Surgery Specialists of New York and New Jersey,
Hackensack University Medical Center,
New York, NY 10022, USA

Department of Dermatology, Mount Sinai School of Medicine,
UMDNJ- New Jersey Medical School, New York, NY 10022, USA

Fordham Law School, New York, NY 10022, USA
e-mail: drdavidgoldberg@skinandlasers.com

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outcomes. The ability to target melanin as a chromophore and its presence in the epidermis in common skin conditions such as lentigines allows for appealing and satisfying cosmetic results. Herein, the justification and approach to treating pigmented lesions will be discussed, along with practical concerns and future directions in treatment.

Keywords Pigmented lesions • Lasers • Q-switched

Introduction

The concept of treating pigmented lesions with laser therapy has been present since the early 1960s, with the observation that the energy of the laser beam (in this case, a long-pulsed Ruby laser) was absorbed "more effectively by colored tissues" [1]. Since then, laser technology has come a long way, with the greatest advancement being the seminal work of Anderson and Parrish in developing selective photothermolysis [2]. With the advent of selective photothermolysis, one was able to target a chromophore in the skin, with relevant chromophores being hemoglobin, water, and of particular interest to this chapter, melanin. In this setup, one would need a laser that is able to target a specific chromophore based on its absorption spectrum. As the absorption spectrum of melanin is rather broad in the UV, visible light, and near-infrared spectrums, the primary interest here would be to achieve a target wavelength and fluence (which, in this regard, can be thought of as the total energy absorbed in a specific area over time) to specifically interact with melanin without damaging surrounding tissues. Thus, one would choose a wavelength where the absorption would be higher for melanin than for other chromophores, i.e. hemoglobin. Additionally, given that the target chromophore in our application can be quite superficial (in epidermal lesions, as opposed to hemoglobin in blood vessels deeper in the dermis), this allows for selective targeting of the melanin, with shorter wavelengths targeting more superficial structures.

The concept of thermal relaxation time should also be briefly reviewed. In the application of lasers to various chromophores, one must keep in mind that the goal is to selectively destroy a target, usually through heat energy. To achieve optimum efficiency, one must heat the chromophore to a time near its thermal relaxation time (the time needed to dissipate half of the heat, specific to the chromophore) but not longer, as this would allow the heat energy to spread to surrounding tissues, leading to unwanted cellular damage to other structures and possibly scarring. In terms of the melanosome, the thermal relaxation time has been postulated to be under one microsecond [3], so a laser capable of firing in nanosecond lasers is necessary and the Quality-switched (QS) laser is ideal for this application. Additionally, given the broad absorption spectrum of melanin that decreases with increasing wavelengths (peak absorbance at about 335 nm) [4], one must balance the specific absorption of laser energy with the depth of tissue penetration afforded by longer wavelengths.

Background

In general, lesions where the pigment is very superficial in the epidermis (such as lentigines) are treated with lasers of shorter wavelengths, such as QS-ruby (694 nm), QS-Nd:YAG (532 nm), QS-KTP (532 nm), or pulsed dye (510 nm) (Figs. 8.1 and 8.2). Deeper lesions, such as tattoo pigment or nevus of Ota, may be treated with QS-Nd:YAG at 1,064 nm or an intermediate laser, such as QS-Alexandrite (755 nm). Recent developments within the past decade have also shown to be effective at treating pigmented lesions, with fractional photothermolysis (FP) being at the leading edge of laser treatment. In this application, the microscopic treatment zones of FP allow for damaged target cells to be incorporated into columns of microscopic epidermal necrotic debris, achieving a more efficient disposition of the destroyed target cells via exfoliation.

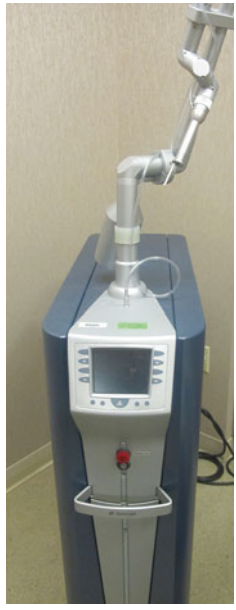

FIGURE 8.1 Q-switched ruby laser

As a corollary to laser therapy, the advent of intense pulsed light (IPL) has also been an interesting and relevant development to this field. Rather than building a laser system from the "ground-up," polychromatic light is emitted from a handpiece and specific filters are put into place to filter the light. With this system, a single device can then be used to target both pigmented and vascular lesions, often at a lower cost than dedicated lasers. However, given that the beam is non-collimated and would rapidly diverge, necessary compromises have to be made in the practical application of IPL, such as the requirement of direct contact of the device with the skin, masking immediate evaluation by the operator and making for difficult treatment in certain locations, such as concave areas of the face [5]. However, IPL remains a useful tool for the treatment of pigmented lesions.

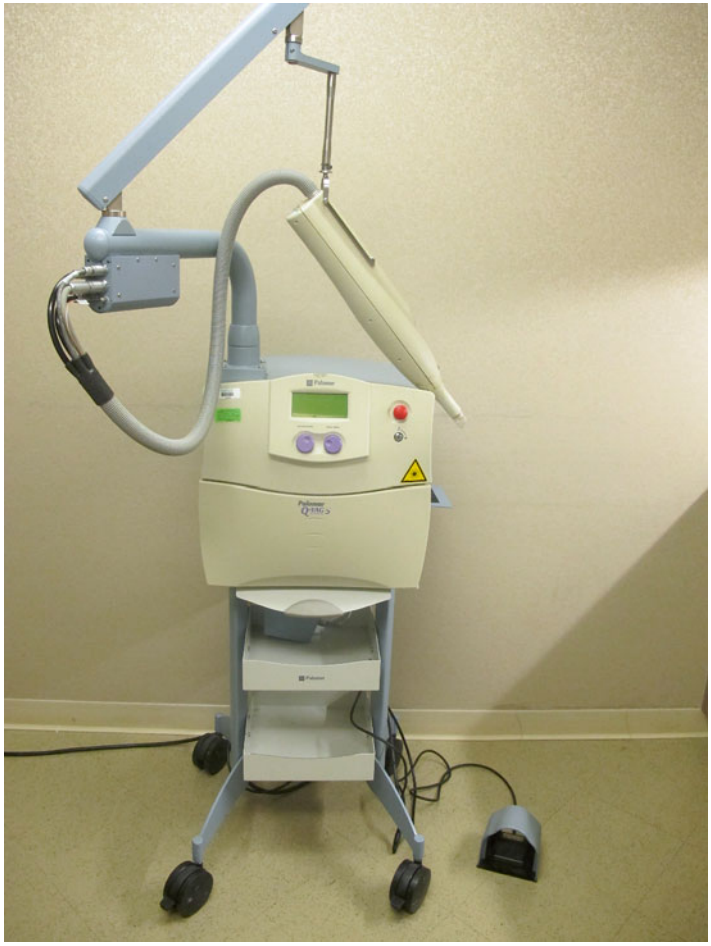

FIGURE 8.2 Q-switched Nd:YAG laser

Indications (Figs. 8.3–8.10)

- Solar Lentigines
- Lentigo Simplex
- Café-au-lait Macules (CALMs)
- Nevus Spilus

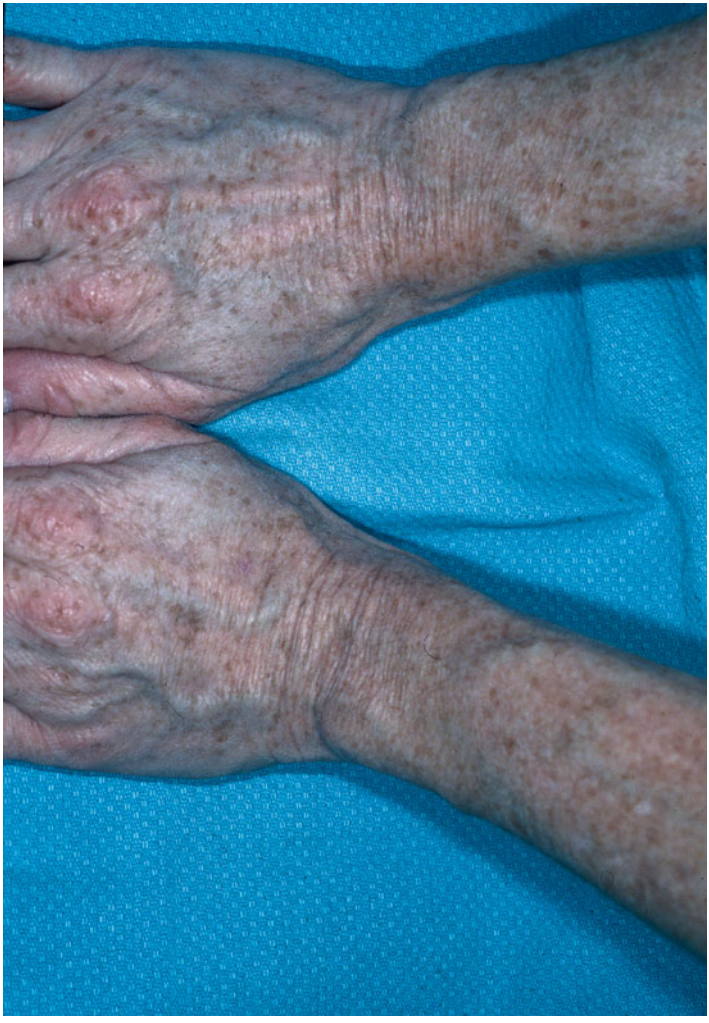

FIGURE 8.3 Lentignes of hands prior to treatment with Q-switched ruby laser

- Seborrheic Keratoses
- Dermatosis Papulosa Nigra
- Post-inflammatory Hyperpigmentation
- Melasma

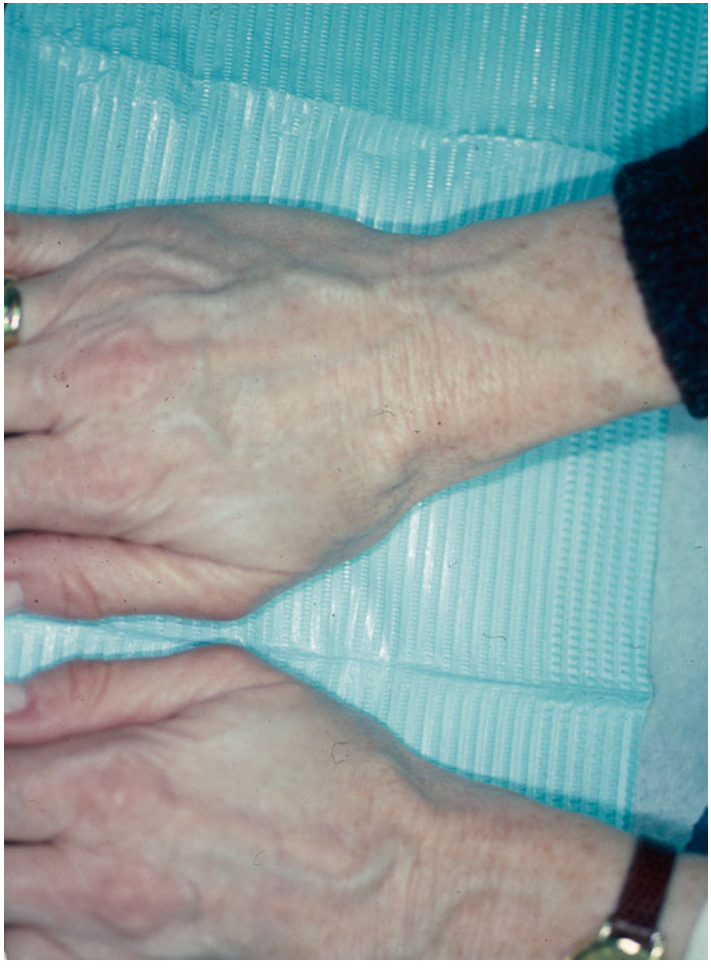

FIGURE 8.4 Lentignes of hands 60 days after treatment with Q-switched ruby laser

- Becker's Nevus
- Melanocytic Nevi
- Nevus of Ota or Nevus of Ito
- Medication-induced Pigmentation
- Tattoo Pigment

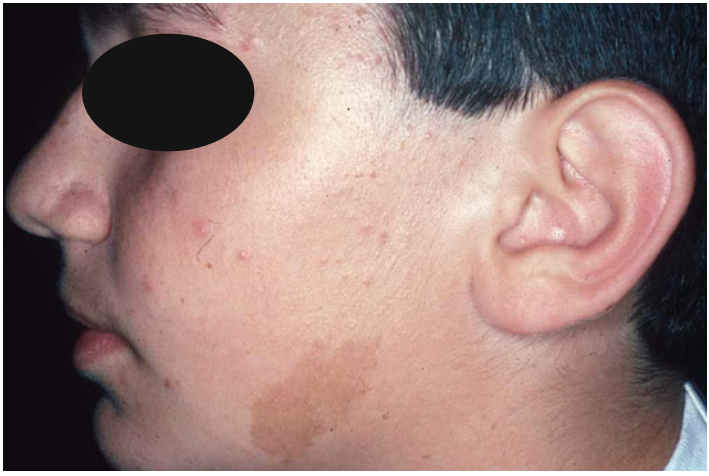

FIGURE 8.5 Café au lait macule prior to treatment with Q-switched ruby laser

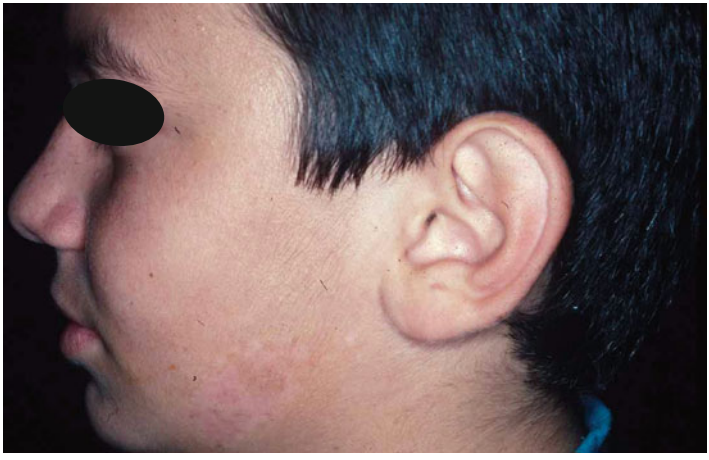

FIGURE 8.6 Café au lait macule after 3 treatments with Q-switched ruby laser

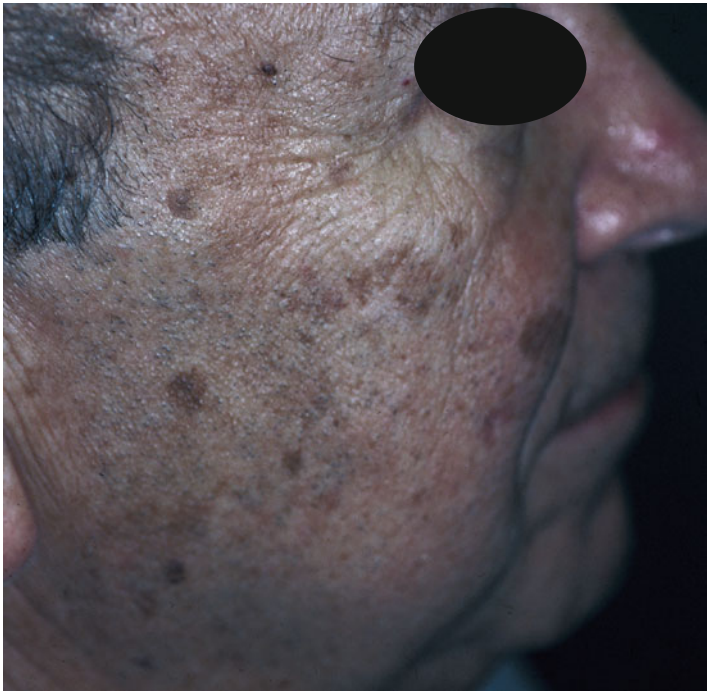

FIGURE 8.7 Lentignes of face prior to treatment with Q-switched Nd:YAG laser

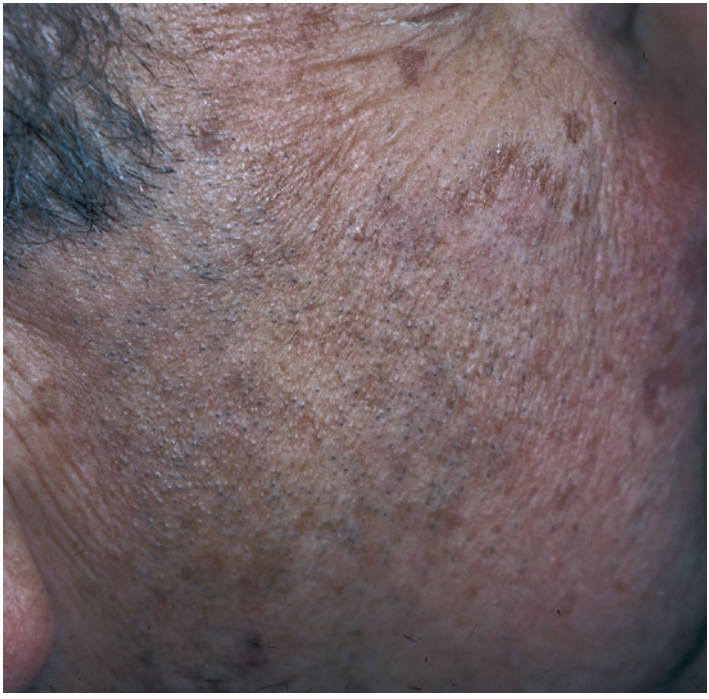

FIGURE 8.8 Lentignes of hands 60 days after treatment with Q-switched Nd:YAG laser

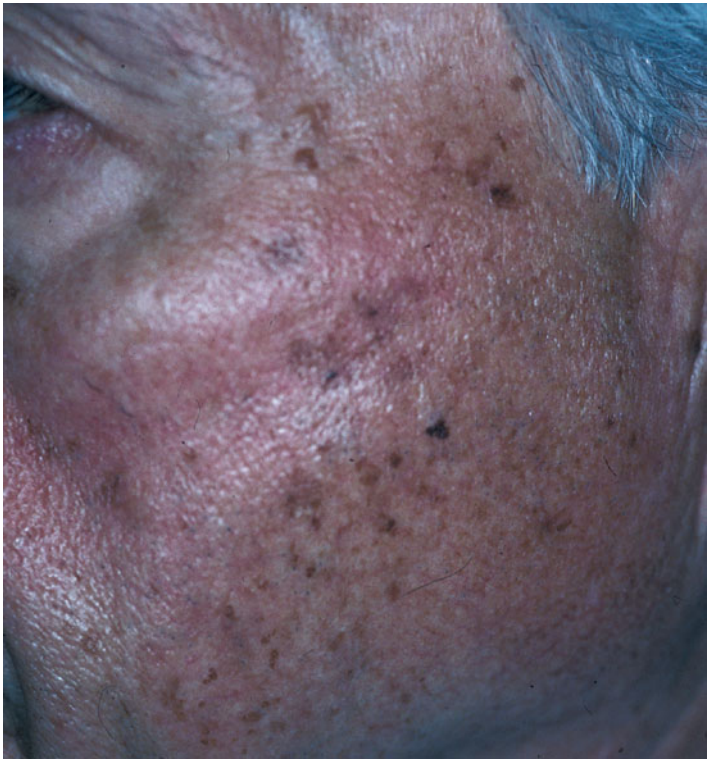

FIGURE 8.9 Lentignes of face prior to treatment with intense pulsed light (IPL)

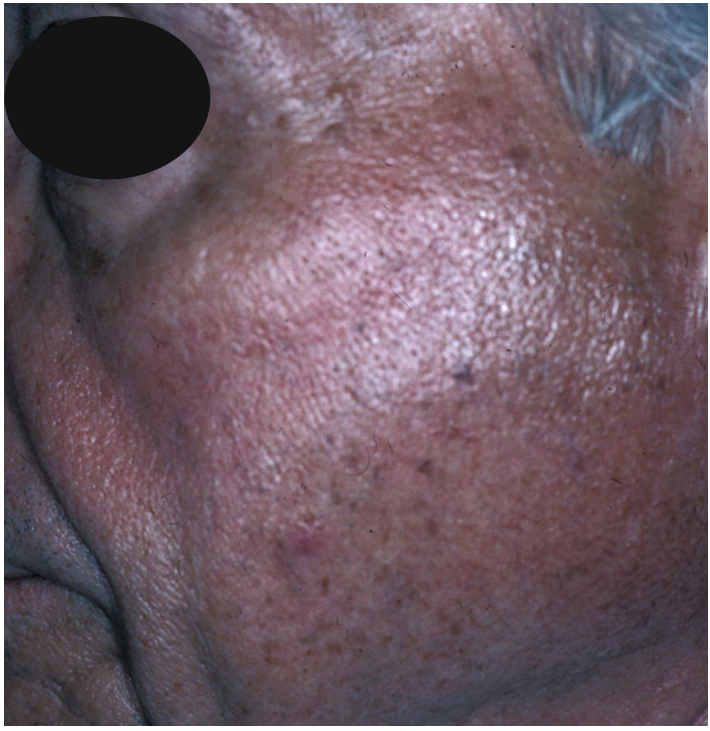

FIGURE 8.10 Lentignes of hands 60 days after four IPL treatments

Contraindications

- As with any procedure, careful consideration of the patient's medical condition and comorbidities must be undertaken, including a full history and medication list. For example, treatment with systemic medications containing gold has been implicated in chrysiasis (blue-gray discoloration in sun-exposed areas caused by cutaneous gold deposits) immediately following treatment with a QS ruby laser [6].
- Any clinical sign of melanoma or a non-benign appearing melanocytic proliferation. Biopsy must be conducted to rule out any significant atypia. Note that the biopsy in this case may also help delineate where the target chromophores reside, i.e. dermal/epidermal.

- Recently suntanned/sunburned skin- this will increase risk of epidermal damage and results in uneven pigmentation. Patients should be advised to wait for several weeks.
- Isotretinoin use within the past 6 months to 1 year- increased risk of hypertrophic scar.
- History of poor wound healing.
- Bleeding disorders.
- Active radiation therapy.
- Personal or family history of melanoma.

Procedural Technique

- Patients should be carefully counseled regarding expectation management in that not all lesions may be amenable to full cosmetic recovery and multiple sessions will be required. The risks of scarring, long-term hypopigmentation (in lighter skin types), and long-term hyperpigmentation (especially in darker skin types, including with IPL) [7] with treatment of pigmented lesions should be discussed.
- Patients should be advised that even in ideal circumstances, they should expect darkening/peeling of lesions that may take several days to heal.
- Darker skin types in general should be targeted with lower fluences, given the increased risk of both hypo- and hyperpigmentation after the procedure. These patients are better candidates for treatment of deeper lesions, as usage of longer wavelength lasers will allow for deeper targeting with reduced epidermal damage.
- A thorough history of tattooing should be obtained, as this can affect response to and selection of laser used.
- Most procedures targeting superficial pigment, such as laser treatment of lentigines, may be tolerated without anesthesia. However, especially with fractional photothermolysis or correction of larger, deeper/dermal lesions, local anesthesia may be required. Depending on the location and area involved, topical anesthetics with lidocaine (such as EMLA), local anesthesia with lidocaine/epinephrine, or

regional nerve blocks may be appropriate. It has been suggested that addition of hyaluronidase to the lidocaine/epinephrine allows for better tissue diffusion and bupivacaine additionally grants a longer duration of anesthesia [8].

- Selection of lasers for treatment are outlined in Table 8.1. Specific treatment considerations are also outlined below.
- For lentigines, cryotherapy has been used to darken lesions prior to treatment with QS Alexandrite laser, allowing for increased efficacy [9].
- Reports indicate that QS Alexandrite laser is preferable for lentigines, nevus of Ota, and dermal melanocytosis, but is susceptible to a high rate of relapse in acquired nevus of Ota-like macules (Hori's nevus), CALMs, and nevus spilus [10].
- One study showed improved efficacy of Er:YAG vs. QS Nd:YAG laser for treatment of Becker's nevus, albeit with a small sample size of only 22 [11].
- The use of laser therapy for post-inflammatory hyperpigmentation is still controversial, as it is one of the possible side effects of fractional photothermolysis itself. Case reports of treatment are sparse, and treatment should be initiated with care (and test spots) only when first-line therapy such as bleaching creams, chemical peels, and topical retinoids have failed.
- Melasma seems to have reasonable treatment success with erbium-doped fractionated laser therapy [12, 13], although the risk of post-inflammatory hyperpigmentation worsening the initial cosmetic insult is concerning.
- Melanocytic Nevi can be treated with laser therapy but its use should be reserved for select cases in which there is no concern for malignancy at all and also either the risk of surgical excision is too great (such as the case with giant congenital nevi) or the cosmetic outcome would be unacceptable. One study focusing on giant congenital nevi had excellent results with a combination of pulsed dye and Q-S laser treatment (one pass of each in multiple rounds of treatment), with a 100 % response rate [4].

Table 8.1 Specific indications for laser therapy and lasers used

Indication	Lasers used	Treatment interval
Lentigines (lentigo simplex or solar lentigo)	QS ruby, QS Nd:YAG (532 nm), QS alexandrite, pulsed dye (510 nm), CO_2, argon, nonablative fractional	4–8 weeks
Seborrheic keratoses and dermatosis papulosa nigra	CO_2, long-pulsed Nd:YAG, KTP, fractionated erbium-doped	
Ephelides	QS alexandrite, long-pulsed Nd:YAG	4–12 weeks
CALMs and nevus spilus	QS ruby, QS Nd:YAG (532 nm and for nevus spilus, 1,064 nm), Er:YAG, QS alexandrite, pulsed-dye	4–8 weeks
Becker's nevus	QS ruby, QS Nd:YAG (532 and 1,064 nm), QS alexandrite, Er:YAG, fractionated erbium-doped	4–8 weeks
Postinflammatory hyperpigmentation	Fractionanted erbium-doped, QS Nd:YAG	2–4 weeks
Melasma	QS ruby, QS Nd:YAG (1,064 nm), QS alexandrite, CO_2, Er:YAG, fractionated erbium-doped	1–4 weeks
Melanocytic nevi	QS ruby, QS alexandrite, QS Nd:YAG, long-pulsed ruby, diode, Er:YAG, CO_2, combinations of the above	1–8 weeks
Nevus of Ota and nevus of Ito	QS ruby, QS Nd:YAG, QS alexandrite, fractionated Nd:YAG	6–12 weeks

(continued)

Table 8.1 (continued)

Indication	Lasers used	Treatment interval
Medication-induced pigmentation	QS ruby, QS Nd:YAG, QS alexandrite	N/A (too few case reports)
Tattoo	QS ruby, QS Nd:YAG (532 and 1,064 nm), QS alexandrite, pulsed dye	6–12 weeks

- Drug-induced hyperpigmentation is a well-known side effect of several drugs, most notably to dermatologists as a result of minocycline, but also with amiodarone, tetracycline, antimalarials, phenytoin, imipramine, chlorpromazine, and ketoconazole.

Pre-operative Care

- Sun exposure should be avoided the week before laser treatment, with broad-spectrum sunblock usage on a daily basis
- Advise patients to stop smoking for at least 2 weeks to 1 month prior to laser treatment to mitigate risk of poor healing
- Anti-viral therapy (such as valacyclovir or famciclovir) for all ablative procedures (such as FP) and in susceptible patients. Consider a 1-week course of oral antibiotics starting the day prior to the procedure (broad-spectrum, such as cephalosporins, penicillin derivatives, azithromycin) for ablative procedures as well.
- Pre-treatment photographs are recommended as documentation for both the physician and patient.
- The area must be carefully and completely cleaned and any alcohol used for cleaning must be allowed to dissipate, to minimize the risk of a flash fire due to a flammable material.

- Eye protection covering the wavelength of the laser being used must be employed by both the patient and any personnel in the room.
- Universal precautions should be respected and equipment protected with plastic coverings as blood spatter can be observed with several treatment modalities.

Post-operative Care

- Cool compresses and emollients should be applied for relief of tingling, burning, and pain. Afterwards, the patient should be advised to place an occlusive dressing with emollients over the area for several days.
- If the patient develops an urticarial reaction, oral antihistamines may be used in addition to the above.
- Patients should clearly understand that they are not to peel off any crust that develops; rather, they should apply emollients to hasten resolution allow the crust to slough off on its own.
- Sun exposure should be avoided the week after laser treatment, with broad-spectrum sunblock usage on a daily basis.
- In general, IPL and fractional photothermolysis may have a shorter recovery time, however the post-treatment darkening and erythema for some time afterwards may be expected as well.

Complications

- Bullous reactions (vesicle formation) may develop in aggressive treatment of deeper dermal lesions, especially if too high a fluence is used.
- Immediate pigment darkening may be observed with laser treatment of tattoos.
- Pupura may form after pulsed-dye laser treatment, which is generally transient and minimized with modern lasers.

- Anaphylaxis has been reported in laser treatment of cosmetic tattoos, presumably by liberating antigenic components of the tattoo pigment [14].

Prevention and Management of Complications

- Occlusive dressings may be applied over vesicles, which should be allowed to rupture on their own. The physician should consider reducing the total energy/fluence applied on subsequent treatments. These vesicles usually heal without scarring unless the wound is complicated, so occlusive dressings and standard wound care is warranted.
- A case report suggests that laser-induced pigment darkening of a cosmetic tattoo (in this case QS-ruby induced) was treated successfully with QS-alexandrite and Nd:YAG lasers [15].
- For anaphylactic reactions, anti-histamines and/or intramuscular epinephrine if available should be used, followed by emergency department consultation.

Future Directions

- New developments in laser technology seek to maximize targeting of chromophores while reducing "collateral damage," however laser therapy is an already-robust field and much of the advancement seems to be focused on minimizing side effects such as scarring and pain or discomfort.
- Randomized controlled trials of laser therapy for specific indications are lacking and the field would benefit from robust, well-designed trials for this purpose.
- IPL is an evolving technology which has a considerable deal of room to grow as far as a mature treatment modality. Future improvements may focus on light sources

(including optimizing efficiency of these sources) and delivery, such as focused treatment handpieces and improved real-time monitoring of treatment [16].

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Chapter 9
Laser Tattoo Removal

Salma Pothiawala, Suzanne L. Kilmer, and Omar A. Ibrahimi

Abstract Tattooing of human skin dates back to prehistoric times, with evidence of tattoos present in artifacts from the Bronze Age and the Paleolithic period. Egyptian mummies have been discovered with tattoos on their bodies (Kent and Graber, Dermatol Surg 38(1):1–13, 2012). Tattoos have been placed for body decoration, as a form of expression, and for cosmetic and medical purposes. Traumatic tattoos

S. Pothiawala, MD, MPH
Department of Dermatology and Cutaneous Surgery, University of South Florida, 13330 USF Laurel Drive, Tampa, FL 33612, USA
e-mail: salma.pothiawala@post.harvard.edu

S.L. Kilmer, MD
Department of Dermatology, Laser and Skin Surgery Center of Northern California, University of California Davis, School of Medicine, 3835 J Street, Sacramento, CA 95816, USA
e-mail: skilmer@skinlasers.com

O.A. Ibrahimi, MD, PhD (✉)
Wellman Center for Photomedicine, Massachusetts General Hospital, 999 Summer Street, Suite 205, Stamford, CT 06905, USA

Connecticut Skin Institute, 999 Summer Street, Suite 205, Stamford, CT 06905, USA
e-mail: omar.ibrahimi@gmail.com

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can also result from injury resulting in implantation of particles in the skin (Bernstein, Clin Dermatol 24(1):43–55, 2006). In the United States, approximately 1 out of every 4 adults ages 18–24 has a tattoo (Armstrong et al., J Adolesc Health 35(1):58–61, 2004; Armstrong et al., Arch Dermatol 132(4):412–416, 1996). Historical methods for tattoo removal have been both mechanical and chemical. These methods have included abrading the skin followed by the application of salt (Manchester, Calif Med 118(3):10–12, 1973), the application of various concentrations of trichloroacetic acid, and dermabrasion, which involves using a wire brush or a diamond fraise wheel to remove skin to the level of the papillary dermis along with tattoo pigment (Kent and Graber, Dermatol Surg 38(1):1–13, 2012; Bernstein, Semin Plast Surg 21(3):175–192, 2007). Electrocautery and liquid nitrogen have been used to try to destroy the skin to remove tattoo pigment. Although tattoo pigment may be removed with the above methods, the rate of scarring and dyspigmentation is very high given that these methods are non-selectively destructive (Gupta, Plast Reconstr Surg 36(3):354–361, 1965; Ruiz-Esparza et al., J Dermatol Surg Oncol 14(12):1372–1376, 1988; Dvir and Hirshowitz, Plast Reconstr Surg 66(3):373–379, 1980; Colver and Dawber Int J Dermatol 24(9):567–568, 1985). Surgical excision of tattoos has also long been an option for removal, but may be difficult given that tattoos are often located on anatomical sites not optimally suited for linear repair, or may require several staged procedures (Buncke and Conway, Plast Reconstr Surg 20(1):67–77, 1957; Bailey, Plast Reconstr Surg 40(4):361–371, 1967; Fujimori, Treatment of nevus of Ota and nevus spilus. In: Kobayashi T, editor. Skin surface surgery. Tokyo: Kokuseido; 1990. p. 181–188; Kobyashi, J Dermatol Surg Oncol 17(12):936–941, 1991; Cosman et al., Ann Plast Surg 22(1):36–42, 1989). Laser tattoo removal began in the 1970s with the argon laser (488 and 514 nm), which was a continuous wave laser and therefore resulted in damage to surrounding tissue and scarring (Apfelberg et al., Br J Plast Surg 32(2):141–144, 1979; Maser et al., World J Surg 7(6):684–691, 1983; Brady et al., Ann Plast Surg 2(6):482–490, 1979;

McBurney South Med J 71(7):795–797, 1978). The ablative CO_2 laser (10,600 nm) has also been use for approximately the past 25 years for tattoo removal, and similarly results in scarring and dyspigmentation given that it non-specifically targets water in the skin (Bailin et al., J Dermatol Surg Oncol 6(12):997–1001, 1980; Reid and Muller Plast Reconstr Surg 65(6):717–721, 1980; Fitzpatrick et al., J Dermatol Surg Oncol 17(4):340–439, 1991; Ruiz-Esparza et al., J Dermatol Surg Oncol 14(12):1372–1376, 1989). Modern tattoo removal involves Q-switched (QS) lasers, which function based on the theory of selective photothermolysis (Anderson and Parrish Science 220(4596):524–527, 1983; Anderson et al., J Invest Dermatol 93(1):28–32).

Keywords Tattoo removal • Selective photothermolysis • Laser technique • Q-switch lasers • Paradoxical darkening

Introduction

- Tattooing of human skin dates back to prehistoric times, with evidence of tattoos present in artifacts from the Bronze Age and the Paleolithic period. Egyptian mummies have been discovered with tattoos on their bodies [1].
- Tattoos have been placed for body decoration, as a form of expression, and for cosmetic and medical purposes. Traumatic tattoos can also result from injury resulting in implantation of particles in the skin [2].
- In the United States, approximately one out of every four adults ages 18–24 has a tattoo [3, 4].
- Historical methods for tattoo removal have been both physical and chemical. These methods have included abrading the skin followed by the application of salt [5], the application of various concentrations of trichloroacetic acid, and dermabrasion, which involves using a wire brush or a diamond fraise wheel to remove skin to the level of the papillary dermis along with tattoo pigment [1, 6]. Electrocautery and liquid nitrogen have been used to try to destroy the skin to remove tattoo pigment.

- Although tattoo pigment may be removed with the above methods, the rate of scarring and dyspigmentation is very high given that these methods are non-selectively destructive [7–10].
- Surgical excision of tattoos has also long been an option for removal, but may be difficult given that tattoos are often located on anatomical sites not optimally suited for linear repair, or may require several staged procedures [11–15].
- Laser tattoo removal began in the 1970s with the argon laser (488 and 514 nm), which was a continuous wave laser and therefore resulted in damage to surrounding tissue and scarring [16–19].
- The ablative CO_2 laser (10,600 nm) has also been use for approximately the past 25 years for tattoo removal, and similarly results in scarring and dyspigmentation given that it non-specifically targets water in the skin [20–23].
- Modern tattoo removal began approximately 25 years ago and involves Q-switched (QS) lasers [24, 25]. These lasers function based on the theory of selective photothermolysis as proposed by Harvard dermatologists R. Rox Anderson and John Parrish.

Background

QS Lasers

- The destruction of tattoos with lasers revolves around the theory of selective photothermolysis. Various chromophores in the skin, such as water, hemoglobin, melanin, or exogenous pigment, each absorb certain wavelengths of light. When a laser emits a wavelength of light that targets a particular chromophore, that energy is absorbed by the chromophore and converted to heat. The heat destroys the target chromophore and may also cause surrounding tissue to be damaged [1].
- For selective destruction, the target chromophore should not be heated for longer than its thermal relaxation time,

which is the time necessary for the chromophore to lose 50 % of its heat [24].

- QS lasers are the mainstay of modern laser tattoo removal; the three main types of QS lasers are the ruby (694 nm), Alexandrite (755 nm), and the neodymium:yttrium-aluminum-garnet (Nd:YAG) lasers (1,064 nm and frequency doubled at 532 nm) [1].
- QS lasers allow for selective photothermolysis by releasing very short (nanosecond), high-power pulses. Rapid heating leads to fragmentation of the target due to its rapid thermal expansion. Further, the high temperature gradients that are produced result in acoustic waves that propagate and lead to mechanical destruction of surrounding structures. It is these photoacoustic waves that are the main workhorses of laser tattoo removal [26].

Types of Tattoos

- Tattoos can either be classified on the basis of color or style [27].
- Several colors of pigment are used to create tattoos, such as green, blue, red, and brown, and black (Table 9.1). Black is the most common. Colors are also mixed to create new shades [27].
- Styles of tattoos include professional, amateur, cosmetic, medical, and traumatic tattoos [27].
- Professional tattoos are placed with the vibrating needle of a tattoo machine, and thus the pigment is placed at an adequate depth and with significant density to persist for a long period of time [27].
- Amateur tattoos are usually black, and they can be composed of a number of substances such as soot, pen ink, or charcoal. They can be created by various methods such as using a needle by hand or a makeshift tattoo machine. The pigment can be placed at varying depths in the skin depending on the tool used to make the tattoo [27].

Table 9.1 Tattoo pigments [41]

Color	Pigment
Brown	Ochre
Yellow	Cadmium sulfide, ochre, curcumin yellow
Blue	Cobalt aluminate
Green	Chromium oxide
Red	Mercury sulfide, cadmium selenide
Violet	Manganese violet
White	Titanium dioxide, zinc oxide
Flesh	Iron oxides
Professional black	Carbon, iron oxide
Amateur black	India ink, carbon
Traumatic	Lead, gunpowder, dirt, other

- Cosmetic tattoos were developed to resemble makeup and enhance physical appearance; red, pink, and brown colors are used on the lips, eyebrows and cheeks. These pigments are usually a mixture of compounds and can contain titanium dioxide and ferric oxide [27].
- Medical tattoos are sometimes placed by medical professionals as markers for sites of radiation or to mark body parts for certain surgeries [27].
- Traumatic tattoos are incurred when the dermis is penetrated by particles, such as dust, gunpowder, or metals, which then become imbedded within it and leave a blue or black tattoo, depending on depth [28–30].

Indications

- Certain laser wavelengths are more effective at targeting certain pigment colors (Table 9.2).
- The 694 nm QS ruby emits red light, which is well absorbed by black and dark blue tattoo pigments and to a lesser extent by other colors. It is well suited to removing amateur

tattoos and darkly colored professional tattoos, as well as many medical and traumatic tattoos [30–33]. Brightly colored tattoos tend not to respond as well [1]. There is a risk of post-treatment hypopigmentation especially in darker skin types with the QS ruby laser as melanin is also a chromophore [31, 34, 35].

- The Nd:YAG laser can emit wavelengths of 1,064 or 532 nm. Like the QS ruby, it is effective at treating black and dark blue tattoos, and not so effective at treating brightly colored tattoos [1]. The QS Nd:YAG (1,064 nm) is better suited to treating tattoos in dark-skinned individuals as its longer wavelength allows it to target pigment in the dermis, and affect superficial melanosomes to a lesser extent than lasers of shorter wavelengths [36].
- The Nd:YAG may be frequency-doubled to emit a 532 nm wavelength, which works well for treating red tattoos [37, 38]. It has been found to be useful for treating patients who have an allergy to red ink when used in combination with corticosteroid application [39]. Hypopigmentation can occur with the 532 nm given that the shorter wavelength can target melanin in the epidermis [35].
- Similar to the QS ruby and QS Nd:YAG, the 755 nm QS Alexandrite works well for black and blue pigment [40]. It has been shown to be effective for green pigment as well [37]. Hypopigmentation is also a potential post-treatment side effect given that 755 nm wavelength can be absorbed by epidermal melanin pigment [34].
- In general, professional and very dark amateur tattoos can be treated effectively with all three of the QS lasers [1].
- The QS ruby has the highest clearance rate but also the highest incidence of hypopigmentation [34].
- Red and green tattoos respond variably to laser removal; some green may respond well to the QS Alexandrite (755 nm), and some red pigment to the Nd:YAG (532 nm) [37].
- Yellow and orange pigments are generally resistant to treatment [1].
- The composition of modern tattoos is variable and it can be difficult to discern composition of pigments and thus appropriate absorption spectra [2].

Table 9.2 Lasers used for tattoo removal [41]

Color	Laser used (nm)
Brown	Tan/light brown: QS Nd:YAG (532), dark brown: QS ruby, QS alexandrite, QS Nd:YAG (1,064)
Yellow	QS Nd:YAG (532)
Blue	QS ruby, QS alexandrite, QS Nd:YAG (1,064)
Green	QS ruby, QS alexandrite
Red	QS Nd:YAG (532)
Violet	QS Nd:YAG (532)
White	QS Nd:YAG (532)
Flesh	QS Nd:YAG (532)
Professional Black	QS ruby, QS alexandrite, QS Nd:YAG (1,064)
Amateur Black	QS ruby, QS alexandrite, QS Nd:YAG (1,064)
Traumatic	QS ruby, QS alexandrite, QS Nd:YAG (1064)

Contraindications

- **Isotretinoin** — the use of laser is controversial in individuals who have taken isotretinoin in the past 6 months due to a potential risk of scarring and keloid formation after laser therapy [42]. However, there is new evidence to suggest that these individuals may not have any increased risk of scarring [43].
- **Gold salts** — Chrysiasis can be induced by the use of gold salts combined and exposure to UV light. Thus, patients who have been treated with gold salts for rheumatologic disorders or other disease should be cautioned on the risk of chryiasis with the use of QS lasers. QS lasers have also been reported to cause further hyperpigmentation in patients with chrysiasis [44, 45].

Procedural Technique/Considerations

Patient Consultation

- The patient should be counseled to have realistic expectations regarding time, expense, possible adverse outcomes, and results of laser tattoo removal: tattoo removal will require several treatment (usually 6–10) (Fig. 9.1) sessions performed at 4–8 week intervals and can cost thousands of dollars. The tattoo may not be fully removed, may not respond, or may become darker. Each treatment also increases the risk of laser-induced side effects [2].

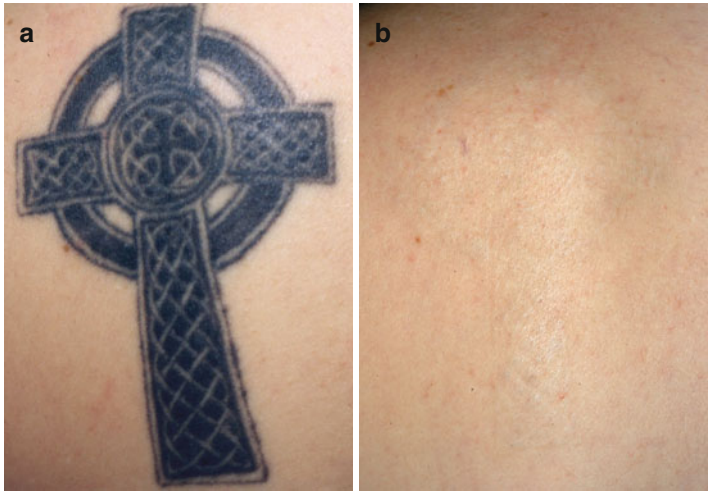

FIGURE 9.1 (**a**) Black tattoo prior to treatment with a Q-switched Nd:YAG laser. (**b**) Appearance following ten treatments

Pretreatment

- Dark-skinned or tan patients can be treated with bleaching agents, such as hydroquinone combined with topical steroids and/or retinoids, prior to treatment in an attempt to reduce the possibility of the laser targeting epidermal melanin [2].
- Tattoos that have dermal post inflammatory hyperpigmentation should not be treated as this can lead to scarring [2].
- The skin should be cleaned and free of any cosmetics or skin care products that may interfere with the absorption of laser light [1].

During Treatment

- As tattoo removal is painful, local anesthesia should be administered. Intradermal lidocaine, topical anesthetics, such as EMLA (lidocane 2.5 % with prilocaine 2.5 %), or regional nerve blocks can be used [1].
- Clear hydrogel dressings (Vigilon) or clear occlusive dressings (Tegaderm) can be applied prior to treatment to reduce heat transfer and thereby safeguard the epidermis. These dressings also protect the operator in the case of aerosolized debris from laser treatment [1, 2]. Use of these dressings may increase the amount of laser beam that is reflected.
- Immediate whitening of the tattoo with laser treatment (Fig. 9.2) should be considered the treatment endpoint [1].

Post Treatment

- Proper wound care is essential to optimize cosmetic outcomes as blisters and crusting can develop and last for a week or more after treatment. Occlusive emollients (such as Aquaphor or petrolatum) should be applied to the treated site and covered if necessary [2].
- Strict sun protection should be practiced for several months after treatment [1].

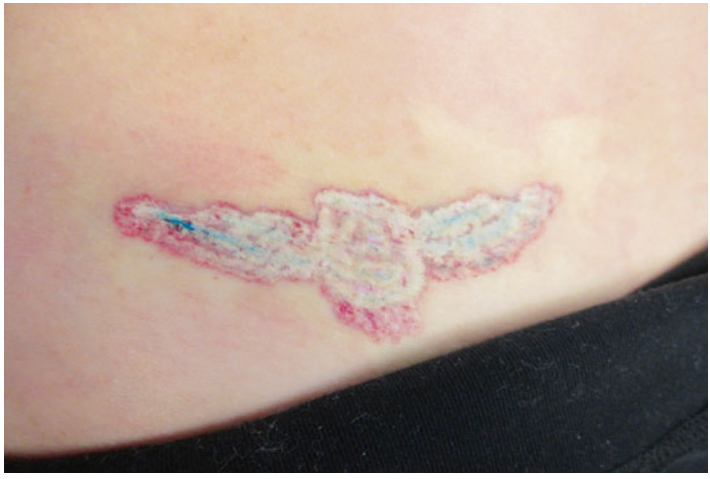

FIGURE 9.2 Desired endpoint of whitening following Q-switched laser treatment

Complications

- **Paradoxical darkening** — Immediate or progressive permanent darkening of tattoo pigments after treatment with QS lasers can occur [27]. It has most commonly been reported with red, pink, brown, yellow, flesh-colored, and white pigments [46, 47]. In terms of mechanism, it is thought to be secondary to ferric oxide and titanium dioxide that is contained certain tattoo pigments. Ferric oxide gets converted to ferrous oxide, which is jet black, and Ti^{4+} to $Ti^{3+,}$ which is blue-black, after treatment with a QS laser [48].
- **Poor response** — The poor response of certain pigments to laser tattoo removal is thought to be secondary to them containing titanium dioxide. Titanium dioxide is found in white and flesh-colored pigments and is also combined with other pigments to enhance their brilliance [1].

- **Dyspigmentation**:
  - Hypopigmenation can occur, especially with shorter wavelength QS lasers, as melanin is a competing chromophore with tattoo pigment [49, 50]. The hypopigmentation has been shown to last longer when induced by the QS ruby versus the 532 nm Nd:YAG or the diode lasers. Hypopigmentation can be treated with other lasers, such as the excimer or 308 nm xenon-chloride [27].
  - Hyperpigmentation can occur and is more of risk in darker skin tones, another reason to a laser with a longer wavelength that will not target the epidermis in treating these patients, such as the Nd:YAG. If the QS Ruby or QS Alexandrite is employed for darker skinned individuals, lower fluences should be used. Tanned individuals should not be treated until their tan has faded [27]. Patients should practice strict photoprotection prior to laser treatments.
- **Allergic reactions** — Tattoo pigments can cause cutaneous allergic reactions. Red pigment composed of cinnabar is the most common pigment to cause such a reaction, which usually presents as a pruritic scaly nodular eruption in the area of the causative ink. Combination of traditional QS lasers with ablative fractional resurfacing has been reported to treat allergic tattoo reactions [38, 51]. Yellow tattoos composed of cadmium are the most common cause of photoallergic reactions [27].
- **Epidermal debris** — The high-energy, short pulses generated by the laser can cause aerosolization of tissue and infectious particles. It is imperative for the operator use adequate protective measures to protect their mucosal surfaces [27].
- **Potential carcinogenicity** — The character of the breakdown products of tattoo pigment after laser treatment has not been well studied. It has been reported that the laser-induced decomposition of azo-containing pigments results in breakdown products such as 2-5-dichloraniline and 4-nito-toluene, which are known to be toxic or even carcinogenic [27, 52].

Prevention and Management of Complications

- Skin pigmentation, spot size, pulse duration, and fluence must be considered when selecting the most appropriate laser in order to achieve optimal results and prevent complications.
- **Use of the appropriate device** — It has been established that pulse in the nanosecond range and shorter and most appropriate for removing melanin-containing structures and small particles [24]. Using a device with pulses in the millisecond range (such as intense pulse light) to remove tattoos results in heating of pigment particles for too long and subsequent spread of heat to surrounding tissue. This transfer of heat energy results in tissue damage and scarring with inadequate tattoo removal. Tattoo removal should only be attempted with QS lasers [2].
- **Treat with appropriate fluence** — Fluence is measured in J/cm^2, and is the energy density of the laser light emitted. The lowest fluence necessary to produce a whitening response should be employed. Using too high fluence can cause epidermal damage. Similarly, greater epidermal absorption of laser light in darker skinned individuals can cause epidermal damage. This can be avoided by using lower fluence in the individuals. However, tattoo pigment may also not be adequately treated with a lower fluence. Thus, it is better to use a laser with a longer wavelength such as the Nd:YAG (1,064 nm) when treated darker skinned individuals so that adequate fluence may be used without risking epidermal damage. If a particular tattoo is refractory to laser therapy, it is oftentimes more beneficial to try another QS laser than to attempt to increase the fluence, which will in most cases increase side effects but not efficacy [1, 2].
- **Darkened tattoos** — Treatments tattoos that have undergone paradoxical darkening after QS laser treatment include continued treatment with QS laser, treatment with nonselective ablative laser, and surgical excision. Continued

treatment with QS laser has been shown to be more effective for red and brown tattoos that have darkened rather than darkened yellow or white tattoos, which are more treatment resistant. For white pigment, which frequently darkens after QS laser therapy, nonselective ablative lasers (pulsed carbon dioxide (10,600 nm) and erbium-doped (Er): YAG (2,940 nm)) tend to be the best option [1]. These lasers, do however, pose an increase risk of scarring and have less predictable outcomes when compared to QS lasers [1].

Future Direction

- Ablative fractional resurfacing has been reported to remove tattoos in combination with QS lasers and by itself [51].
- Multiple treatments in the same day with 20 min intervals has also been shown to lead to faster clearance of tattoos [53].
- **Picosecond lasers** — Lasers with shorter pulses in the picosecond range were first tested at Harvard Medical School over 15 years ago. These lasers may be more effective than QS lasers at targeting pigment particles and may causeless damage to surrounding tissue. The shorter pulse duration of the picosecond lasers causes more rapid photothermolysis than QS lasers, and thereby results in a greater destructive force [54]. The use of these lasers commercially has been hampered by the ability to develop a stable version of the picosecond laser that is not cost prohibitive.
- **Scatter reduction** — The laser energy that is absorbed by a target chromophore is greatly reduced by the absorption and scattering of laser light as it passes through tissue. Intradermal injections of hyperosmotic substances such as glycerol, glucose, and dimethylsuloxide have been effective at reducing scatter in animal studies [55]. However, tissue necrosis and scarring was also seen with these intradermal injections [55]. Safer injectable and topical compounds which will reduce scatter of laser light, make tattoo

pigments easier to see, and enable a more significant portion of the emitted laser energy to be absorbed by dermal tattoo pigments are being developed [56].

- **Safer tattoo** — Currently there are no FDA regulations on tattoo pigments. Many pigments that are commonly used were initially created for alternate purposes, and their safety profiles are not well known. The removal of these pigments is also difficult as their composition is unknown and thus it can be difficult to select the most appropriate laser. In 2009, a new tattoo pigment Infinitink (Freedom Inc., Cherry Hill, NJ), composed of bioresorbable dyes encapsulated in polymethylmethacrylate beads, was developed. It can be removed with fewer treatments as compared to conventional pigments as its beads contain additional pigments that are designed to be absorbed by certain laser wavelengths [1].
- **Imiquimod** — Imiqimod in combination with QS laser may help clear tattoos better than just QS laser alone. Human studies have shown conflicting results, however, and more studies are needed [27, 57].

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Chapter 10
Laser Hair Removal

Jennifer A. Ledon, Jessica A. Savas, Katlein Franca, and Keyvan Nouri

Abstract Laser hair removal is one of the most common non-surgical procedures performed in the United States. Excessive, unwanted hair can be seen in all ages, ethnicities and skin types and lasers can help provide a permanent reduction in hair growth. Professional and home-based laser and light systems are both currently available, with professional systems including the 694 nm ruby laser, 755 nm Alexandrite laser, the 800 nm diode laser, the long-pulsed 1,064 nm Neodymium doped: yttrium aluminum garnet (Nd:YAG) laser, intense pulsed light (IPL), and radiofrequency. While generally safe, side effects from laser hair removal are possible and should only be used by trained medical professionals after performing a thorough history and physical examination. This chapter will provide a succinct approach to laser hair removal, including but not limited to available modalities, patient selection, reported side effects and management of care.

J.A. Ledon, MD (✉) • J.A. Savas, MD
K. Franca, MD, MS • K. Nouri, MD
Department of Dermatology and Cutaneous Surgery,
University of Miami—Miller School of Medicine,
1475 NW 12th Avenue, 2nd Floor, Miami, FL 33136, USA
e-mail: jledon1@med.miami.edu; jsavas@med.miami.edu;
k.franca@med.miami.edu; knouri@med.miami.edu,
knourimd@gmail.com

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Introduction

- Laser hair removal is one of the most common non-surgical procedures performed in the United States.
- Professional and home-based laser and light systems are both currently available. Professional laser and light systems for hair removal include the: 694 nm ruby laser, 755 nm Alexandrite laser, the 800 nm diode laser, the 1,064 nm Neodymium doped: yttrium aluminum garnet (Nd:YAG) laser, intense pulsed light (IPL), and radiofrequency. In the United States, home-based systems include only diode and IPL systems [1].
- Excessive, unwanted hair can be seen in all ages, ethnicities and skin types.
- Laser hair removal results in a permanent reduction in hair growth and not total permanent hair loss.
- A complete, but temporary hair loss can be seen for 1–3 months after treatment. Hair re-growth after laser hair removal may be finer and fairer, more closely resembling velus hair. This may change over time, ultimately appearing akin to terminal hair.
- Laser hair removal functions on the principle of selective photothermolysis, with melanin serving as the target chromophore [2]. This increases the incidence of side effects in patients with darker Fitzpatrick skin types.
- Laser hair removal of white, blonde or red hairs is generally ineffective due to decreased quantities of eumelanin (dark melanin) [3].
- Aside from general cosmesis, laser hair removal may also help to improve the untoward effects from conditions such as pseudofolliculitis barbae and acne keloidalis nuchae [4].
- Paradoxical hypertrichosis is an uncommon, yet possible side effect with a reported incidence between 0.05 and 10.2 % [5–8].

Background

Long-Pulsed 694 nm Ruby Laser

- The long-pulsed 694 nm Ruby laser is the oldest laser used for hair removal.
- In patients with fair skin and dark course hair, it is highly effective with few side effects [9].
- Due to its highly selective targeting of melanin, it is not recommended for patients with greater than Fitzpatrick type III skin or patients with recent sun exposure. For this reason, it has fallen out of favor.

755 nm Alexandrite Laser

- Synthetic alexandrite crystal is used to emit energy at 755 nm wavelength, corresponding to the middle of the melanin absorption spectrum.
- The 755 nm Alexandrite laser typically has a larger spot size and higher repetition rate than 694 nm Ruby laser.
- The longer wavelength of the 755 nm laser results in slightly deeper penetration and avoidance of epidermal melanin when compared to the long-pulsed 694 nm Ruby laser, yet is still not ideal for darker skin types.

800 nm Diode Laser

- Like the 755 nm Alexandrite, the 800 nm diode produces light in the middle of the melanin absorption spectrum, with greater depth penetration than the 694 nm Ruby and 755 nm Alexandrite lasers.
- It has been suggested that lower fluences with either longer pulse durations or higher repetition rates may help when treating ethnic skin in order to avoid epidermal damage, however it is not the wavelength of choice for darker skin [10].

1,064 nm Long-Pulsed Nd:YAG Laser

- The 1,064 nm Nd:YAG possesses the single deepest-penetrating wavelength of all the laser systems used for hair removal.
- When compared to other available wavelengths, due to its deeper penetration, as well as the fact that the 1,064 nm wavelength is on the tail end of the melanin absorption spectrum, it is more effective in bypassing epidermal melanin absorption.
- For this reason, this wavelength may cause fewer side effects when treating Fitzpatrick skin phenotypes IV–VI, but is generally less effective [11, 12].

IPL (515–1,200 nm)

- IPL systems emit broadband non-coherent light, targeting chromophores such as water and hemoglobin, in addition to melanin.
- Its larger spot size (120–450 mm^2) allows it to treat large areas such as the back or chest.
- Due to their broad emission spectrum, and thus decreased selectivity, efficacy and side effect rates may be extremely varied.
- Spectra may be tailored with the addition of optical filters [13].

Q-Switched Nd:YAG Lasers

- Q-switched, as opposed to long-pulsed, delivers energy through an aperture-like device, maximizing energy and peak power with a short pulse duration (nanosecond range).
- Efficacy for this form of delivery is varied as some authors suggest the pulse duration is too short to properly heat the target hair follicle [14]. Others report moderate efficacy

with high patient satisfaction [15, 16]. The long-pulsed Nd:YAG is nonetheless more commonly used.
- The Q-switched 1,064 nm Nd:YAG has also been shown to be effective in improving symptoms of pseudofolliculitis barbae [4].

Radiofrequency

- Radiofrequency devices do not specifically target melanin.
- They, however, have been studied in conjunction with IPL and diode lasers to increase effectiveness, particularly with difficult to treat fine or fair hairs [17, 18].
- One study found that the addition of aminolevulinic acid to radiofrequency/IPL hair removal increased efficacy in removal of white terminal hairs [19].

Indications

- Aesthetic removal/reduction of unsightly or unwanted hair.
- Medical conditions where excessive hair growth may be characteristic, or conditions where hair removal may improve course of disease.[1] These include:
  - Idiopathic hirsutism: male-pattern, androgen-dependent hair growth in women not secondary to any identifiable factor.
  - Local acquired hypertrichosis[2].
  - Pseudofolliculitis barbae.

[1]When evaluating for idiopathic hirsutism, it is important to rule out conditions in which increased hair growth may be a harbinger for more serious underlying conditions. These may include polycystic ovarian syndrome (PCOS), congenital andrenal hyperplasia (CAH), or malignancies (Table 10.1).
[2]Generalized secondary hypertrichosis, typically drug-induced, may resolve with removal of the inciting agent (Table 10.2).

- Laser hair removal has been shown to be most safe and effective in patients with fair skin and dark, course hair due to the ability for laser wavelengths to more selectively target melanin in the hair follicle.
- With proper wavelength, fluence, spot size and pulse duration selection, patients with Fitzpatrick skin types IV or greater may be treated with variable success.

Contraindications

- Unable to tolerate other forms of light therapy, such as:
  - Patients with seizure disorders triggered by light
  - Patients with lupus erythematosus
  - Patients who have received or are currently receiving gold therapy
  - Patients with a light sensitivity disorder
  - Patients taking medication that increases sensitivity to light
- Active local infections.
- Pregnant (effects on fetus are unknown).
- Patients with tattoos in the area to be treated should be advised that changes in tattoo color might occur.
- History of depilation within 2 weeks prior to treatment. Removal of the hair follicle prior to laser therapy may decrease effectiveness.

Procedural Technique/Considerations

Pre-op Care

- A full medical history should be obtained prior to the first laser hair removal session. This should include:
  - Current medications
  - History of recent sun exposure
  - Endocrine status
  - History of light insensitivity

  - Scarring tendencies
  - Recent hair removal methods that may have been performed as well as any side effects that may have been experienced with them

- Conditions and medications that may cause hirsutism or hypertrichosis can be found in Tables 10.1 and 10.2.
- Patient expectations should be discussed prior to treatment.
  - Laser hair removal has only been shown to result in the permanent reduction of hair quantity, not in permanent total hair loss (no matter how many sessions are performed).
  - While total hair loss may be seen for some weeks to months, hair re-growth is expected.
  - Hair loss may not occur immediately after treatment. It may take up to 2 weeks for affected hair to fall out.
  - Fair or velus hair that grows from treated areas may darken over time.

- Patients should be counseled to avoid plucking or electrolysis 4 weeks prior to treatment.
- Sun exposure to treated areas should be none to minimal beginning 6 weeks before the procedure to 6 weeks after the procedure, especially if at risk for hyperpigmentation.
- If there is a history of herpes simplex virus (HSV) outbreaks in the area to be treated, antiviral prophylaxis can be given for 1 week, started 2–3 days prior to laser treatment.
- A test spot may be performed in an area that is discrete, yet similar in skin color, sun exposure and hair density to the treated area.

  - Each setting should be tested with four, 10 % overlapping spots.
  - It may take 1–2 days to demonstrate side effects.
  - Erythema and perifollicular edema are expected (Fig. 10.1).
  - Intolerable pain, erythema and edema that last for longer than a few hours, blistering or crusting are all indications that fluence should be decreased.

Table 10.1 Conditions that may result in unwanted hair growth, hirsutism and hypertrichosis [20–22]

Underlying condition	Types	Associated symptoms	Possible sequelae
Hirsutism			
PCOS	n/a	Menstrual irregularities	Mood irregularities
		Male-pattern balding	Metabolic disorders
		Acne	Subfertility
		High serum androgens	
		Central obesity	
Ovarian hyperthecosis[a]	n/a	Same as above	Insulin resistance
		Post-menopausal	Cardiovascular disease
CAH	Non-classic (late-onset)	Premature pubarche	Subfertility
		Acne	
		Accelerated bone age	
		Menstrual irregularities	

Insulin resistance syndromes	Type A, Type B syndromes	Virilization	Acanthosis nigricans
		Amenorrhea	Subfertility
		Lipoatrophy/dystrophy	Other autoimmune disorders
Tumors	Adrenal	Virilization	Usually malignant
		Amenorrhea	
		Cushing's syndrome	
	Ovarian	Refractory hypertension	Usually malignant
		Hypokalemia	
		Abdominal pain	
		Palpable mass	
	Pituitary adenoma	Cushing's syndrome (disease)	

(continued)

Table 10.1 (continued)

Underlying condition	Types	Associated symptoms	Possible sequelae
Hypertrichosis			
Hypothyroidism	n/a	Course, dull scalp hair	Resolves with hormone replacement
		Pretibial myxedema	
Anorexia nervosa	n/a	Generalized lanugo	Malnutrition
			Electrolyte abnormalities
			Death
Porphyria	Cutaneous	Sensitivity to light	Hepatic fibrosis
			Cirrhosis
Dermatomyositis	Juvenile	Proximal muscle weakness with dermato®logic manifestations	Internal malignancies
		Pain	
Polymyositis	Adult-onset	Proximal muscle weakness	Blood and solid organ malignancies
			Interstitial lung disease

PCOS polycystic ovarian syndrome, *CAH* congenital adrenal hyperplasia
[a]Unclear if ovarian hyperthecosis is on the spectrum of disease for polycystic ovarian syndrome

Table 10.2 Agents that may result in hirsutism or hypertrichosis [20, 23]

Drugs that may cause unwanted hair growth	
Hirsutism	**Hypertrichosis**
Danazol	Phenytoin
Testosterone	Cyclosporine
Metyrapone	Penicillamine
Corticotropin	Diazoxide
Glucocorticoids	Minoxidil
	Psoralen
	Streptomycin
	Valproic acid

Technical Considerations

- Protective eyewear must always be used.
- Consult laser manual for specific fluences, spot sizes and pulse durations as these differ between laser systems. Many programs have pre-set parameters based on skin phenotype.
- Larger spot sizes may be more effective for hair removal at identical fluences [24].
- Hair in the treated area should be shaved or trimmed to avoid thermal damage from heat diffusion.
- A mild cooling spray or dynamic cooling device can be used to improve patient safety and comfort.
- Topical anesthetics may be used for patient comfort.

Post-op Care

- Wound care and/or dressings are typically not necessary following treatment.
- Arrange open lines of communication should any adverse events occur.
- Multiple laser treatments may be necessary to yield effective clinical results [25].

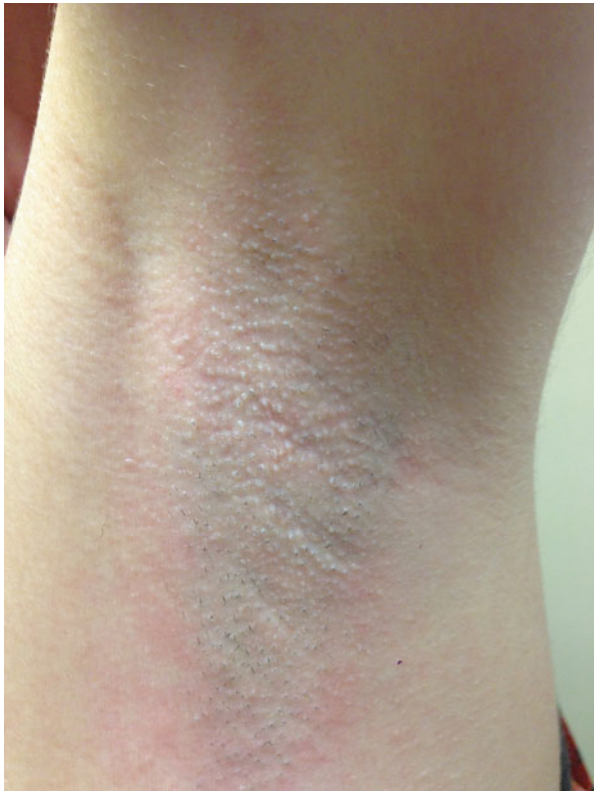

Figure 10.1 Expected erythema and perifollicular edema immediately after procedure

Complications

The reported incidence of complications following laser for hair removal is low, however side effects are more common in patients with Fitzpatrick skin types IV–VI due to competition with epidermal melanin.

- Expected side effects:
  - Pain (mild to moderate)
  - Erythema
  - Perifollicular edema

- Unwanted side effects:
  - Temporary dyspigmentation
  - Blistering
  - Crusting
  - Infection
  - Scarring
  - Hypertrichosis

Prevention and Management of Complications

- Topical anesthetics may be used. If pain is intolerable, however, strength may be too high.
- The risk of blistering and crusting, and thereafter infection and scarring are more common when treating patients with darker pigmentation or patients who have had recent sun exposure to the treated area [26]. Careful selection of wavelength, fluence and pulse duration can help minimize the risk of these effects [27]. Test spots may also help identify settings.
- The etiology of paradoxical hypertrichosis is unknown, yet it is thought to be related to sub-therapeutic dosing [28]. It is more common in Fitzpatrick skin types III and IV, particularly patients of Mediterranean or Pacific Asian descent, as well as patients with hirsutism [6, 7].
- Patients should be reassured regarding expected side effects of erythema and perifollicular edema.
- Physicians should always make themselves available to address any and all questions and concerns patients may have.

Conclusion

- Lasers and IPL are an effective means of reducing hair growth.
- Laser hair removal does not result in the total, permanent loss of hair.
- Treatment typically requires several sessions to maintain hair loss.

- Home-based systems are not as effective as professional systems.
- Future studies are needed to optimize laser hair removal of white, blonde, and red hairs.
- A highly effective and safe hair removal system for patients with deeply pigmented skin is still currently not available.

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Chapter 11
Resurfacing

Jill S. Waibel and Chad Hivnor

Abstract One of the most popular treatments for rejuvenation of aging skin is resurfacing. Skin resurfacing removes the outer layers of photodamaged skin with subsequent re-epithelization and neocollagenosis. Resurfacing procedures create a controlled injury to the skin to a desired depth to stimulate new epidermis and dermis with improved skin characteristics. Of all of the possible procedures for resurfacing, lasers offer the most precision.

Ablative resurfacing with carbon dioxide (CO_2) is considered the gold standard for laser resurfacing (Lask et al.,

J.S. Waibel, MD (✉)
Miami Dermatology and Laser Institute,
7800 SW 87th Avenue, Suite B-200, Miami, FL 33173, USA

Department of Dermatology and Cutaneous Surgery,
University of Miami, Miller School of Medicine,
Miami, FL, USA

Department of Internal Medicine, Baptist Hospital,
Miami, FL, USA
e-mail: jwaibelmd@miamidermlaser.com

C. Hivnor, MD
Dermatology Department, San Antonio Uniformed Health Education Consortium, 3600 Berquist Av Ste 1, 59 MDSP/SGO7D, Lackland, AFB, TX 78236, USA
e-mail: chivnor@gmail.com

K. Nouri (ed.), *Handbook of Lasers in Dermatology*,
DOI 10.1007/978-1-4471-5322-1_11,

Dermatol Surg 21(12):1021–1024, 1995). CO_2 lasers emit light at 10,600nm and are either continuous (CW) or pulsed. The degree of thermal damage is dependent on laser wavelength, irradiance and duration of laser exposure. Continuous wave CO_2 lasers have a myriad of adverse effects. In the 1980s, researchers created short pulsed CO_2 lasers. By using pulse durations shorter than the thermal relaxation time, thermal damage zones were reduced and thus improved the safety profile (Shim et al., Dermatol Surg 24(1):113–117, 1998). Next, pulsed ablative CO_2 lasers were created giving more control of tissue vaporization, decreased thermal damage and improved hemostasis(Dover and Hruza, Semin Cutan Med Surg 15(3):177–188, 1996; Lowe et al., Dermatol Surg 21(12):1025–1029, 1995).

The 2,940 nm Er:YAG device was then developed to reduce adverse effects associated with CO_2 laser. The Er:YAG is absorbed 16 times more strongly by water than the CO_2 laser. Er:YAG ablation is more precise with less thermal damage than the CO_2 laser. Thus Er:YAG resurfacing efficacy increases with increasing depth of ablation (via multiple passes) and increased thermal damage (Ross et al., Lasers Surg Med 30:93–100, 2002)

Although extremely effective for repairing aging skin the adverse events of traditional ablative laser including long post-operative recovery times, significant pigmentary changes and often prolonged erythema caused physicians to search for new options.

In the 1990s non-ablative resurfacing emerged with vascular lasers, mid infrared lasers and Q-switched asers which had modest collagen remodeling with minimal clinical efficacy.

To address the adverse sequelae of ablative resurfacing and limited efficacy of nonablative laser the concept of fractional photothermolysis was developed (Manstein et al., Lasers Surg Med 34:426–438, 2004). In fractional photothermolysis scanners create array of microscopic wounds at deep dermal depths with controlled collateral coagulation. These microscopic wounds result in zones surrounded by normal tissue which allow for rapid healing of the laser treated columns. Fractional laser wounds can be tuned to specific depths with controlled collateral thermal damage. The first fractional

device was the nonablative 1550 nm erbium glass laser. Patients needed multiple nonablative treatments monthly to achieve significant clinical results. Next was the development of fractional ablative CO_2 and Er:YAG devices with impressive histologic and clinical effects (Reilly et al., Arch Facial Plastic Surg 12:321–325, 2010). Non-ablative fractional resurfacing (NAFR) results are less robust, but have minimal downtime whereas ablative fractional resurfacing (AFR) and traditional resurfacing have variable degrees of downtime, but greater efficacy. Adverse events appear highest with traditional resurfacing (Tanzi and Alster, Plast Reconstr Surg 111(4):1524–1529, 2003).

Now with a greater understanding of the pros and cons of all resurfacing modalities we are experiencing a laser resurfacing renaissance. Laser physicians are now combining modalities such as traditional resurfacing to difficult rhytides (periorally) and treating the rest of the face with fractional lasers. Fractional lasers are emerging as an important modality in the treatment of scars (Reilly et al., Arch Facial Plastic Surg 12:321–325, 2010; Tanzi and Alster, Plast Reconstr Surg 111(4):1524–1529, 2003; Waibel and Beer, J Drugs Dermatol 7(1):59–61, 2008; Tierney et al. Dermatol Surg 35(8):1172–1180, 2009). Individualized skin rejuvenation for patients include fully ablative, fractional ablative, non-ablative fractional lasers with injectables and surgical interventions or any combination of these techniques.

Keywords Traditional ablative resurfacing • Fractional ablative resurfacing • Non-ablative fractional laser • Scar laser resurfacing • Carbon dioxide laser • Erbium-YAG laser

Introduction

Skin resurfacing refers to the removal of outer layers of photodamaged skin to stimulate epidermal re-epithelization and dermal neocollagenosis. The need for resurfacing may be a result of aging, sun exposure, burns, radiation, trauma,

heredity and other lifestyle factors which can include nutrition, alcohol consumption and smoking. These alterations may occur with age, hormonal alterations, or other genetic factors. Finally, prior acne and other types of scars may leave pigmentary changes and deeper scar tissue in the dermis may leave uneven surface contours. Resurfacing of the skin and tissues include the process via thermal, mechanical or chemical means to replace damaged skin with healthier epidermis and dermis. Pigmentary alteration, such as blotchiness or brown spots, may be another reason for resurfacing (Fig. 11.1a, b). As you can see skin resurfacing can improve multiple conditions in multiple areas as noted but also scars from surgery, trauma, acne, or burns may be improved by skin resurfacing (Figs. 11.2a, b, 11.3a, b, and 11.4a, b).

Aesthetic resurfacing may be accomplished using multiple modalities all of which have varying efficacies and side effect profiles. Resurfacing procedures include chemical peeling, dermabrasion, and laser. Dermabrasion and chemical peeling improve texture and rhytids by damaging the superficial layers of the skin. Results are unpredictable due

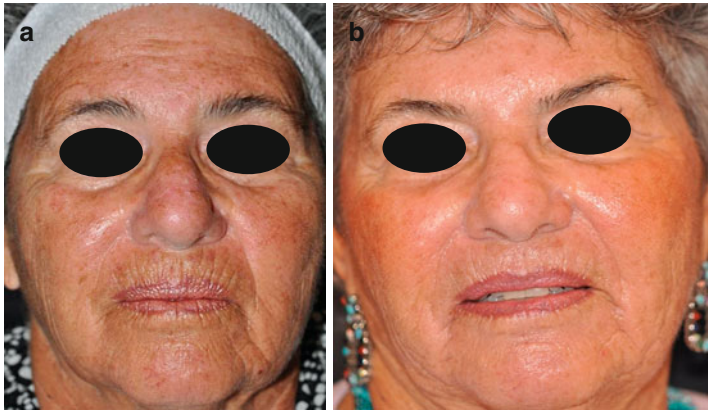

FIGURE 11.1 (**a**, **b**) Baseline and 3 months post ablative fractional resurfacing (AFR)

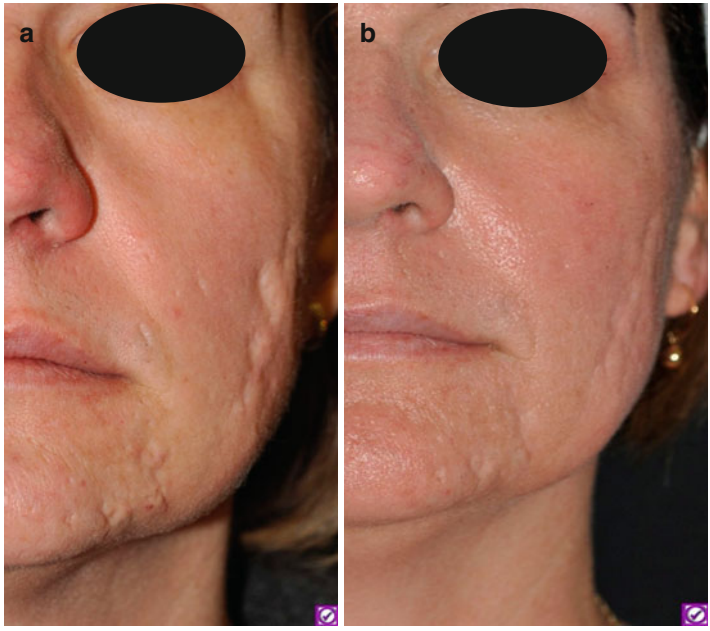

FIGURE 11.2 (**a**, **b**) Surgery Acne scars before and after a series of AFR

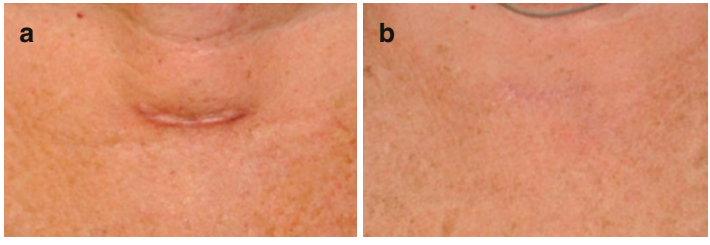

FIGURE 11.3 (**a**, **b**) Thyroidectomy surgical scar before and after AFR

to lack of ability to control the depth of tissue removal with accuracy. Lasers are precise tools based on physics and thus the preferred choice for resurfacing. This chapter primarily addresses laser resurfacing.

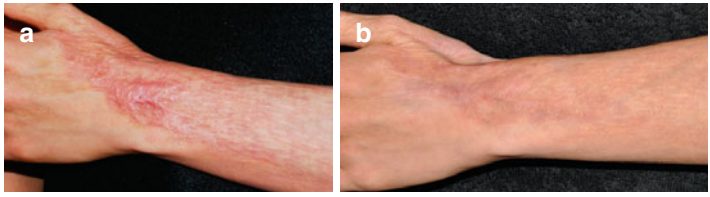

FIGURE 11.4 (**a**, **b**) Burn scar before and after AFR

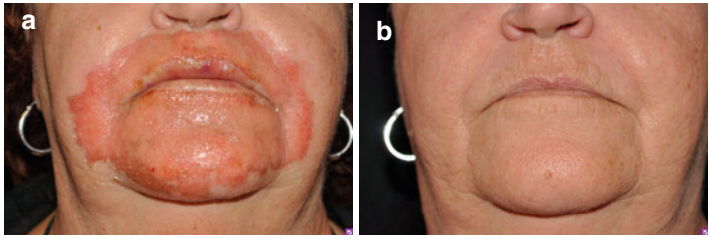

FIGURE 11.5 (**a**,**b**) Downtime traditional ablative resurfacing 10–14 days

Historically, traditional resurfacing with carbon dioxide (CO_2) and erbium yttrium aluminum garnet (Er:YAG) lasers had excellent clinical outcomes for photodamaged skin but had increased post-operative recovery and unacceptable rate of potential side effects [10]. These problems led the laser industry to create non-ablative laser devices with limited clinical effectiveness. In 2004 fractional photothermolysis emerged into the laser world giving physicians and patients a tool that had significant results with decreased post-operative healing and increased safety profile [6]. Fractionated technology was developed as both non-ablative fractional resurfacing (NAFR) devices and ablative fractional resurfacing (AFR) devices (Figs. 11.5a, b, 11.6a, b, and 11.7a, b). Fractional lasers have proven to be a mainstay in laser resurfacing for both photoaging and all types of scars. Today physicians are able to customize treatments for a patient by traditional ablative and fractional lasers as well as other aesthetic procedures.

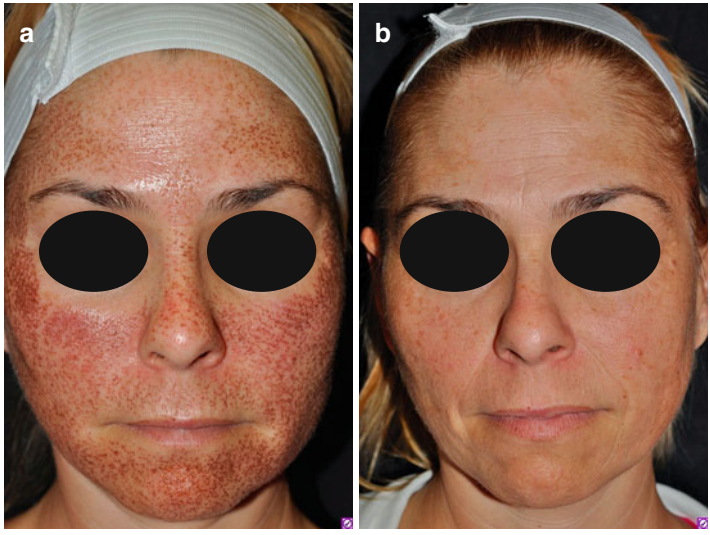

FIGURE 11.6 (**a**, **b**) Downtime fractional ablative resurfacing (AFR) 5–7 days

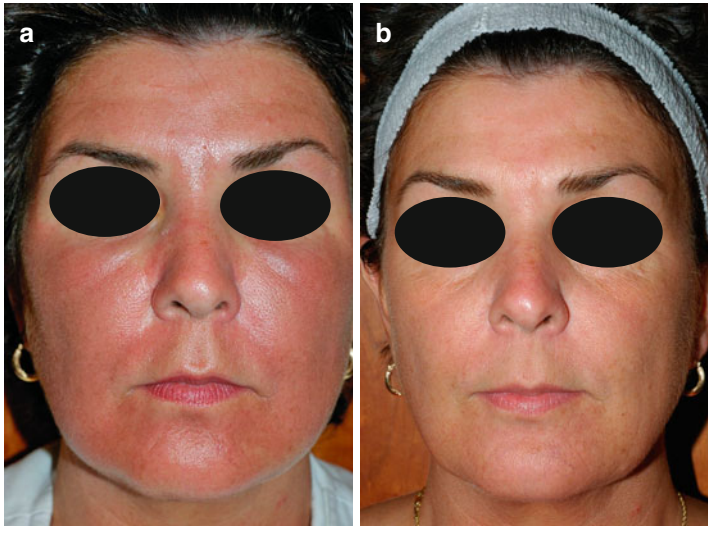

FIGURE 11.7 (**a**, **b**) Downtime non-ablative fractional resurfacing (NAFR) – 3–4 days

Background

During the 1990s and early 2000s the gold standard for the treatment of facial rhytides and photodamage from a laser perspective was traditional CO_2 resurfacing [11]. These lasers were either continuous (CW) or pulsed beams that removed all of the epidermis and a portion of the dermis [3]. The traditional resurfacing laser injury would heal with fibroplasia and neocollagenosis with excellent results. CO_2 laser technology was developed with shorter pulse durations or in the case of continuous mode laser devices with scanning technology both of which left shorter dwell times to minimize thermal damage [1, 2]. Pulsed ablative CO_2 lasers with pulse durations shorter than the thermal relaxation times allowed more precision of tissue vaporization, minimal thermal damage, and hemostasis [4]. The effectiveness of CO_2 devices was undermined by its side effect profile which included prolonged erythema, infection, delayed onset hypopigmentation and scarring. Next the Er:YAG laser was studied for traditional resurfacing. Er:YAG has a higher absorption coefficient for water (16 times) than CO_2 laser and thus results in more shallow ablation depths in tissue. The Erbium proved to be a good resurfacing tool especially when the pulse width was lengthened which allowed for more of an effect [5]. With this added effect increased the side effect profile to that of traditional CO_2. Traditional ablative laser resurfacing is considered the gold standard, however due to the increased risk for prolonged wound healing, permanent hypopigmentation, infection and scarring physicians and industry continued to search for other solutions [8].

Fractional photothermolysis was first described by Manstein et al. [6] as a new method for delivery of laser energy with the potential for improved safety. The nonablative resurfacing device produced an array of microthermal zones creating small columns of thermal injury to the skin. Fractional treatments have small areas of tissue removed

or destroyed with large perimeter-to-area ratio for fast healing. The goal of fractional resurfacing is less downtime however multiple treatments may be necessary to achieve the same results as traditional ablative lasers. Non-ablative fractional lasers give less downtime, less discomfort but also less results per treatment. The drawbacks of non-ablative fractional lasers are that it requires multiple treatments; erythema and edema post-operatively; and incomplete treatment of epidermal damage.

Ablative fractional laser resurfacing (AFR) has precise and deep ablation with control of depth of tissue heating and vaporization [7, 12]. The use of AFR has tried to balance the benefit of traditional resurfacing with the minimization of risk.

The rapid recovery times seen with fractional ablative resurfacing are most likely due to the healing of the wound from adjacent keratinocyte stem cells versus traditional ablative laser wounds healed via migration of stem cells from the hair follicles [13]. This is demonstrated by even some ablative fractionated lasers healing the epidermis within 24–48 h depending on the diameter of the column and depth of penetration to obtain the fractionating. Overall fractional ablative devices appear to have an improved safety profile versus traditional ablative resurfacing. Fractional treatment parameters need to be decreased when treating off-face anatomic locations. The risk of scarring is greater in the neck and chest because these nonfacial areas have fewer pilosebaceous units versus the facial region. Fractional laser treatments have been reported in the literature to cause hypertrophic scars in the neck [14].

Compared with traditional ablative resurfacing wound healing times after ablative fractional treatment is more rapid, infections are less frequent and post-operative downtime is less.

The availability of traditional resurfacing, non-ablative fractional resurfacing and ablative fractional resurfacing give

the physician the ability to customize treatments for patients depending on the patient's goals for resurfacing and their ability to accommodate post-operative downtime.

The remaining sections in this chapter will be broken down by traditional resurfacing, non-ablative fractional resurfacing and ablative fractional resurfacing.

Indications

Traditional Ablative Resurfacing (Fig. 11.8a, b)

- Patients with moderate – severe periorbital and perioral rhytides are best candidates
- Other significant signs of photodamage
  - Actinic keratosis
  - Diffuse solar lentigines and other pigmentary dyschromias
  - Actinically damaged skin

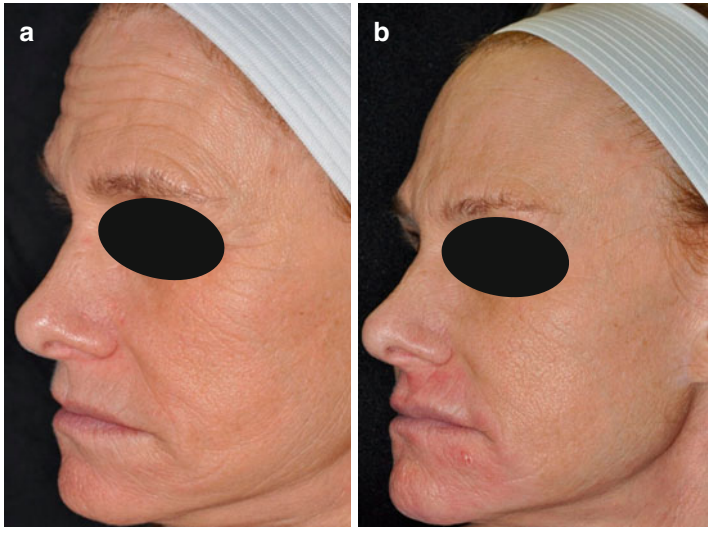

FIGURE 11.8 (**a**, **b**) Traditional erbium ablative surfacing

- Severe Acne scars
- Benign age or genetically related growths (recommend ablative to growths only then fractionating the remainder of skin)

Non-ablative Fractional Resurfacing (NAFR)

- Mild – moderate photoaging safe on all body locations with appropriate settings. Decrease fluence off face, caution in thinner areas of skin such as neck. Appropriate cooling in between passes to avoid bulk heating. Decreased density in skin of color (Fig. 11.9a, b).
- Fine rhytides
- Mild dyschromia
- Scars — atrophic scars, mild acne scars, hypertrophic scars, traumatic and burn scars.
- Striae
- Prominent pores
- Melasma
- Poikiloderma of Civatte
- Minocycline induced facial hyperpigmentation
- Nevus of Ota
- Residual hemangioma
- Disseminated superficial actinic porokeratosis

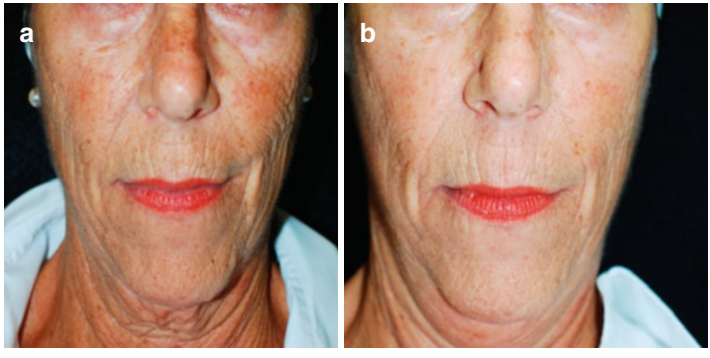

FIGURE 11.9 (**a**, **b**) Actinic damage: combination non-ablative fractional laser treatment & one IPL

Ablative Fractional Resurfacing (AFR)

Many of the indications above, especially when more diffuse and extensive

- Photoaging moderate to severe
  - Face, neck, chest and hands (Figs. 11.10a, b and 11.11a, b)
- Moderate – severe rhytides (Figs. 11.12a, b and 11.13a, b)
- Moderate dyschromia and melasma
- Dermatochalasis, festooning
- Eyelid tightening (Figs. 11.14a, b and 11.15a, b)
- Scars — atrophic, acne, surgical, burn and traumatic
- Benign growths
- Colloid milium
- Seborrheic keratoses
- Sebaceous hyperplasia

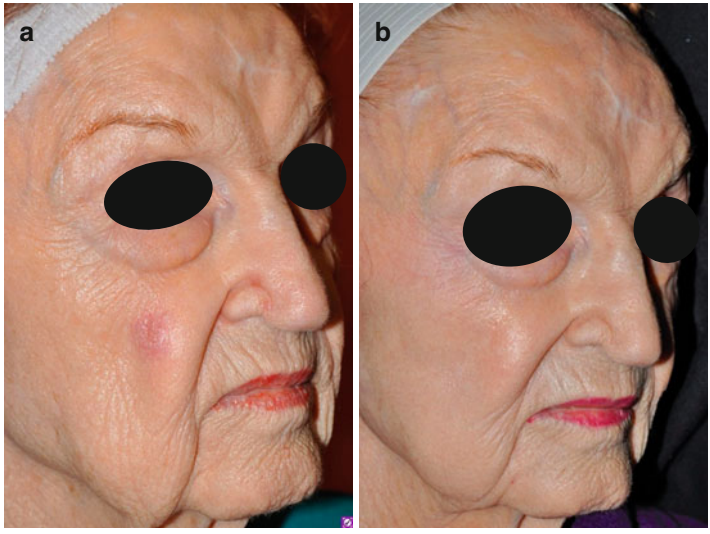

FIGURE 11.10 (**a**, **b**) Before and after fractional ablative resurfacing

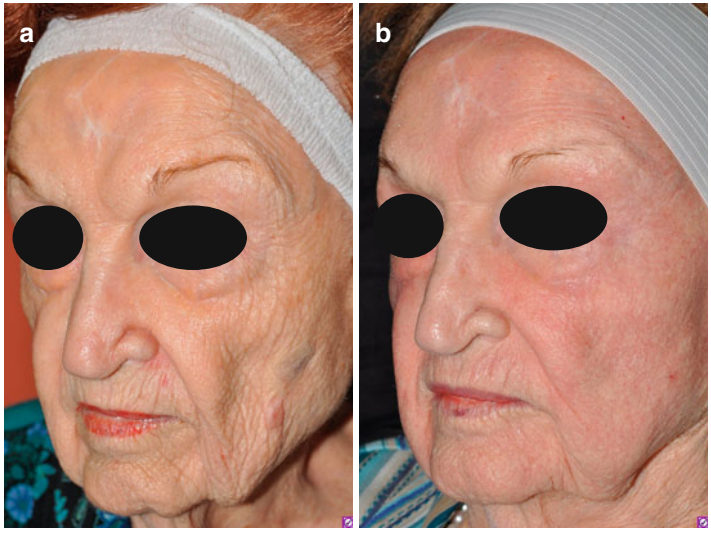

FIGURE 11.11 (**a**, **b**) Before and after fractional ablative resurfacing

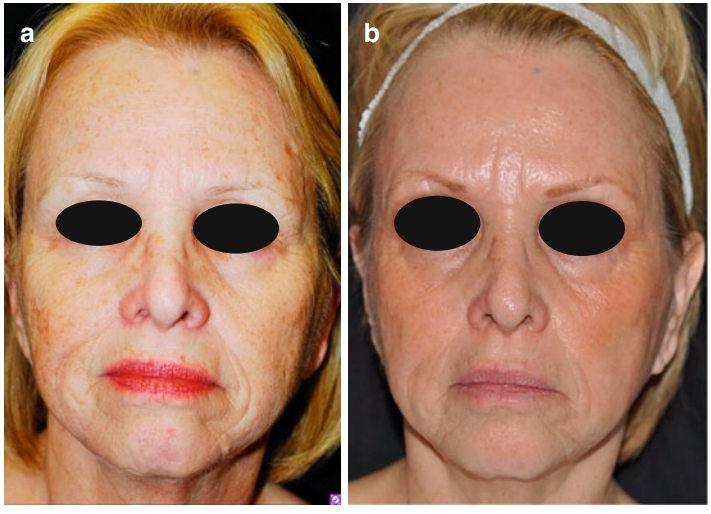

FIGURE 11.12 (**a**, **b**) Before and after fractional ablative resurfacing

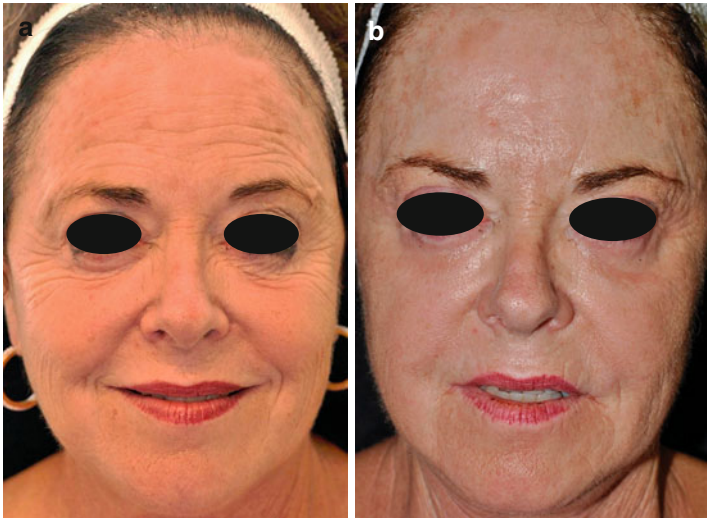

FIGURE 11.13 (**a**, **b**) Before and after fractional ablative resurfacing

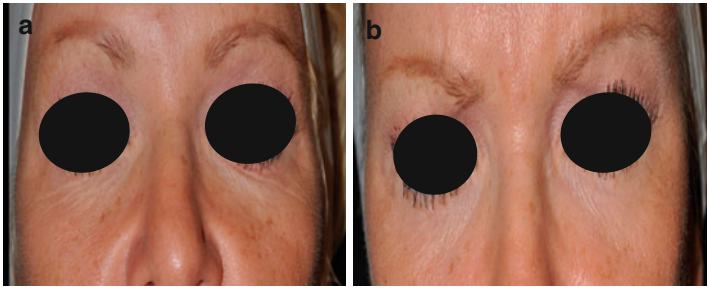

FIGURE 11.14 (**a**, **b**) Before and after fractional ablative periocular resurfacing

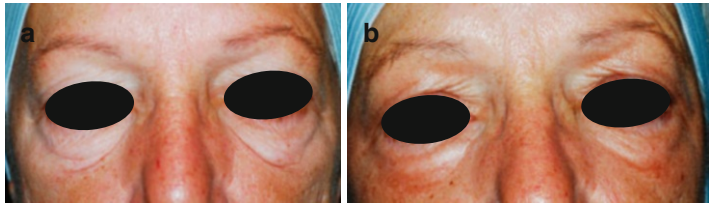

FIGURE 11.15 (**a**, **b**) Before and after fractional ablative periocular resurfacing

Contraindications

Traditional Ablative Resurfacing

- Active infection
- Appendageal abnormality
- Oral retinoids, extensive electrolysis, radiation, autoimmune disease (ie scleroderma), Graft versus Host Disease, or skin grafts after burn or traumatic injury
- Caution in patients with previous lower lid blepharoplasty
- Previous deep chemical peel and dermabrasion within last 3–12 months
- Relative contraindication:
  - Unrealistic expectation
  - Inability to comply with post-operative wound care
  - Regional resurfacing in darker skinned patients
  - History of therapeutic radiation exposure

Fractional Resurfacing Both NAFR and AFR

- Isotretinoin (or associated oral retinoid) current use or 6 months prior
- Active infection
- Unrealistic expectations or inability to comply with post-operative instructions

- Relative contraindication: skin sensitivity to light either from collagen vascular disease or medication
- Relative contraindication: pregnant or breastfeeding mothers should discuss risk and benefit ratio with both laser physician and obstetrician.
- Deep chemical peels and radiation treated patients should be conservative
- History of lower lip blepharoplasty should be conservative

Procedural Technique/Considerations

Pre-operative Considerations Traditional Resurfacing, NAFR and AFR

- As with any procedure a realistic discussion of therapeutic goals, limitations, and potential complications followed by written informed consent should be obtained.
- Pertinent historical information during the initial evaluation includes patient's skin type, has the patient experienced herpes simplex virus, previous eyelid surgery, scar history (does patient form hypertrophic or keloid scars), other medical conditions, radiation therapy, current medications (including herbals), allergies should be documented.
- Physical examination should be performed and document photodamage and scar characteristics. Sclera show, lid lag and eyelid evaluation snap test should be evaluated to determine preoperative eyelid skin elasticity to avoid ectropion formation. Scar characteristics such as the presence of residual erosions and ulcers, erythema, pliability, textural irregularity, dyspigmentation, and scar thickness and degree of restriction. Ensure no active skin cancer is present as the treatment may only treat the superficial aspect.
- Topical or oral antibiotics are not employed under routine circumstances for NAFR, though they may certainly be entertained on a case-by-case basis. Many physicians use drugs against *methicillin resistant staph aureus* (MRSA) when doing traditional resurfacing and AFR.

- When treating facial areas, viral prophylaxis should be considered for both NAFR and AFR and traditional resurfacing. Highly recommend to prophylax all patients with history of herpes simplex virus when doing any laser resurfacing procedure.
- High quality pre-operative photographs need to be obtained.
- The vast majority of traditional and fractionated laser treatments occur in the clinic setting following topical or local anesthesia alone. However, sedation or even general anesthesia may be utilized if requested by patient. If general anesthesia is required recommend a through pre-operative surgical evaluation from patient's internist and other specialist such as cardiologist.

Laser Selection

- Physicians should give patients different laser treatment options depending on the degree of photodamage and the downtime the patient's life can accommodate. Individualized treatment plans are easily obtained with the ability to tune the laser parameters.
- First is the selection of traditional versus fractionated resurfacing

Patients with skin phototypes I and II are best candidates for traditional laser resurfacing.

Severe periocular and periorbital rhytids respond best to traditional resurfacing.

- AFR or NAFR: This is often determined based on the clinical need of the patient (i.e. severity of photodamage or location and thickness of the scar). But this may be determined by post-operative downtime and the amount of peri-operative pain that the patient will be able to tolerate. NAFR and AFR can treat all skin types safely, although it is recommended to turn down density in darker phototype patients and off-facial anatomic locations.

- Few controlled, prospective studies evaluating the comparative efficacy of various fractional devices have been performed, but early reports and the clinical experience of the authors suggests that AFR has the capacity to induce a more robust remodeling response than NAFR.
- Scars should be treated with fractional technology either NAFR or AFR. Traditional resurfacing may worsen scars.
- With fractional non-ablative and fractional ablative resurfacing parameters are decreased for off-face anatomical sites. The risk of scarring is greater in the neck and chest versus the face due to the paucity of pilosebaceous units.

Laser Treatment Technique

- The majority of treatments are performed in the clinic setting using commercially available topical anesthetic preparations under occlusion for 1 h or more prior to treatment.
- Injectable local anesthetics may be utilized in focal areas, and these measures are often supplemented during treatment with a forced chilled-air device (Zimmer Cryo, Zimmer MedizinSystems, Irvine, CA). Some patients may benefit from systemic pre-operative analgesics or anxiolytics. Conscious sedation or even general anesthesia can be employed in instances of large surface area involvement or anticipated poor patient tolerance of the procedure while awake.
- With previous discussion in mind, fractional laser treatment technique, parameters, and adjunctive treatments should be applied thoughtfully to minimize the degree of cumulative thermal injury to the tissue. Each treatment is customized at every session according to the individual SKIN characteristics and interval changes.
- Aggressive pulse energy settings require a concomitant reduction in the treatment density AND/OR rate the potential for bulk heating.
- Adequate procedural documentation should take place by physician at the time of the procedure with appropriate laser logs.

Post-operative Care

- Immediately after traditional and ablative treatments, petrolatum or a petrolatum-based ointment is applied and continued several times daily until the site is fully epithelialized. Inadequate moisturization may lead to irritation and potential of scarring. Too much may increase risk for milia and acne formation. Thus, use of thin layers versus icing on a cake should be employed.
- Patients may resume showering the following day and begin gentle daily cleansing of the area.
- Acetic acid (i.e. dilute vinegar) compresses may be initiated according to the preference of the treating surgeon.
- Photo-protection should be advocated, including avoidance of sun in the early post-treatment period. Start the application of bland sunscreens after reepithelization for traditional resurfacing and AFR and up to 3 months.
- Non-ablative treatments proceed in a similar fashion, but bland emollients and sunblock may be initiated immediately since the epithelium essentially remains intact

Complications

- Infections — viral such as herpes simplex or herpes zoster. For severe progressive viral infection after traditional resurfacing may need IV antivirals.
- Infections — bacterial most common *S. aureus*, *MRSA and pseudomonas*. Treatment includes culture, remove occlusion, broad spectrum antibiotics and acetic acid soaks (*Pseudomonas*).
- Fungal or yeast (candida) infections are rare and after cultured best treated with topical or oral antifungal.
- Post inflammatory hyperpigmentation
- Hypopigmentation from traditional resurfacing. Current data shows that traditional resurfacing had up to 40 % patients with hypopigmentation. Hypopigmentation is rare and usually transient with NAFR and AFR.

- Hypertrophic scars
- Acneiform and milia (thought secondary to occlusion)
- Telangiectasia
- Capillary fragility
- Irritant or contact dermatitis
- Ectropion
- Synechia
- Persistent erythema
- Pruritus
- Pain during procedure
- Scarring
- Lack of satisfaction with the procedure

Prevention and Management of Complications

- Caution advised with traditional resurfacing if significant lower eyelid laxity, neck and body resurfacing or Fitzpatrick skin types 5 or 6.
- Consider antiviral prophylaxis for all traditional ablative resurfacing and fractional ablative resurfacing. Start medication 1 day prior and continue until full repithelization, usually 7–10 days.
- Antiviral prophylaxis for non-ablative fractional laser treatments in patients with history of herpes simplex virus. Start 1 day prior and use for 7 days.
- Antibiotic prophylaxis with the purpose of avoiding bacterial infection is controversial. Many physicians use for traditional resurfacing and AFR until re-epithelization is complete to prevent MRSA infections.
- Epithelialized skin after resurfacing is very sensitive so warn patients to be careful with any topical products for 1 month. A common encountered problem within this time frame is irritant contact dermatitis.
- Post-inflammatory hyperpigmentation (PIH) — there is no need for hyperpigmentation prophylaxis for deep laser resurfacing because melanocytes are destroyed with first laser pass. If PIH develops recommend sun avoidance,

retinoid cream and hydroquinone cream every night with judicious sunblock every morning. If resistant PIH consider use of Thulium or Q-switched laser.

- Current long term data reports numbers as high as 40 % of patients with traditional CO_2 resurfacing had hypopigmentation.
- Early treatment of hypertrophic scars from laser resurfacing includes topical and intralesional steroids, occlusion therapy and vascular or NAFR laser.
- If acne outbreak after laser resurfacing recommend stopping occlusive agents, consider oral tetracycline antibiotic. Milia can be opened with 18–30 gauge needle or just let them self-resolve with time.
- Telangiectasia or capillary fragility may develop from healing of laser resurfacing or by topical steroid application. Telangiectasia may be treated with vascular lasers such as pulsed dye, KTP or long pulsed Nd:YAG.
- Dermatitis is common if active ingredient introduced too soon after laser resurfacing. Recommend gradual reintroduction of topical and retinoids after 1 month. Contact dermatitis is common after topical antibiotic ointment. It is important to discontinue product causing dermatitis.
- Ectropion tends to be temporary and usually resolves 3–4 months. Treatment involves massage and cathopexy if does not correct after 6 months.
- Synechia is more commonly seen with Erbium resurfacing and may be treated by a small incision into the synechia.

Future Directions

In recent years there has been a transition from traditional resurfacing to fractional laser for aging, photodamaged and scarred skin. The non-ablative therapies are less robust but have minimal downtime whereas ablative and traditional have variable degrees of downtime but greater efficacy. Now with a greater understanding of the pros and cons of all resurfacing modalities we are again experiencing a laser resurfacing

renaissance. Laser physicians are now combining modalities such as traditional resurfacing to difficult rhytides periorally and treating the rest of the face with AFR or NAFR lasers in the same treatment session. Laser resurfacing treatments are customized to treat the photodamage and rhytides in each area with precision of depth, patient's ability to tolerate post-operative downtime and best safety profile. Laser resurfacing procedures are often used in conjunction at same visits of dermal fillers for concomitant volume restorers.

Fractional lasers are emerging as gold standard in the treatment of scars. Much like the cosmetic patient each scar patient should have customized treatment. Fractional lasers have given new hope to all scar patients. Lasers can be used to treat and favorably modify many if not all of these abnormal scar characteristics.

Lastly we are seeing the emergence of using fractional lasers for preventative aging. Younger patients are seeking NAFR for skin health maintenance and for anti-aging purposes. Laser physicians have noticed patients with regular maintenance laser sessions seem to age more gracefully with healthier skin. More studies are needed to fully understand the effects of photons on the prevention of aging.

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Chapter 12
Fractional Devices

Jill S. Waibel

Abstract Fractional photothermolysis has been a significant breakthrough in clinical laser science. Fractional lasers employ technology which splits the laser beam into hundreds of microbeams, creating patterns of thermal microscopic wounds that reach deep dermal depths. These small wounds allow a rapid healing response. This method of fractional skin resurfacing has led to clinical efficacy in aesthetic and scar treatments with high physician and patient satisfaction. Fractional lasers have a superior safety profile when compared with traditional resurfacing techniques.

Fractional laser devices may be either non-ablative or ablative. Non-ablative fractional resurfacing (NAFR) heats up the dermis from 50 to 100 °C; which induces collagen to undergo irreversible coagulation of proteins. Ablative fractional resurfacing (AFR) heats up the dermis to greater than

J.S. Waibel, MD
Miami Dermatology and Laser Institute,
7800 SW 87th Avenue, Suite B-200, Miami, FL 33173, USA

Department of Dermatology and Cutaneous Surgery,
University of Miami, Miller School of Medicine,
Miami, FL, USA

Department of Internal Medicine, Baptist Hospital,
Miami, FL, USA
e-mail: jwaibelmd@miamidermlaser.com

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100 °C; causing vaporization of tissue within the immediate area surrounded by a thermal coagulation zone.

NAFR devices were introduced in 2004 with a better safety profile but decreased efficacy versus traditional resurfacing devices (Manstein et al., Lasers Surg Med 34:426–438, 2004). NAFR has become a popular worldwide procedure due to its effective epidermal and dermal rejuvenation, increased safety profile, decreased post-operative downtime, use on all anatomical areas, and wide spectrum of medical and aesthetic indications. NAFR can be used for mild-moderate rhytids, leukoderma, atrophic and hypertrophic scars and many other indications.

Despite the success of non-ablative fractional lasers there remained a need for more aggressive tissue ablation for the purposes of rejuvenation of severely photodamaged skin, deeper rhytids and severe scars. AFR devices entered the market in 2007 with improved efficacy over NAFR.

There are many fractional devices currently on the market. Many of these devices have distinct technological characteristics that maximize safety and efficacy. This chapter reviews and discusses fractional devices and fractional treatment pearls.

Keywords Fractional lasers • Non-ablative fractional lasers • Ablative fractional lasers • Resurfacing • Scars • Laser complications

Introduction

Fractional photothermolysis was a significant breakthrough in laser technology that occurred in 2004 [1]. This unique concept of wounding creates a pattern of hundreds of microscopic thermal injuries to the skin. These fractionated laser beams create wounds with diameters ranging from 120 to 500 μm that reach deep dermal depths with rapid wound

healing. Due to the small size of the fractional wounds, there is a unique molecular cascade of healing which stimulates prolonged neocollagenesis and a rapid healing response [2]. This method of fractional resurfacing has proven clinically efficacious for aesthetic procedures, scar rehabilitation and many other clinical indications. Fractional lasers have a better safety profile than traditional resurfacing techniques.

Fractional lasers may be either non-ablative or ablative. Non-ablative devices deliver less thermal energy (usually <70 °C) and work by coagulation of collagen. This thermal damage leads to an increased expression of heat shock proteins which activate epidermal stem cells to proliferate and replace damaged photoaged or scarred tissue. Non-ablative fractional resurfacing (NAFR) has become widely recognized for cosmetic improvement of photoaged skin [3] as well as improvement for acne, surgical, traumatic and burn scars [4, 5].

Ablative fractional resurfacing (AFR) emerged in 2007. The mechanism of action for ablative fractional therapy is more complex with ablation temperatures reaching in excess of 100 °C causing fractionated columns of epidermis and dermis to be vaporized. AFR create focal microscopic full thickness wounds. Elimination of the damaged epithelia and shrinkage of collagen fibers occurs immediately after AFR. Over the next 6 months, neocollagenesis ensues in the treated tissue. Remodeling after AFR is started by regrowth of the epidermal compartment followed by healing of ablated zones of dermal collagen. In scar rehabilitation, there also is evidence of recreation of dermal epidermal ridges, returning skin histologically to normal skin.

Multiple reports suggest AFR is emerging as a gold standard for the treatment of scars [6, 7]. Traditional ablative resurfacing is the gold standard for treatment of wrinkles and photoaged skin. In 2010, Orringer quantitatively compared molecular changes after traditional resurfacing to the changes that laser resurfacing showing ablative fractional resurfacing was 65 % as effective as traditional resurfacing [8].

Background

Non-ablative Fractional Resurfacing (NAFR)

Fractional photothermolysis was first described by Manstein et al. [1] as a new method for delivery of laser energy with improved safety over traditional resurfacing. Through the delivery of microscopic, non-contiguous zones of thermal damage using a mid-infrared laser source the surrounding untreated islands of dermal and epidermal cells facilitated post-treatment collagen remodeling. The depth of epidermal and dermal coagulation is proportional to treatment energy (mJ) and is tunable. The first commercially available device for NAFR was introduced by Reliant Technologies in 2004. This device showed complete reepithelization in 24 h and collagen denaturation from papillary dermis to mid-reticular dermis depending on the treatment energy. The healing response occurs from the zones of spared tissue by activating epidermal stem cells. Non-ablative fractional light sources including a 1,550, 1,540 and 1,440 nm wavelengths are reviewed in Table 12.1.

Another novel non-ablative fractional laser is the Thulium 1,927 nm. It has moderate to high water absorption—making it ideal for superficial resurfacing. The 1,927 nm wavelength is very useful for the treatment of dyschromias including photodamage, photoinflammatory hyperpigmentation and hemosiderin deposition.

Ablative Fractional Resurfacing

Non-ablative fractional devices have achieved worldwide popularity due to their effectiveness, safety and decreased post-operative downtime. However, review of the literature has shown AFR produces superior clinical results to NAFR in fewer treatment sessions [9, 10, 11].

There are many ablative fractional devices available in the market with a myriad of differences (Table 12.2). Some

Table 12.1 Non-ablative fractional devices

Device	Manufacturer	Laser	Wavelength (nm)
Affirm	Cynosure	Nd:YAG and xenon pulsed light	1,440 ± 1,320
Fraxel dual	Valeant Pharmaceuticals	Erbium fiber	1,550
		Thulium fiber	1,927
ResurFX	Lumenis	Er:Glass fiber	1565
Lux 1540	Palomar	Er:Glass	1,540
Lux 1440		Nd:YAG	1,440
Lux deep IR		Infrared	850–1,350
Halo	Sciton	Hybrid fractional	1470
eMatrix	Syneron/ Candela	Diode/bipolar radiofrequency	

of these differences include wavelength, spot size, delivery method (stamped vs scanning), depth of ablation, amount of coagulation (extent of total thermal damage) and speed of treatment.

Fractional ablative lasers have had ongoing innovation with second generation devices on the market. Syneron Candela Corporation put forth the CO_2RE resurfacing system which has the ability in fusion mode to have one laser pulse with two simultaneous depths of penetration to treat both epidermis and dermis at the same time. Palomar Medical Technologies introduced the erbium yttrium aluminum garnet (Er:YAG) laser plus groove optic as the first AFR device to induce a noncylinder fractional injury (Fig. 12.1). These fractional grooves generate a directional injury and crossed linear patterns that can be customized by the physician. Lumenis' SCAAR FX (Synergistic Coagulation and Ablation for Advanced Resurfacing). Provides 150 mJ per pulse; and by reaching up to 4.0 mm into the dermis, this mode can treat all depths of complex, deep lesions effectively.

Table 12.2 Ablative fractional devices

Device	Manufacturer	Laser	Wavelength (nm)
Affirm CO_2	Cynosure	CO_2	10,600
CO_2RE	Syneron/ Candela	CO_2	10,600
eCO_2	Lutronic	CO_2	10,600
Fraxel Re:pair	Solta medical	CO_2	10,600
Juvia	Ellipse Inc	CO_2	10,600
Lux 2940	Cynosure Palomar	Er:YAG	2,940
Groove	Cynosure Palomar	Er:YAG	2,940
Mixto SX	Lasering	CO_2	10,600
Pearl fractional	Cutera	YSGG	2,790
Pixel harmony	Alma	Er:YAG	2,940
Pixel CO_2	Alma	CO_2	10,600
Profractional	Sciton	Er:YAG	2,940
SmartXide DOT	Eclipsemed	CO_2	10,600
Halo	Sciton	Hybrid Erbium fractional	1470 & 2940
SP plus	Fontana	Nd;YAG/ Er:YAG	
SP dualis		Nd:YAG/ Er:YAG	
XS dualis		Er:YAG	
XS fidelis		Er:YAG	
Ultrapulse active FX	Lumenis	CO_2	10,600
Ultrapulse deep FX			
SCAAR FX			

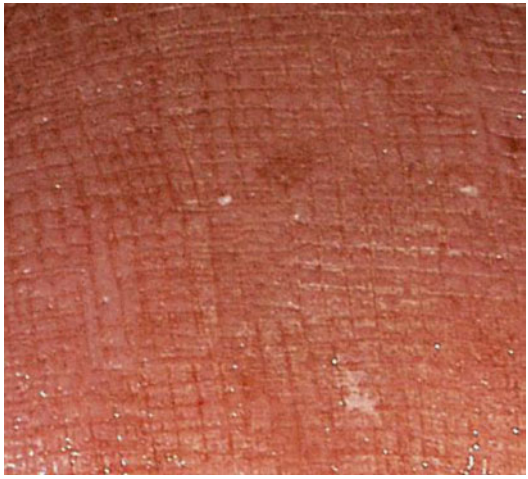

FIGURE 12.1 Lines of ablations with 2,940 Er:YAG laser plus groove optic

Indications

Non-ablative Fractional Resurfacing

- Photoaging of face, neck, hands – (Fig. 12.2)
- Fine rhytides
- Mild dyschromia and post-inflammatory hyperpigmentation (PIH) (Fig. 12.3)
- Scars — atrophic, hypopigmented, acne, hypertrophic, traumatic and burn scars (Fig. 12.4)
- Striae distensae (Fig. 12.5)
- Prominent pores (Fig. 12.6)
- Melasma (Fig. 12.7)
- Poikiloderma of Civatte temporary improvement of melasma, not curative
- Minocycline induced facial hyperpigmentation
- Nevus of Ota

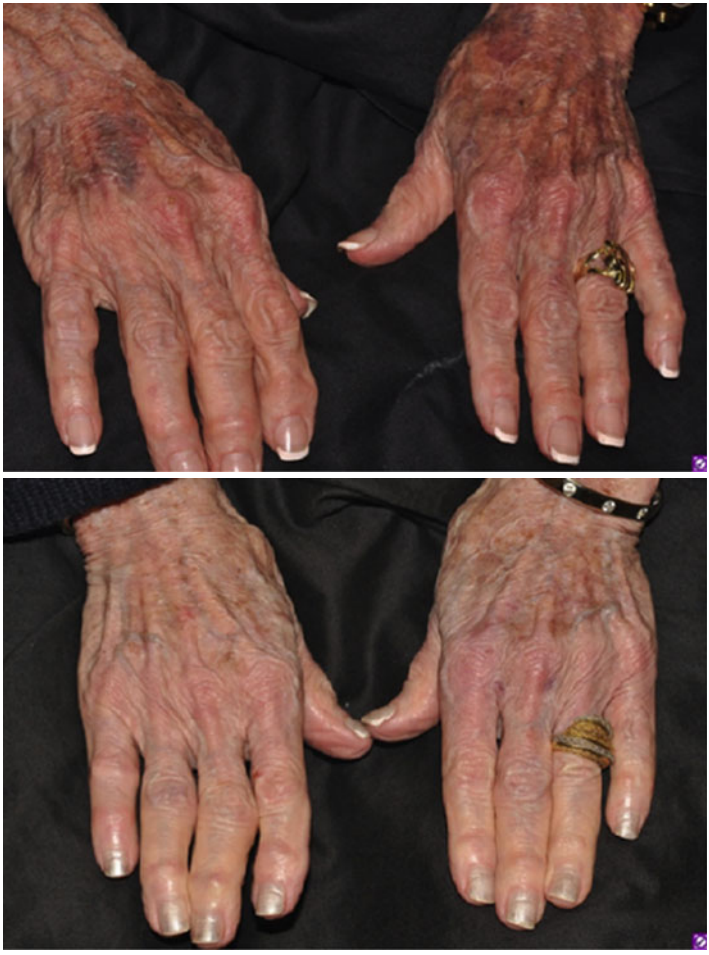

FIGURE 12.2 Before and after 2 treatments of 1,927 nm Thulium non-ablative fractional laser for severely actinic damaged hands

- Residual hemangioma
- Disseminated granuloma annulare
- Disseminated superficial actinic porokeratosis
- Colloid milium
- Telangiectatic matting

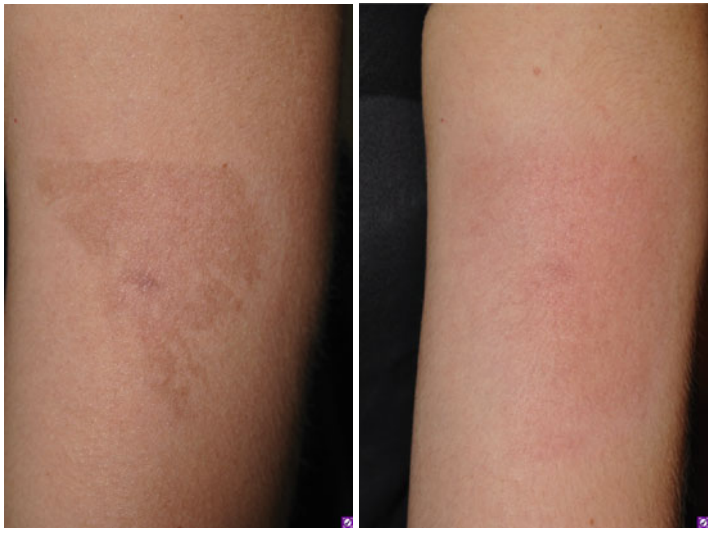

FIGURE 12.3 Before and after 3 treatments of 1,927 nm Thulium fractional laser treatment for post-inflammatory hyperpigmentation

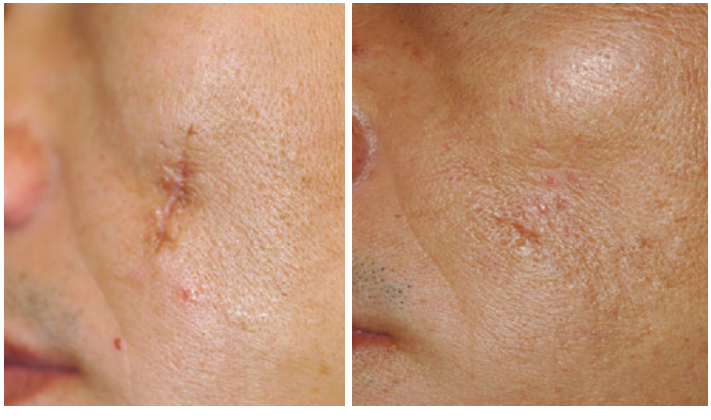

FIGURE 12.4 Before and after 3 treatments of non-ablative fractional laser treatment for surgical scar

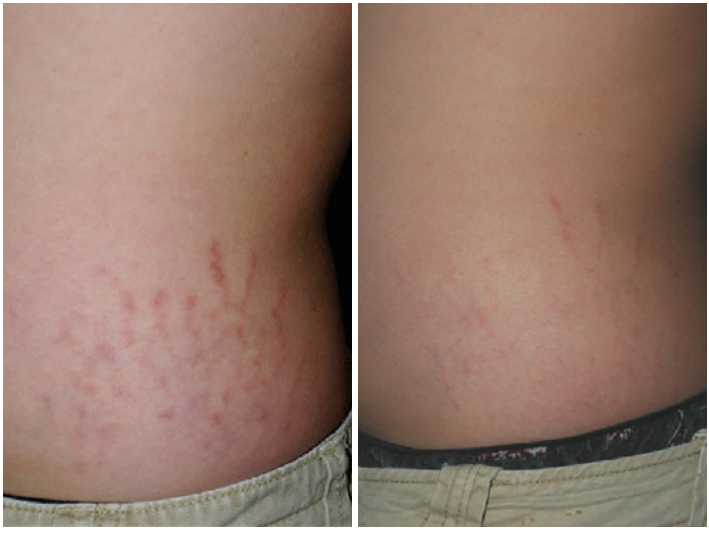

FIGURE 12.5 Before and after 3 treatments of non-ablative fractional laser treatment for striae rubra distensae

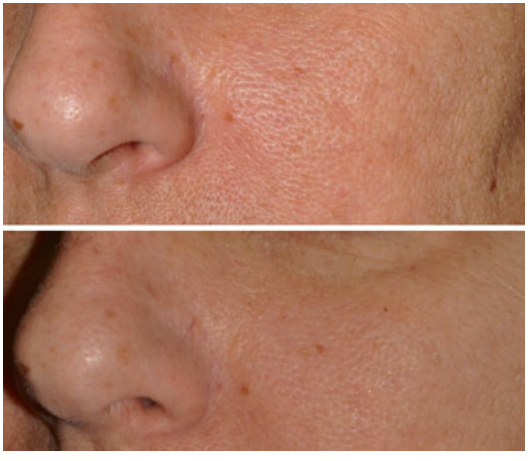

FIGURE 12.6 Before and after 1 non-ablative fractional laser treatment for patient with prominent pores

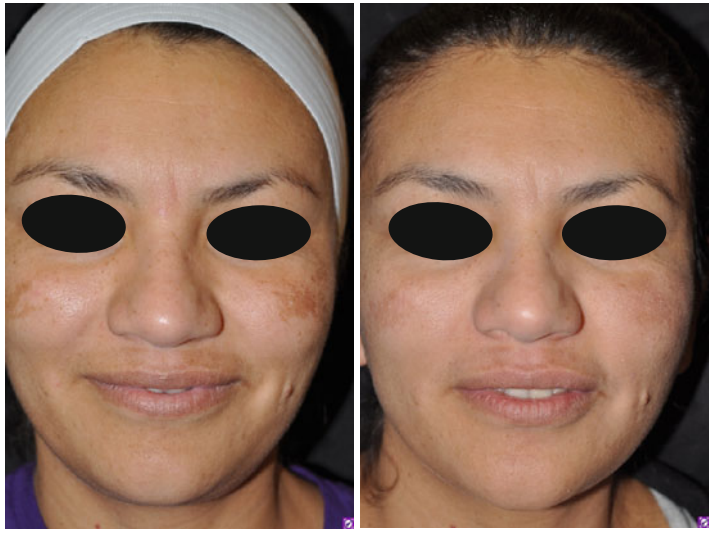

FIGURE 12.7 Before and after 1 treatment of Thulium laser treatment with improvement of her melasma

Ablative Fractional Resurfacing

- Photoaging face, neck, chest and hands (Fig. 12.8)
- Moderate – severe rhytides (Fig. 12.9)
- Moderate dyschromia (Fig. 12.10)
- Dermatochalasis, festooning
- Eyelid tightening
- Scars — atrophic, acne (Fig. 12.11), surgical (Fig. 12.12), burn (Fig. 12.13) and traumatic

Contraindications

- Isotretinoin (or associated oral retinoid) current use or 6 months prior
- Active infection

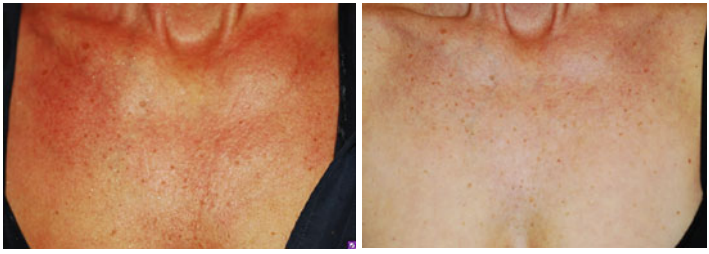

FIGURE 12.8 Before and after 2 treatments of nonablative and ablative fractional laser treatment for photoaging and rhytids decollette

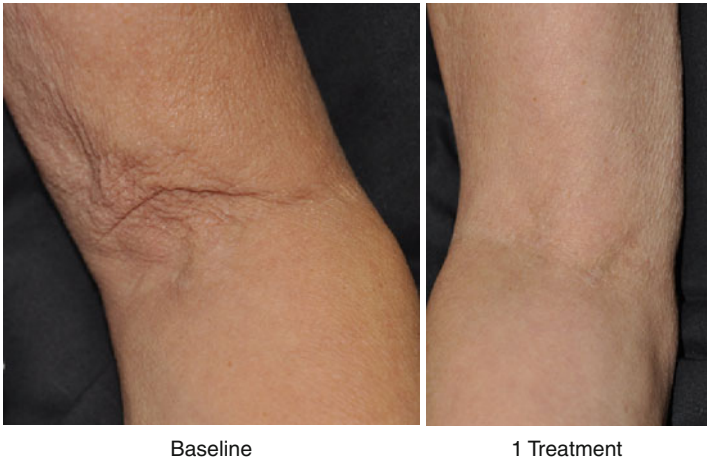

FIGURE 12.9 Before and after 1 treatment of ablative fractional resurfacing for laxity on arms

- Unrealistic expectations
- Relative contraindication: prior skin sensitivity to light either from collagen vascular disease or medication
- Relative contraindication: pregnant or breastfeeding mothers should discuss risk and benefit ratio with laser physician, obstetrician and/or pediatrician.

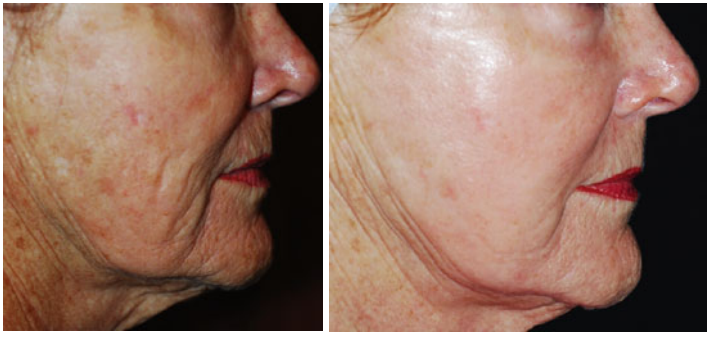

FIGURE 12.10 Before and after 1 treatment of ablative fractional resurfacing for moderate dyschromia

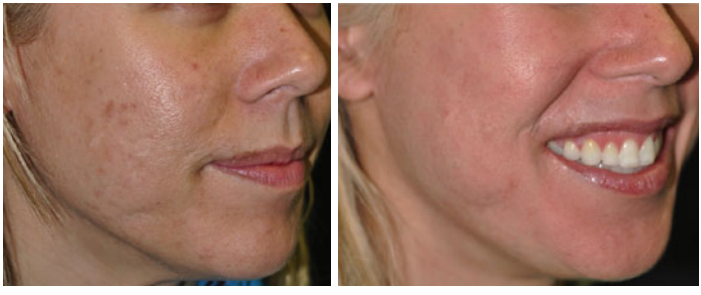

FIGURE 12.11 Before and after 1 CO_2 fractional ablative laser treatment for acne scars

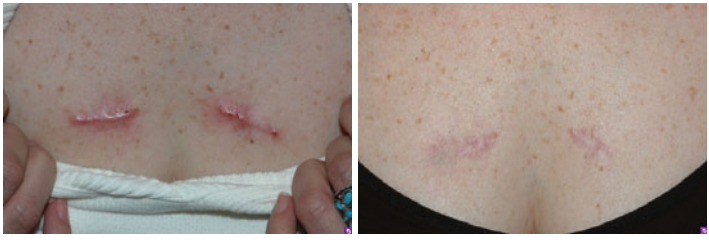

FIGURE 12.12 Before and after 3 treatments of ablative fractional resurfacing and topical corticosteroid application for scars on chest

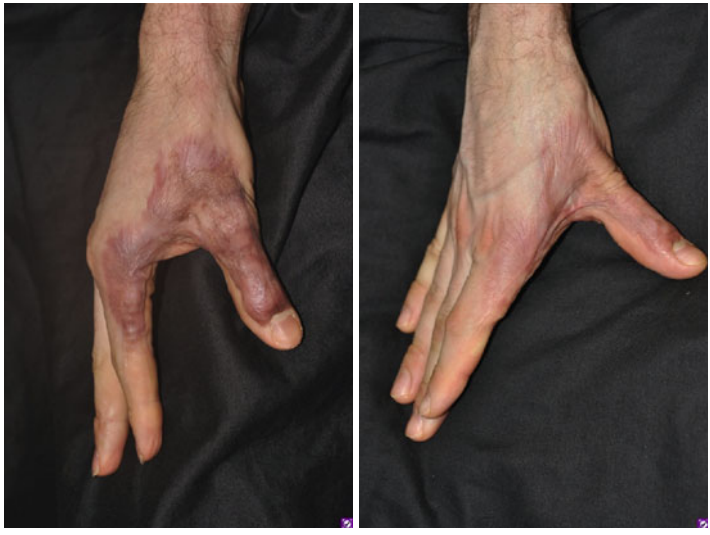

FIGURE 12.13 Before and after 2 treatments of Thulium and Erbium ablative fractional resurfacing for burn scars on hand with significant improvement in range of motion

Procedural Technique/Considerations

Pre-operative Considerations Both NAFR and AFR

- As with any procedure a realistic discussion of therapeutic goals, limitations, and potential complications followed by written informed consent should be obtained.
- Pertinent historical information during the initial evaluation includes patient's skin type, has the patient experienced herpes simplex virus, previous eyelid surgery, scar history (does patient form hypertrophic or keloid scars), other medical conditions, current medications, allergies should be documented.
- Physical examination should be performed and document photodamage and scar characteristics.

- Eyelid evaluation snap test should be performed to determine preoperative eyelid skin elasticity to avoid ectropion formation.
- Scar characteristics such as the presence of residual erosions and ulcers, erythema, pliability, textural irregularity, dyspigmentation, scar thickness and degree of restriction should be evaluated and documented.
- Topical or oral antibiotics are not employed under routine circumstances for NAFR, though they may certainly be entertained on a case-by-case basis. Many physicians use drugs against methicillin resistant *Staphylococcus aureus* (MRSA) when doing AFR.
- When treating facial areas, viral prophylaxis should be considered for both NAFR and AFR. Highly recommend prophylaxis to all patients with history of herpes simplex virus whether doing NAFR or AFR.
- High quality pre-operative photographs need to be obtained.
- The vast majority of fractionated laser treatments occur in the clinic setting following topical or local anesthesia alone. However, sedation or even general anesthesia may be utilized if requested by patient. If general anesthesia is required recommend a through pre-operative surgical evaluation from patient's internist and other specialist such as cardiologist.

Laser Selection

- First is the selection of AFR or NAFR. This is often determined based on the clinical need of the patient (i.e.: severity of photodamage or thickness of scar) but may be determined by post-operative downtime tolerated by a patient's lifestyle.
- Few controlled, prospective studies evaluating the comparative efficacy of various fractional devices have been performed, but early reports and the clinical experience of the authors suggests that AFR has the capacity to induce a more robust remodeling response than NAFR [10, 11].

FIGURE 12.14 Numbing procedure for fractional ablative laser treatment performed in the clinic setting using commercially available topical anesthetic preparations under occlusion for 1 h prior to treatment

Fractional Laser Treatment Technique

- The majority of treatments are performed in the clinic setting using commercially available topical anesthetic preparations under occlusion for 1 h or more prior to treatment (<30 mL) (Fig. 12.14). Recommend use caution with topical anesthesia using thin layers, <30 mL due to potential for lidocaine toxicity.

- Injectable local anesthetics may be utilized in focal areas, and these measures are often supplemented during treatment with a forced chilled-air device (Zimmer Cryo, Zimmer MedizinSystems, Irvine, CA). Some patients may benefit from systemic pre-operative analgesics or anxiolytics. Conscious sedation or even general anesthesia or conscious sedation can be employed in instances of large surface area involvement or anticipated poor patient tolerance of the procedure while awake.
- With previous discussion in mind, fractional laser treatment technique, parameters, and adjunctive treatments should be applied thoughtfully to minimize the degree of cumulative thermal injury to the tissue. Each treatment is customized at every session according to individual photodamage and scar characteristics and interval improvements with previous treatment sessions.
- Adequate procedural documentation should take place by physician at the time of the procedure with appropriate laser logs.

Post-operative Care

- Immediately after ablative treatments, petrolatum or a petrolatum-based ointment is applied and continued several times daily until the site is fully epithelialized, usually within 2–3 days. A bland moisturizer may be used after epithelization for up to 1 week.
- Patients may resume showering the following day and begin gentle daily cleansing of the area.
- Dilute vinegar compresses may be initiated according to the preference of the treating surgeon.
- Patients are allowed to resume essentially normal activity after treatment.
- Photo-protection should be advocated, including avoidance in the early post-treatment period and application of a bland sunblock once epithelial integrity is restored. Non-ablative treatments proceed in a similar fashion, but

bland emollients and sunblock may be initiated immediately since the epithelium essentially remains intact

Complications

Common Complications

- Procedural pain
- Immediate onset transient erythema is an expected consequence of NAFR and AFR which usually subsides within 3–4 days.
- Immediate onset of localized edema
- Pinpoint bleeding with AFR more common with Er:YAG devices versus carbon dioxide (CO_2) devices
- Mild serous drainage for 24–48 h
- Mild post procedure pain
- Acne and milia
- Delayed purpura
- Contact dermatitis

Infrequent Complications

- Prolonged erythema is defined as post-treatment redness persisting longer than 4 days with NAFR and beyond 1 month for AFR. The majority of erythema resolves within 3 months.
- Post procedure pain requiring medications
- Infection
- Transient post-inflammatory hyperpigmentation
- Scarring – hypertrophic scarring is a rare complication of AFR. Published reports show most cases involved AFR of the neck [12–14].
- Anesthesia toxicity
- Eruptive keratoacanthomas [15]
- Ectropion formation – lower eyelid is most commonly involved [12].

Prevention and Management of Complications

- Do not treat patients with unrealistic expectations
- Do not laser patients on isotretinoin, advised to wait 6–12 months after cessation of isotretinoin
- Do not treat patient if active bacterial, viral, fungal or yeast infection.
- Most infections occur within the first week postoperatively. Patients with increased itching, pain or focal redness should alert the physician of possible infection. If infection is suspected, a wound culture should be performed, and antibiotics should be started empirically. The antibiotic can later be adjusted based on the results of the culture and antibiotic sensitivity. It is recommended to have follow-up phone calls and/or office visits within first week of AFR to ensure patient is healing without complication.
- Recommend prophylactic antibiotics in patients who have a history of infection with *Staphylococcus aureus,* immunosuppressed or have valvular heart disease.
- Caution is advised in patients with ectropion and prior blepharoplasty surgery if treating periocular area.
- Decrease post-procedure erythema with use of light emitting diode (LED) array
- Topical ascorbic acid should be considered post AFR due to its wound healing properties to decrease post-operative recovery time [16].
- To decrease acne and milia formation, consider non-occlusive post-operative care moisturizers. If patient develops moderate-severe acne flares, a short course of oral acne antibiotic may be prescribed.
- To prevent post-inflammatory hyperpigmentation, it is recommended that with fractional resurfacing to use higher fluences but lower density settings. Patients should be advised to avoid sun exposure 2 weeks before and 4 weeks after to prevent PIH. If PIH develops, treatment

regimens include time, topical bleaching agents, mild chemical peels and physical sunblocks.
- When contact dermatitis is suspected, it is most commonly due to topical ointments applied by patients. Instruct patients not to use any non-prescribed topicals during the acute healing phase. Recommend your office give or sell skin care products for patients to use including mild cleanser, mild moisturizer, vitamin-C and physical sunblock as post recovery care kit.
- Hypopigmentation is uncommon after fractional resurfacing and the only reported cases have been transient unless scarring has occurred.
- Cautious treatment with AFR on the neck is recommended to decrease both depth and density in certain anatomic areas.
- If treating the periocular area, avoid excessive collagen contraction by decreasing energy and density settings.
- If hypertrophic scarring occurs, it is recommended to commence early treatment with topical or injected corticosteroids, compression therapy, pulsed dye or NAFR [17].
- Recommend complete removal of topical anesthesia prior to laser to avoid percutaneous absorption through fractional laser channels. Recommend using <30 mL of topical lidocaine.

Future Directions

Fractional lasers have been a transformational technology. Fractional lasers have increased the physician's ability to treat and improve photodamage, rhytids and scars in patients.

The next frontier of fractional lasers will be laser assisted delivery systems using the fractional channels to deliver pharmaceuticals and other bioactive materials. Laser assisted drug delivery is an evolving modality which may allow for topical medications to be delivered to a precise depth within the skin, more efficient transcutaneous delivery of large drug molecules, and even systemic drug administration via a

transcutaneous laser entry route. Laser therapy is a unique ablative modality, which has the ability to destroy the stratum corneum and other epidermal and dermal layers in a predictable and controlled manner, resulting in the potential for increased penetration of a variety of bioactive molecules.

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Chapter 13
Lasers for Scars

Anna H. Chacon, Jennifer A. Ledon, and Keyvan Nouri

Abstract There are various laser therapies available for scar revision that can be tailored according to the patient's characteristics such as age and expectations, as well as the scar's appearance.

Laser applications can serve as prophylactic measures of adverse scar formation, definitive therapy, or temporary intervention until further surgical repair is needed.

Keywords Scars • Cicatrix • Lasers • Keloids • Hypertrophic scars • Atrophic scars

Introduction

- There are various laser therapies available for scar revision that can be tailored according to scar appearance and patient's age and expectations.

A.H. Chacon, MD (✉) • J.A. Ledon, MD • K. Nouri, MD
Department of Dermatology and Cutaneous Surgery,
University of Miami—Miller School of Medicine,
1475 NW 12th Avenue, 2nd Floor, Miami, FL 33136, USA
e-mail: a.chacon@med.miami.edu; annachaconmd@gmail.com;
jledon1@med.miami.edu; knouri@med.miami.edu;
knourimd@gmail.com

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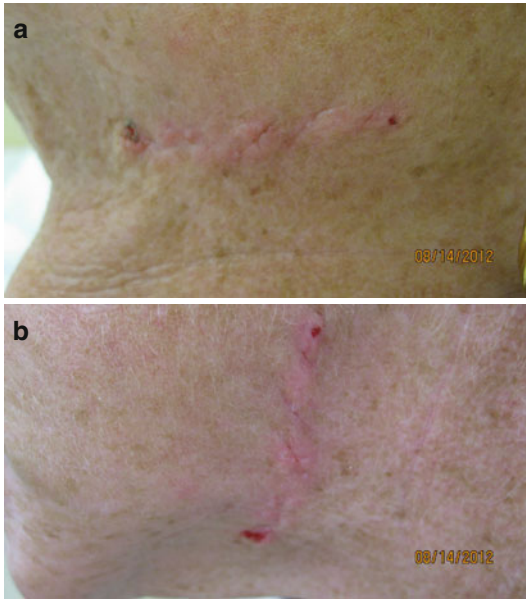

FIGURE 13.1 A 52-year-old female who underwent laser treatment with a 585 nm pulsed dye laser, 10 mm spot size, 10 % overlap on a hypertrophic scar in her left neck resulting from reconstruction after Mohs surgery (**a**) Pre-operative (**b**) Post-operative

- Laser can be used as prophylaxis against adverse scar formation, definitive therapy with scar revision, or temporary intervention until further surgical repair is needed.
- For keloids and hypertrophic scars, the 585 nm pulsed dye laser (PDL) is the gold standard (Fig. 13.1) [1].
- Though atrophic scars may be treated with carbon dioxide (CO_2) and Erbium:Yttrium-Aluminum-Garnet (Er:YAG) lasers, there is a need for less invasive procedures with reduced morbidity, such as nonablative lasers [2].

Background

- Scars result from cutaneous injury due to trauma or disease process [3]. Other types of residual scarring may occur as a result of acne, contractures, or burns.

Table 13.1 Characteristics and types of scars [4–6]

Type of scar	Physical features
Hypertrophic	Pink, raised, firm erythematous scars [4]
Keloids	Raised, reddish-purple nodular scars
	Firmer than hypertrophic scars [4]
Atrophic	Dermal depressions due to collagen destruction
Elevated	Raised, firm scars commonly caused by decreased expression of collagenase
Ice-pick	Narrow <2 mm sharply demarcated tracts that extend deep into the dermis or subcutis [5]
Boxcar	Round-to-oval shaped skin dimples with sharp margins [5]
Rolling	Shallow 4–6 mm wide [5]
	Undulating appearance
Striae distensae	Linear bands of atrophic or wrinkled skin [6]
Striae rubra	Early stages of striae distensae
	Erythematous with pink, lavender or purple hue [6]
Striae alba	Later stages of striae distensae
	Hypopigmented and sclerotic [6]

- When the normal process of wound healing is altered, abnormal scar formation occurs.
- Although scars do not pose a significant health risk, they can be cosmetically displeasing which can be detrimental to a patient's psychosocial well-being.
- Scars can be classified as atrophic, normotrophic, or hypertrophic depending on physical features (Table 13.1).
- Atrophic scars include: epidermal and dermal atrophy, panatrophy, or striae distensae.
- Keloids and hypertrophic scars fall into the category of raised and/or hypertrophic scars.
- The mechanism by which lasers work in treating hypertrophic scars and keloids has not been clearly elucidated, in

spite of the leading principle of vascular proliferation and its role in scar formation [7].
- Selective photothermolysis refers to the advent of pulsed lasers with more specific and selective targets [8].
- As a consequence of this theory, unwanted adverse effects as well as thermal damage and scarring were significantly reduced.

585 nm Pulsed Dye Laser

- First-line for keloids and hypertrophic scars [1].
- Technique: serial, non-overlapping pulses that cover entire area.
- Fluences and energy densities positively correlate with the scar's fibrosis [9].
- Start at low fluences, increasing to higher fluences depending on the scar's previous response to laser [10].
- If the response is favorable, keep energy density constant [10].
- If minimal response, increase the fluence by 10 % during the next session [11].
- 50–80 % improvement rate after two sessions for hypertrophic scars [12].
- Keloids and severe hypertrophic scars may require more sessions.

10,600 nm CO_2 Laser

- Ablative resurfacing for recontouring atrophic scars.
- Attains reproducible tissue vaporization by selective ablation of water-containing tissue, achieving greater precision than dermabrasion [13].
- Depth of vaporization and residual necrosis is directly proportional to number of laser pulses and pulse energy [13].
- Results in greater collagen shrinkage and offers more collagen remodeling [14].

- De-epithelialization usually requires one pass.
- Re-epithelialization takes place within 7–10 days [14].

2,940 nm Er:YAG Laser

- Very popular choice for laser vaporization of facial atrophic scars
- Approximately ten times more selective for water than CO_2 lasers, resulting in greater tissue vaporization and less dermal residual thermal damage [15].
- De-epithelialization requires 2–3 passes [16].
- Hair-bearing areas will need to be wiped down to decrease thermal conduction to skin through seared surface hairs [15].
- Less overall risk of erythema [16].
- Preferable for mild atrophic scars due to short-term recovery.
- Bleeding may be observed during the third pass secondary to penetration of the dermis and inability for photocoagulation of vessels [15].
- Re-epithelialization takes place within 4–7 days.

1,064 nm Neodynium:Yttrium-Alunimum-Garnet (Nd:YAG)

- Safe and effective alternative for mild-moderate atrophic acne scars.
- Minimal side effects (moderate erythema, petechiae, and discomfort).
- Nearly 40 % decrease in scar size at 6 month follow-up [17].
- Effects of collagen remodeling are ongoing after treatment sessions have been completed.

1,320 nm Nd:YAG

- Atrophic scars [18].
- Reasonable alternative for acne scars

- Often used along with concomitant cryogen cooling spray
- More favorable response seen in scars without fibrosis [18].
- Better results may be observed if combined with other treatment modalities such as surgery or intense pulsed light (IPL).

Other Lasers

1,540 nm Erbium: Glass Fractional Laser

- Surgical and post-traumatic scars.
- Re-epithelialization within 72 h of treatment [19].
- Rearrangement of dermal collagen and tissue remodeling evident at 2 weeks [19].

1,550 nm Erbium-Doped Fiber Laser

- Fractional photothermolysis of atrophic facial acne scars
- Significant improvement with good-to-excellent results in 1 month [20].

1,450 nm Diode Laser

- Atrophic facial scars [21].
- Transient erythema and hyper pigmentation reported in darker skin types (IV–VI) [22].

Low-Fluence 2,940 nm Er:YAG Laser

- Mild-moderate clinical improvement in atrophic acne scars
- Usually well tolerated [23].

Combined 585/1,064 nm Laser

- More effective for deep boxcar scars compared to long-pulsed Nd:YAG.
- Histological evaluation shows significantly greater collagen deposition [24].

Indications

- Classification and comprehensive assessment of scar including: color, vascular supply, texture, surface area, thickness or height, and pliability (Table 13.2).
- Patient has failed or chooses not to undergo other treatment modalities.
- Depending on type of laser being used, patients with lighter Fitzpatrick skin types (I–III) are more amenable to treatment.
- Previously treated scars are typically more difficult to treat, and may require adjustment of laser parameters.
- Realistic goals and expectations: no treatment is perfect and patients should understand that multiple treatments may be required. Physicians should advise patients regarding compliance with appropriate follow-up to minimize possible complications.

Contraindications

- Coexisting infection:
  - Patients should be free of infection prior to initiating laser therapy.
  - Laser therapy to infected skin may result in dissemination of infection.
- Coexisting inflammatory disorder:
  - Dermal inflammation may hinder efficacy of treatment and interfere with the healing process.

Table 13.2 Important scar variables to consider [24–26]

Scar variable	Important considerations
Color [24]	Mismatch in pigmentation
	Subjective measurements: non, slight, obvious, or gross
	Objective methods: instruments to measure erythema and melanin indices
	Flow Dopplers: measures amount of blood flow that contributes to scar's pigmentation
	Eye: powerful visual tool to detect imperfections
Vascularity [25]	Normal, pink, red or purple
	May be evaluated using Vancouver Burn Scar Scale among other instruments
Scar thickness and height [26]	Ultrasound is reliable and accurate to detect scar thickness
Pliability [24]	Refers to mobility, laxity, stiffness, elasticity, contraction
	To measure, attempt to fold scar
	Grading: normal, supple, yielding, firm, banding or contracture
	Functionality
Texture [24]	Difficult to estimate
	Examples of measurement devices: optical and mechanical profilometers
Surface area [26]	Planimetry
	Tracing scars helps to estimate contraction margins (short-term)
	Photography: most common, reliable, and accurate measurement
	Gold standard: digital photography

  - i.e. psoriasis, severe acne, and dermatitis may worsen after laser [15].

- Medications:
  - Isotretinoin
    - Alters wound healing and impairs production of collagenase [27].
    - Concurrent laser therapy may lead to unsightly hypertrophic scarring [27].
    - Recommendation: cease isotretinoin at least 6 months prior to laser therapy.
  - Anticoagulants
    - May lead to more intraoperative bleeding

Procedural Technique/Considerations

Pre-operative Care

- History: onset, location, associated symptoms, changes previous attempted therapies.
- Treat scars early (preferably within a few months) due to the abundant vascularity during this time.
- Adjust laser parameters for previous attempted therapies that may have contributed to fibrosis.
- Location: facial, arm and shoulder scars respond better to lasers than those on the anterior chest [7].

Technical Considerations

- Outpatient setting.
- Anesthesia: usually not required under normal circumstances.
  - Topical anesthesia, such as lidocaine may be applied within an hour before treatment.

Table 13.3 Non-laser treatment modalities

Non-laser treatment modalities
Dermabrasion
Chemical peels (glycolic acid, lactic acid, salicylic acid, trichloroacetic acid, phenol [carbolic acid])
Microneedling
Topical therapy (antihistamines, pressure dressings, silicone, onion extract, etc.)
Injections (corticosteroids, 5-fluorouracil, bleomycin)
Surgical removal
Cryotherapy

- Clean area and remove any makeup or creams.
- Photography: may be used to compare before/after each treatment session and to monitor response to therapy.
- Eye safety: every individual present should wear approved safety goggles to protect from retinal and ocular damage.

Post-operative Care

- Avoidance of sun exposure to minimize dyschromia
- Appropriate gentle cleansing
- Avoidance of trauma
- Follow-up treatments with further laser applications if necessary in 4–6 weeks (Table 13.3)

Complications

- Purpura
  - Most commonly reported side effect
  - Appears immediately and lasts approximately 1 week

- Pain during treatment
  - Common, yet uncomfortable, similar to the snapping of a rubber band. Consider pretreatment with topical anesthetic.
- Other symptoms: burning, pruritus
  - Common, typically subside within days
- Post-inflammatory pigmentary alterations
  - Difficult to treat
  - May be managed with bleaching creams.

Prevention and Management of Complications

- Postpone further treatment sessions until the affected area has healed completely.

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Chapter 14
Lights and Lasers for Acne

Katlein França, Jennifer A. Ledon, Jessica A. Savas, and Keyvan Nouri

Abstract Acne is one of the most common dermatological conditions. It can be psychologically devastating and impact quality of life. The use of lasers and lights to treat acne has increased dramatically in the past decade due to its efficacy and minimal side effects. This chapter presents an overview of the use of lights and lasers to treat acne.

Keywords Acne • Lasers • Lights • Intense Pulse light • Photopneumatic devices • Photodynamic Therapy

Introduction

Acne is one of the most common dermatologic disorders and affects almost all individuals at some point in their life [1, 2]. This condition can be psychologically devastating and greatly impact

K. França, MD, MS (✉) • J.A. Ledon, MD • J.A. Savas, MD
K. Nouri, MD
Department of Dermatology and Cutaneous Surgery,
University of Miami—Miller School of Medicine,
1475 NW 12th Avenue, 2nd Floor, Miami, FL 33136, USA
e-mail: k.franca@med.miami.edu; jledon1@med.miami.edu;
jsavas@med.miami.edu; knouri@med.miami.edu,
knourimd@gmail.com

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quality of life [3]. The pathogenesis of acne is multifactorial and the pathophysiology is still not completely clear. It is known that an increase in sebum production, hyperkeratinization, inflammation and colonization by *Propionibacterium acnes* are all related to the process [4]. Medical treatments for acne include the use of topical and oral medications as well as lasers and lights devices [5].

Background

In the past decade, the use of lasers and lights to treat acne has increased dramatically due to its efficacy and minimal side effects [1, 5]. These devices act by targeting the *Propionibacterium acnes* bacteria, reducing the inflammation and reducing sebaceous glands activity [5]. Short wavelengths target the P. acnes bacteria while long wavelengths target the sebaceous glands. This chapter will address the use of the blue light, red light, intense pulsed light (IPL), photopneumatic devices, photodynamic therapy (PDT), pulsed dye laser (PDL), potassium-titanyl-phosphate (KTP) laser, 1,450 nm diode laser, erbium glass laser, and the neodium: yttrium-aluminum-garnet (Nd: YAG) laser to treat acne lesions.

Blue Light (405–470 nm)

Blue light irradiation is known to be an effective therapy for the treatment of acne vulgaris. It uses blue light (405–470 nm) to destroy the *P. acnes* [1, 6]. The skin should be exposed to the blue light source for a short period of time ranging from a few seconds up to 15 min, depending on the product [6, 7]. Patients without nodulocystic lesions are better candidates for blue light irradiation [6].

Red Light Phototherapy (600–650 nm)

Red light therapy (600–650 nm) penetrates deeper in skin than the blue light and has been traditionally used in combination with the blue light. Alternating treatment between blue light and red light has also been employed. The use of this combination can be performed two times a week for 8 weeks [8]. Red light has been documented to activate the porphyrins produced by *P. acnes* and consequently decrease the inflammatory process [9]. The procedure is well-tolerated, safe, and effective [8]. A study that tested the efficacy of red light phototherapy alone for the treatment of acne vulgaris showed a significant improvement in non-inflammatory and inflammatory acne lesions with phototherapy performed for 15 min twice a day for 8 weeks [10].

Intense Pulsed Light

The use of intense pulsed light is a light-based therapy that has shown promising results in patients with acne. It uses a flashlamp to deliver non-coherent, wide spectrum visible light to near-infrared wavelengths [9]. This device works by utilizing photodynamic therapy and causes the selective destruction of the P. acnes [11]. A study that evaluated the use of short contact aminolevulenic acid and IPL and IPL alone showed that the degree of improvement was better and remained longer with the combined regimen [12].

Photopneumatic Devices

Photopneumatic technology combines the use of a vacuum pressure with a broadband source to treat acne. It is considered an effective and safe modality for the treatment of comedonal and mild to moderate inflammatory acne vulgaris [13].

Gold and colleagues found a 57.8 % reduction in non-inflammatory acne lesions and 57.8 % reduction in inflammatory lesions in a study group with 11 patients [14].

Photodynamic Therapy

Photodynamic therapy is a light-based treatment that uses topical precursors of porphyrins [15]. Topical application of aminolevulinic acid (ALA) or methylaminolevulinate (MAL) followed by light exposure after a period of incubation causes the buildup of porphyrins and damage to sebaceous glands, improving acne lesions [16]. It is an off-label alternative treatment for acne and more research is required to improve treatment tolerability and to determine the optimal treatment parameters [15, 16].

Pulse Dye Laser (585 and 595 nm)

Pulsed dye lasers (PDL) emit high-energy laser light with short pulse durations with long intervals between each pulse [17]. Research has shown controversial results regarding the use of this laser for the treatment of acne [17, 18]. A study performed with 45 patients compared the efficacy of the PDL, topical treatment and chemical peels. The authors found that at 12 weeks of treatment the best results were seen in the group treated with the PDL; the remission in the follow-up period was also higher in this group [17]. The use of PDL-assisted photodynamic therapy with MAL has been suggested to be superior to laser alone for the treatment of acne vulgaris [18].

KTP Laser (532 nm)

The Potassium titanyl phosphate (KTP) laser produces a green light with a wavelength of 532 nm [19]. A low power KTP laser can be used to activate the *P. acnes* porphyrins,

releasing free radical molecules that will destroy the bacteria. In a study performed with 25 patients at fluences ranging from 6 to 12 J/cm^2, a clearing of 60–70 % was achieved after six treatments [20].

1,450 nm Diode Laser

The 1,450 nm diode laser is a long wavelength that thermally alters sebaceous glands and is an effective treatment of inflammatory facial acne [9, 21]. A study performed with 27 female patients showed reduction in the number of skin lesions by 51.7 % at 8 weeks and 63.0 % at 10 weeks [22]. This laser has also shown good results and minimal side effects even in patients with Fitzpatrick skin phototypes IV–VI [21].

Erbium Glass Laser (1,540 nm)

The erbium glass laser (1,540 nm) provides deep dermal penetration and affects the sebaceous activity, improving inflammatory acne lesions [9]. A study performed with 15 patients evaluated the use of the 1,540 nm erbium:glass laser in the treatment of moderate to severe inflammatory acne on the face. The laser was used four times at 2-week intervals. The authors found that papules, pustules, and nodules all responded well to this therapy [22]. Reduction of skin oiliness can occur after the laser treatment [23].

Nd:YAG Laser (1,320 nm)

The neodymium: yttrium aluminum garnet (Nd:YAG) laser has thermolytic effects upon sebaceous glands [9]. Acne vulgaris has been treated with this long wavelength laser with promising results. A study performed with 35 patients with moderate-to-severe acne showed the reduction of inflammatory lesions by 57 % and the reduction of non-inflammatory

lesions by 35 %. These patients received six treatment sessions at a 2-week interval [24]. This treatment modality is considered effective, safe and well tolerated by patients with acne [25].

Indications

- Patients with contraindications to other therapies (topical and/or oral medications) [1, 2].
- Topical or oral medication failure [1–3]
- Patients looking for fast results [3, 26, 27]
- Patients with inflammatory acne

Contraindications

- Pregnancy [28, 29]
- History of poor wound healing [28, 29]
- Patients taking medication that causes light sensitivity [28, 29]
- Patients using oral retinoids within the past 6 months
- Patients prone to keloid scarring [28, 29]
- Patients presenting with or who have a tendency to develop skin discolorations [28, 29]
- Presence of local infection [28, 29]

Procedural Technique/Considerations (Including Pre-operative and Post-operative Care)

Pre-operative Care

- Consider the patient's skin type
- Consider the patient's medical history, comorbidities and current and past use of topical and/or oral medications

Procedural Technique/Considerations

- Consider each laser technology individually: laser parameters and number of passes may differ with laser type and device.
- The effectiveness varies from patient to patient. Some patients will require follow up treatments that should be determined by the physician.

See the background section for more information regarding each device.

Post-operative Care

- Sun exposure avoidance
- Use of sunscreen recommendation
- Use of topical medications and other products should be determined by the physician
- If HSV outbreaks, consider the use of antiviral medications prophylactically

Complications

- Long lasting erythema and edema [5]
- Bruising [5]
- Post inflammatory hyperpigmentation [5]
- Pustules [5]
- Infection [5]

Prevention and Management of Complications

Prevention

- Detailed clinical history and physical exam should be made before the procedure [5]

- Skin type selection: Patients with skin type 4 or more may present more complications [5]
- Use of pre laser topical tretinoin and hydroquinone for patients with skin type 4 or more [5]

Management of Complications

- Use of topical and oral antibiotics in case of infection [5, 30]
- Use of bleaching creams in case of post-inflammatory hyperpigmentation [5, 30]

Future Directions

The treatment of acne can be challenging due to the multifactorial pathogenesis of this condition. In the past decade, new studies have suggested the efficacy of several lasers to treat the different stages of acne and its etiopathogenesis. A recent study performed by Sakamoto and colleagues studied the wavelengths of a free electron laser that would specifically target the sebaceous glands. Based on the selective photothermolysis theory, these authors found that optical pulses at ~1,720 or ~1,210 nm delivered with large beam diameter and appropriate skin cooling in approximately 0.1 s could provide an alternative treatment for acne [31]. Lasers can have a significant role in the future of acne therapy, however new studies are necessary to determine safety, parameters, and long-term efficacy.

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Chapter 15
Use of Lasers for the Treatment of Psoriasis and Vitiligo

Maya G. Debbaneh, Eric S. Lee, John Koo, and Judith Hong

Abstract Psoriasis and vitiligo are two chronic inflammatory skin conditions that have long been treated with phototherapy. Recently, laser theropy has become an alternative to generalized light treatment, as lesions can be targeted more directly and generally require less treatment sessions. While a variety of lasers have been tested for both the treatment of psoriasis and vitiligo, the most commonly used laser for

M.G. Debbaneh, BA (✉)
Department of Dermatology, University of California, Irvine,
515 Spruce Street, San Francisco, CA 94118, USA
e-mail: maya.debbaneh@gmail.com

E.S. Lee, MD
Department of Dermatology and Cutaneous Surgery,
University of Miami—Miller School of Medicine,
1600 NW 10th Avenue, Miami, FL 33125, USA
e-mail: elee3@med.miami.ediu

J. Koo, MD
Department of Dermatology, University of California,
San Francisco Psoriasis Center, 515 Spruce Street,
San Francisco, CA 94118, USA
e-mail: john.koo@ucsfmedctr.org

J. Hong, MD
Department of Dermatology, San Francisco Veteran Affairs
Medical Center, 3841 Brickway Blvd, Santa Rosa, CA 95403, USA
e-mail: judithhong81@gmail.com

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this purpose is the excimer laser, which uses a wavelength of 308 nm. This chapter discusses the indications and use of lasers in the treatment of psoriasis and vitiligo.

Keywords Laser • Psoriasis • Vitiligo • Hypopigmentation • Phototherapy • Excimer

Introduction

Psoriasis has long been effectively alleviated by various phototherapy modalities, including Narrow Band UVB (NB-UVB) (308–312 nm), Broad Band UVB not mentioned. Again, but could not BBUVB (290–320 nm) and psoralen with UVA (PUVA). Though effective the dose has been limited by wonszefifiz. Tissue damage of uninvolued skin. The limit, termed the minimal erythema dose (MED), is the lowest dose of light required to cause erythema in non-targeted skin. The use of lasers has provided a way to administer phototherapy directly to lesional plaques, therefore avoiding unaffected skin and allowing for higher doses of light per treatment. The excimer laser is the most widely used laser for this purpose, providing a way to deliver targeted doses of 308-nm light to psoriasis [1]. Lasers utilize the concept of "supra-erythemogenic phototherapy," in which optimized doses are significantly higher than the MED of non-psoriatic skin [2]. Because the laser is applied specifically to psoriatic skin, which is able to tolerate much higher doses of light, the clinician is able to dose more aggressively, resulting in faster clearing rates [2, 3].

Similarly, the excimer laser has become a therapy option for patients with vitiligo, a condition that remains a challenge to treat. While both PUVA and NB-UVB have had some success in controlling the progression of depigmentation, and at times leading to repigmentation, laser therapy has gained a reputation for treating localized vitiligo possibly more effectively than PUVA or NB-UVB. A recent review article on excimer laser therapy for the treatment of vitiligo

suggests that it should be considered as a possible first-line therapy in localized vitiligo on the face and neck, where it is most effective [4].

Background

Psoriasis

Psoriasis is a potentially debilitating skin condition affecting anywhere from 2 to 3 % of the U.S. population [5]. This often visually striking condition can not only cause physical discomfort but can also negatively affect psychological and social aspects of patient's lives [6, 7]. Fortunately, many treatment options now exist to clear and control the symptoms of psoriasis. Generalized phototherapy has become one of the most effective treatments for this condition, especially NB-UVB and PUVA, and is thought to be effective through several mechanisms, including apoptosis of T-cells and decreasing the activity of antigen presenting cells in the skin [8, 9]. However, this form of treatment carries a risk of irritating and burning non-involved skin, which can theoretically lead to photoaging and higher incidence of skin cancer [10]. The advent of targeted laser phototherapy has minimized unwanted effects on non-psoriatic skin while simultaneously increasing the effectiveness of each treatment. While several laser types have been studied for psoriasis treatment, including the carbon dioxide laser, the pulsed-dye laser and nonexcimer home units, the most commonly used and effective machine for this purpose is the excimer laser [11]. It is a gas laser utilizing a xenon-chloride medium, which is delivered through a fiberoptic handpiece, producing UV light at a wavelength of 308 nm [10]. The newer excimer laser models are also significantly more powerful than earlier versions. For example, the PhotoMedex XTRAC Velocity is three to four times more powerful than the previously developed XTRAC Ultra machine, which has decreased the time necessary for treatment [3]. The efficacy of the 308 nm excimer UVB laser

was tested in several studies including a multicenter open trial for localized plaque psoriasis. Seventy-two percent of participants achieved PASI 75 after an average of 6 treatments and 84 % showed PASI 75 after 10 or fewer treatments [12]. Trehan, et al. observed an average remission time of 3.5 months in 15 of 20 treated patients with plaque psoriasis. In a study with 1 year or greater follow-up, 13 of 26 patients with plaque psoriasis either had continued clearance or long-term improvement [13].

Compared with whole-body phototherapy, which generally requires about 20–30 treatments for clearance, the 308 nm excimer laser requires only six to ten treatments [1, 12–14]. Although no hard guidelines exist, laser treatment appears most practical for localized psoriasis with an affected body surface area (BSA) of less than 10 %. Additionally, using the excimer laser in combination with topical, or even systemic therapies can potentially lead to even faster and more extensive clearing. A recent blinded study comparing the use of combination of flumetasone ointment and excimer laser therapy to laser monotherapy showed no significant difference between PASI scores by the end of 5 weeks, but the group receiving combination therapy required less cumulative laser dosage during treatment, resulting in less side effects [15]. Moreover, Wong et al. presented two cases studies in which clobex spray and calcitriol ointment were used in conjunction with excimer laser treatments resulting in 12 months of clearance after treatment [16].

Vitiligo

Vitiligo is a depigmenting disorder that affects 0.1–2 % of the world's population [17]. Much like psoriasis, vitiligo can have a marked impact on quality of life and psychological health, often leading to feelings of embarrassment potentially causing social isolation, and is associated with conditions such as anxiety and depression [18]. Although several options for treatments exist, such as topical steroids, topical calcineurin

inhibitors, and phototherapy, results are often unsatisfying to the patient. Currently, the most effective modality is phototherapy, which is thought to target many of the same immune cells in psoriasis, including inducing apopotosis of cytotoxic T cells that are responsible for melanocyte destruction. Additionally, phototherapy enhances the migration and proliferation of melanocytes resulting in repigmentation [19–22].

After NB-UVB was established as the more effective treatment for vitiligo when compared to PUVA, it became the preferred treatment for this condition [23–26]. Similar to psoriasis, the excimer laser makes use of this technology to target affected areas at a much higher dose of light than what is tolerated with generalized phototherapy. Excimer laser therapy and NB-UVB phototherapy was compared in a randomized, investigator-blinded half side comparison involving 21 patients in which symmetrical lesions on one side of the body were treated twice a week for 6 months with 308 nm excimer laser, while NB-UVB was used to treat the opposite side. Repigmentation was graded on a scale of zero to four with zero representing no repigmentation and a score of four being excellent repigmentation (between 76 and 100 % repigmentation). Results showed that six lesions (37.5 %) treated with excimer laser and only one lesion (6 %) treated with NB-UVB achieved an excellent repigmentation score while four lesions (25 %) treated with a 308 nm excimer laser and five lesions (31 %) treated with NB-UVB achieved a good repigmentation score of three (between 51 and 75 % repigmentation). Moreover, lesions treated with a 308 nm excimer laser obtained moderate repigmentation within a mean of 21.6 ± 8.08 treatments while lesions treated with NB-UVB required 27.6 ± 10.29 treatments to achieve the same result ($P = 0.004$) indicating that fewer laser treatments are needed than NB-UVB to obtain the same level of repigmentation [17].

Additional studies have shown that it is particularly useful in stable, localized vitiligo [27] and darker skin types, specifically Fitzpatrick skin types III and IV [28]. The most responsive sites have been the face followed by the neck,

trunk and extremities, with the hands and feet being the least responsive areas. Other factors that make repigmentation more likely with excimer laser are smaller, newer lesions and younger age of the patients, as children seem to respond better than adults [4].

Indications

Psoriasis

- **General Indications** Indications for excimer laser treatment are similar to those for generalized phototherapy, namely failure of, or contraindications to, topical therapies. It is generally recommended that laser therapy be reserved for patients with localized psoriasis confined to less than 10 % BSA, although this is not a strict guideline. The maximum BSA treated was in a pilot study by Gattu, et al., for which generalized psoriasis of up to 30 % BSA was treated effectively with excimer laser; a PASI improvement of at least 75 % was seen in 54 % of patients in the study [2]. Patients must be amenable to biweekly treatment sessions. Laser therapy for psoriasis is currently only indicated for plaque psoriasis and palmoplantar psoriasis, as it has not been established as a reliable treatment for other subtypes.
- **Scalp Psoriasis** The excimer laser has been shown to improve scalp psoriasis in two studies in which the hair was parted manually to deliver the pulses [29, 30]. It has also been used successfully in a case of recalcitrant scalp psoriasis in combination with twice daily clobetasol spray [31].
- **Palmoplantar Psoriasis** Palmoplantar psoriasis refractory to topical treatments has been shown to be an effectively treated using excimer laser therapy [32–35], however it was shown to have similar efficacy as cream PUVA treatment [34].
- **Nail Psoriasis** The excimer laser has not been established as an effective treatment for nail psoriasis. A pilot study

involving four patients showed no improvement in nail psoriasis with the excimer laser [36]. In contrast, the pulsed dye laser (PDL) has been shown to be a treatment option for nail psoriasis refractory to biologics. Several studies utilizing 595 nm pulsed dye laser treatment for nail psoriasis showed significant improvement in NAPSI scores after 3 months of once monthly treatments [37, 38]. One randomized double blind study comparing long and short pulse durations showed a significant reduction in NAPSI score after 3 months of treatment with no significant difference in outcome between the long and short pulse groups. The most common side effects were hyperpigmentation and petechiae that later resolved [38].

- **Pediatrics** While most studies involving excimer lasers involve patients 18 years and older, a pilot study by Pahlajani, et al. did not report any greater incidence of side effects in children, with a median age of 11 years old, as compared to adults [39]. However, the long-term outcomes of laser treatments on children have not been studied.
- **Pregnancy** Excimer laser therapy is generally considered to be safe, as UVB therapy is a commonly employed treatment modality for severe psoriasis during pregnancy [40].
- **Presence of a Pacemaker** It is safe for a patient with a pacemaker to undergo laser therapy.

Vitiligo

- **General Indications** Laser treatment should be considered in vitiligo refractory to topical steroids and topical calcineurin inhibitors alone. As described previously, it is particularly useful in stable, localized vitiligo [27] and darker skin types, specifically Fitzpatrick skin types III and IV [28]. The most responsive site has been observed to be the face followed by the neck, trunk and extremities, with the hands and feet being the least responsive areas. Other factors that make repigmentation more likely with excimer laser are smaller and newer lesions [4].

- **Pediatrics** Excimer laser treatment for vitiligo has been shown to be safe, and in fact, more effective, in childhood [4, 41, 42].

Contraindications

- Because no absolute contraindications to laser therapy have been established, the practitioner must rely on his or her clinical judgment and the patient's individual possible adverse reaction to therapy.
- **Photosensitizing Medications** Phototherapy is a relative contraindication in patients who are unable to tolerate phototherapy either due to medication (Table 15.1) or secondary to a photosensitizing condition [43]. However, these are not absolute contraindications and phototherapy can still be utilized with caution if exposing a selected test area of the skin to UVB light elicits no reaction. There is the option of timing phototherapy sessions in order to maximize the time between the use of the photosensitizing medication and laser therapy, allowing systemic levels of the photosensitizing medication to reach minimal levels by the time of treatment. For example, the patient can take their medication immediately following the phototherapy session so that it is at a minimal level by the time the patient is due for another treatment [1].
- **Photosensitizing Conditions** Phototherapy in general is contraindicated in photosensitizing disorders (i.e. systemic lupus erythematosus, xeroderma pigmentosum, etc.) so a thorough history and physical must be obtained prior to initiating treatment.
- **History of Skin Cancer** Although the long-term skin cancer risk is unknown for patients undergoing excimer laser treatment for psoriasis, a patient's history of melanoma or non-melanoma skin cancer should be considered. NB-UVB therapy, which encompasses the 308 nm wavelength has not been found to significantly increase the risk of skin cancer [44]. While targeted laser therapy does deliver a

Table 15.1 Commonly known medications that can cause photosensitivity

Class of drug	Examples
Acne medications	Tretinoin (Retin-A)
Anticancer drugs	Dacarbazine
	Fluorouracil
	Methotrexate
	Procarbazine
	Vinblastine
Antidepressants	Amitriptyline, Amoxapine, Desipramine, Isocarboxazid, Maprotiline, Nortriptyline, Trimipramine
Antihistamines	Cyproheptadine, Diphenhydramine
Antimicrobials	Demeclocycline, Doxycycline, Grisefulvin, Tetracyclines, Nalidixic acid, Oxytetracycline, Sulfacytine, Tremethoprim
Antifungals	Fentichlor, Jadit, Multifungin
Antiparasitics	Bithionol, Pyrvinium pamoate, Quinine
Antipsychotics	Chlorpromazine, Fluphenazine, Haloperidol, Piperacetazine, Prochloperazine, Promethazine, Thioridazine, Triflupromazine
Contraceptives	Estrogens, Norgestrel
Diuretics	Amitriptyline, Acetazolamine, Chlorothiazide, Furosemide
Hypoglycemics	Acetohexamide, Chloropropamide, Glipizide, Glyburide, Tolazamide, Tolbutamide
Non-steroidal anti-inflammatories	Ketoprofen, Naproxen, Phenylbutazone, Piroxicam, Sulindac
Others	Artificial sweeteners, deodorants, Psorolenes, Amiodarone, bergamot oil, oils of citron, lavender, lime, sandalwood, cedar, Benzocaine, Captopril, Carbamazepine

Table 15.2 Fitzpatrick skin type classification

Skin type	Sunburn and tanning history
I	Always burns, never tans, sensitive
II	Burns easily, tans minimally
III	Burns moderately, tans gradually to light brown
IV	Burns minimally, always tans well to moderately brown
V	Rarely burns, tans profusely
VI	Never burns, deeply pigmented, not sensitive

greater dose of light, therapy is often of shorter duration than generalized phototherapy.

- **Hyperkeratotic Lesions** It was noted in one study that hyperkeratotic lesions were less responsive to laser therapy and may require more treatment sessions [2].
- **Fitzpatrick Type I Skin** Patients with Fitzpatrick skin type I have been reported to experience more blistering than other skin types, which may limit the amount of dose increase per treatment session [2]. A description of the Fitzpatrick skin categorization is included in Table 15.2.
- Caution should be taken in patients with a history of keloid formation or heightened Koebner reactions, which is the appearance of psoriasis in areas of trauma.

Procedural Technique/Considerations for Excimer Laser

Psoriasis

- Preoperative Considerations:
  - Properly screen the patient by taking a full history and physical, paying special attention to current medications, and screening for the above-mentioned contraindications. Also, note the affected areas on physical exam

to be treated along with the induration of the lesions and whether the lesions are located in sensitive areas such as the armpit, face or groin, as they may be less tolerant to laser treatment.
- Advise the patient to come to the treatment sessions without applying lotions, creams, deodorants, and especially sunscreen, making sure the skin is as clean as possible.
- Some clinicians may apply mineral oil prior to treatment, although it has not been shown to be beneficial to treatment and may damage the laser handpiece [45].
- Make sure the clinician, the patient and any observers in the treatment room wear the proper protective eyewear.
- Have the patient sign the consent form after discussing all possible side effects and patient expectations of treatment outcomes.

- Procedural Considerations:
  - The treatment schedule is generally conducted twice a week for at least ten treatments to start and there should be a minimum of 48 h between treatments. Patients may see a response in as little as one treatment, with a 75 % or greater clearance in as little as six to ten treatments [43].
  - **Dosing** The initial treatment dose can be determined by either the MED or based on other factors such as plaque thickness and Fitzpatrick skin type [43].
    - Formal MED testing involves sequentially exposing small areas of skin to different intensities of UVB laser doses. The MED is defined as the amount of UVB that produces barely perceptible erythema in noninvolved skin 12–18 h after exposure. In generalized phototherapy the initial exposure may range anywhere from 50 to 100 % of the MED, but with the excimer laser, the MED can be initiated from 100 to 400 %, depending on the plaque location, thickness of the plaque and plaque color. For example, if the plaque is located in thicker (the knees, elbows, hands or feet), if the plaque is thick and tough and if the

plaque is tanned we can start the first dose at four times the determined MED. A sample protocol for initial treatment is shown in Table 15.3 and a sample protocol for dosing subsequent treatments is shown in Table 15.4 [43].

- Alternatively, dose can be immediately determined based on plaque thickness, plaque induration, and Fitzpatrick skin type. Because of convenience, this has become the preferred method of dosing because it is less time consuming than conducting MED testing (Table 15.5). In subsequent treatments, doses are adjusted based on clinical observation and patients' ability to tolerate the previous treatment. A sample protocol for dosing changes is included in Table 15.6 [43].
  - To avoid unwanted side effects, be sure not to treat the same area twice during one treatment session.
- **Photosensitizing Medication** If a patient is started on a photosensitizing drug during treatment, the drug can be scheduled to maximize the time between when the medication is to be taken and when the next phototherapy session is to take place. Medications should be reviewed prior to each treatment session.
- **Maintenance** When plaques are largely diminished, tapering the frequency of treatment for several additional treatments is advised and may help extend the duration of remission. Tenja, et al. described administering four additional treatments after there was no induration observed [46]. Housman, et al. described a maintenance protocol that included "one treatment a week for 4 weeks, one treatment every other week for 4 weeks and one final treatment 4 weeks later for a total of seven treatments [47]."
- **Failure of Treatment** If a psoriasis patient has not had a significant reduction of their plaque psoriasis after about 20 treatments, and the recommended treatment guidelines of two to three treatments per week have been followed, the adequacy of dosing should be reviewed. If the dose appears to be adequate, then cessation of this form of treatment should be considered.

Table 15.3 Excimer laser MED-Based Psoriasis Protocol for determining dose for first treatment

Plaque location	Plaque thickness	Plaque tan	Multiplier for first dose	MED (or Fitzpatrick Skin Type as proxy for MED) in mJ/cm²					
				MED = Fitz. Type 1	MED = Fitz. Type 2	MED = Fitz. Type 3	MED = Fitz. Type 4	MED = Fitz. Type 5	MED = Fitz. Type 6
Knees, elbows, hands, feet	Thick, tough	Tanned	4 (or 400 %)	400	600	800	1,000	1,200	1,400
Knees, elbows, hands, feet	Thick, tough	Not tanned	3 (or 300 %)	300	450	600	750	900	1,050
Knees, elbows, hands, feet	Thin, moderate	Tanned	3 (or 300 %)	300	450	600	750	900	1,050
Knees, elbows, hands, feet	Thin, moderate	Not tanned	2 (or 200 %)	200	300	400	500	600	700
All other locations	Thick, tough	Tanned	3 (or 300 %)	300	450	600	750	900	1,050
All other locations	Thick, tough	Not tanned	2 (or 200 %)	200	300	400	500	600	700

(continued)

Table 15.3 (continued)

Plaque location	Plaque thickness	Plaque tan	Multiplier for first dose	MED (or Fitzpatrick Skin Type as proxy for MED) in mJ/cm^2					
				MED = Fitz. Type 1	MED = Fitz. Type 2	MED = Fitz. Type 3	MED = Fitz. Type 4	MED = Fitz. Type 5	MED = Fitz. Type 6
All other locations	Thin, moderate	Tanned	2 (or 200 %)	200	300	400	500	600	700
All other locations	Thin, moderate	Not tanned	1 (or 100 %)	100	150	200	250	300	350

An example of how to determine the initial dose is as follows: if the patient has a thick, tough plaque located on the knee and that plaque is tanned, we can multiply the MED by a factor of four. For example if the MED is 400 or, as a substitute, the patient has Fitzpatrick skin type I, we can multiply the MED by four, resulting in an initial dose of 1,600 mJ/cm^2

Table 15.4 Excimer laser MED-Based Psoriasis Protocol determining dose for subsequent treatments

Effect	Description of effect	Dose change
No effect	No erythema at 12–24 h and no plaque improvement or pigmentation	Increase dose by 25 % (or increase MULT by 1)
Good effect	Mild erythema at 12–24 h OR plaque thinning OR reduced scaliness OR pigmentation occurred	Maintain dose
Considerable plaque improvement achieved	Good effect (see above) with considerable plaque improvement achieved at previous dose level	Reduce dose by 25 % (or reduce MULT by 1): [reduction intended to minimize hyperpigmentation effect and/or to avoid increased erythema]
Too much effect with or without blistering	Moderate/severe erythema with or without blistering	Reduce dose by 25 % (or reduce MULT by 1) treat around any blistered area; do not treat blistered area until healed (crust disappeared).

Table 15.5 Sample protocol for determining dose for first excimer laser treatment of psoriasis

Plaque thickness	Induration score	Fitzpatrick skin type I–III (mJ/cm^2)	Fitzpatrick skin type IV–VI (mJ/cm^2)
Mild	1	300	400
Moderate	2	500	600
Severe	3	700	900

Table 15.6 Sample protocol for dosing on subsequent excimer laser treatments for psoriasis

Clinical observation	Patient able to tolerate previous treatment	Dosing change from prior dose
[a]No effect: no erythema, no tenderness, no plaque improvement	Yes	Increase dose by 25 %
	No	Increase dose by 15 %
[a]Minimal effect: slight erythema, slight tenderness, no significant improvement	Yes	Increase dose by 15 %
	No	Maintain dose
[a]Moderate-good effect: moderate erythema, moderate tenderness	Yes	Maintain dose
	No	Reduce dose by 15 %
Severe effect: extreme erythema and/or tenderness without blisters	Yes	Reduce dose by 15 %
	No	Reduce dose by 25 %
Blistering	Yes or no	Reduce dose by 25 %

[a]24–72 h after treatment

- **Missed Treatments** When laser treatment sessions are missed, the dosage of the subsequent treatment will have to be adjusted. The XTRAC Best Practice Committee provides a sample guideline listed below in Table 15.7. These guidelines assume that the patient's last dose resulted in the expected mild to moderate erythema lasting 24–48 h from the last treatment .
- Postoperative Considerations:
  - Clinician should record areas treated, dose setting, total body surface area treated and total energy used.
  - Keep treated areas free from excessive sun exposure following treatments.

Table 15.7 Protocol for missed excimer laser treatments for psoriasis

Number of weeks missed	Dose to be administered
One week	Last administered dose
Two weeks	Decrease dose by 25 % of last administered dose
Three weeks	Reassess according to original dosing guidelines

  - The clinician may require that the patient record their skin response 12–24 h following the treatment session to track side effects.

Vitiligo

- Preoperative Considerations: Please see "Preoperative Considerations" under Psoriasis
- Procedural Considerations:
  - It is recommended that treatments be given two to three times per week and some improvement is typically noticeable within ten treatments. Most patients will require 25–30 treatments to see the full effect.
  - **Dosing** The initial dose used in vitiligo treatment is dependent on the location of the area treated. Since certain areas seem to be less responsive to laser therapy, a higher initial dose is likely needed. For example, hands and feet are treated with an initial dose of 400 mJ/cm^2. A sample protocol is shown in Table 15.8. Similarly, determining the dose for subsequent treatment is dependent on clinical observations (Table 15.9).
  - To avoid unwanted side effects, be sure not to treat the same area twice and not to overlap areas of treatment.
- **Photosensitizing Medications** If a patient is started on a photosensitizing drug during treatment, clinicians must be cautious when beginning laser treatment. The drug can be scheduled to maximize the time between the next photo-

Table 15.8 Sample protocol for determining the first excimer laser treatment dose for vitiligo

Vitiligo location	Initial dose (mJ/cm^2)
Periocular	100
Face, scalp, ear, neck, axilla, bikini	150
Arm, leg, trunk	200
Wrist	250
Elbow	300
Knees	350
Hands, feet	400
Finger, toes	600

Table 15.9 Sample protocol for determining subsequent excimer laser treatments for vitiligo

Clinical observation	Typical dosing change
No effect: no erythema or mild erythema at 12–24 h	Increase dose by 50 mJ/cm^2
Good effect: mild to moderate erythema response for 24–48 h	Maintain dose
Moderate erythema: erythema still evident at 48–60 h	Decrease dose by 50 mJ/cm^2
Severe erythema: erythema still evident at 60–72 h or blistering has occurred	Postpone treatment until resolved, then reduce dose by 100 mJ/cm^2

therapy session and medication use, which may require, for example, that the medication be taken immediately following a phototherapy session. This would ensure that amount of medication in the patient's system is at it's lowest by the next laser treatment appointment. Please see Table 15.1 for a list of photosensitizing medications.

- **Missed Treatment** When treatments are missed, dosing must be adjusted accordingly. A sample protocol for this is included in Table 15.10, which assumes that the patient's

Table 15.10 Protocol for missed excimer laser treatments for vitiligo

Number of weeks missed	Dose to be administered
One week*	Same as last administered dose
If desired 48-h level of tenderness reached	Decrease dose by 25 mJ/cm^2
Two weeks	Decrease dose by 50 mJ/cm^2
Three weeks	Reassess according to original dosing guidelines

last administered dose resulted in a mild to moderate erythema lasting up to 48 h after treatment [42].

- **Failure of Treatment** If a vitiligo patient has had no response after about 30 treatments, and has followed the recommended guidelines of two to three treatments per week with adequate dosing, cessation of this form of treatment should be considered [42].
- **Postoperative Procedures** Please see "Postoperative Procedures" for Psoriasis.

Complications

- The most common side effects of the excimer laser include erythema, blistering and hyperpigmentation, which are limited to localized areas in contrast to large areas seen with full body treatments using traditional phototherapy [1, 12, 14, 15, 48]. Some of these adverse effects can cause the patient a fair amount of discomfort or pain.
- **Hyperpigmentation** There can be areas of hyperpigmentation of prior sites of psoriatic lesions following laser therapy, although pigmentation generally normalizes with time.
- **Photoaging** UV treatments are known to age the skin over time and may increase freckles and pigmentation of the skin. However, the localized application of laser therapy minimizes this affect on non-lesional skin.

- **Skin Cancer** As stated, there is a theoretical risk of increased skin cancer risk with phototherapy in general, but studies have not shown there to be an association with UVB light treatment and skin cancer [44].
- **Eye Damage** If eye protection is not worn, retinal damage and possibly cataracts can occur if eye protection is not worn. Each individual in a treatment room should wear the proper eye protection provided [43].

Prevention and Management of Complications

- The potential side effects of erythema and blistering can be prevented by properly screening patients in the preoperative period, as discussed. Special attention should be paid to avoiding or noting the presence of photosensitizing medications or conditions. Additionally, the clinician should take care in adjusting the light dose according to clinical observation and patient tolerance. Please refer to "Procedural Technique and Consideration."
- To relieve or prevent minor discomfort following treatment, or simply as an adjunct to laser therapy, patients may use topical steroids following a laser treatment session. Additionally, non-steroidal anti-inflammatories can be taken to alleviate any discomfort.

Future Directions

As laser technology continues to advance alongside our knowledge of disease pathogenesis, it is prudent to not only further develop current modalities of treatment but to consider entirely novel approaches to these complex and life-altering conditions.

The traditional concept of requiring repeated laser treatments has recently been challenged. The excimer laser has recently been tested using a single dose of excimer laser at

ten times the MED, referred to as "TURBO UVB", during one treatment session. By week four, results showed a decrease in median PASI score from 16.2 to 8.0 and 7.2 at week eight. In addition, PASI values at 8 weeks were reduced, on average, by 42 % from baseline. On histopathology, there was a decrease in epidermal thickness and T cell apoptosis following this one-time treatment [49].

Additionally, a new laser utilizing the UVA spectrum, called the Alba 355, delivers light at a 355 nm wavelength and employs a solid-state neodymiumdoped yttrium orthovanadate medium. Zerbinati, et al. determined that 12 out of 14 patients achieved PASI 75 following four treatments a week for 3 weeks, with no side effects reported in this particular study. However, treatments require 25 min for treatment over a single lesion, with sessions lasting up to an hour and 40 min, which may limit the practicality of this laser treatment [50].

While these novel approaches show promise in improving our treatment of chronic skin disorders, more research is required to refine these emerging modalities. By exploring new technologies and different methods of delivering existing treatments, patients suffering from these disorders will continue to have expanded treatment options for these often debilitating diseases.

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Chapter 16
Lasers and Lights for Onychomycosis

Jennifer A. Ledon, Jessica A. Savas, Katlein França, Anna H. Chacon, and Keyvan Nouri

Abstract In the armamentarium of available treatment strategies for onychomycosis, lasers are a relatively new approach for this difficult-to-treat disorder. Although initial studies evaluating lasers for onychomycosis appeared nearly 30 years ago with the carbon dioxide (CO_2) laser (Apfelberg et al., J Am Podiatry Assoc 74(10):509–513, 1984), clinical use has not gained popularity until recent years. Currently, several laser modalities are approved by the Food and Drug Administration (FDA) for the temporary increase of clear nail growth in patients with onychomycosis (Ledon et al., Laser Med Sci 29:823–829, 2014). These include the 532, 630–680, 1,064 and 1,320 nm Neodynium-doped yttrium aluminum garnet (Nd:YAG) lasers, as well as the 870/930 nm combination and 980 nm diode lasers. This chapter will provide a succinct approach to treatment of oncyhomycosis with

J.A. Ledon, MD (✉) • J.A. Savas, MD • K. França, MD, MS
A.H. Chacon, MD • K. Nouri, MD
Department of Dermatology and Cutaneous Surgery,
University of Miami—Miller School of Medicine,
1475 NW 12th Avenue, 2nd Floor, Miami, FL 33136, USA
e-mail: jledon1@med.miami.edu; jsavas@med.miami.edu;
k.franca@med.miami.edu; a.chacon@med.miami.edu;
annachaconmd@gmail.com; knouri@med.miami.edu;
knourimd@gmail.com

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lasers or light therapy, as well as short background on each of the laser modalities being studied for this indication.

Keywords Lasers • Lights • Onychomycosis • Nail fungus • Dermatophyte • Tinea rubrum • Treatment

Introduction

In the armamentarium of available treatment strategies for onychomycosis, lasers are a relatively new approach for this difficult-to-treat disorder. Although initial studies evaluating lasers for onychomycosis appeared nearly 30 years ago with the carbon dioxide (CO_2) laser [1] clinical use has not gained popularity until recent years. Currently, several laser modalities are approved by the Food and Drug Administration (FDA) for the temporary increase of clear nail growth in patients with onychomycosis [2]. These include the 532, 630–680, 1,064 and 1,320 nm Neodynium-doped yttrium aluminum garnet (Nd:YAG) lasers, as well as the 870/930 nm combination and 980 nm diode lasers. Although literature evaluating the efficacy of lasers for onychomycosis is scant, studies have also included ultraviolet (UV) light, photodynamic therapy (PDT), the femtosecond infrared titanium sapphire 800 nm laser, the ablative CO_2, Nd:YAG, and diode lasers, as mentioned previously. Randomized controlled trials are still needed to fully assess the efficacy of these modalities.

Background

Onychomycosis is a disorder of hyperkeratinization of the nail bed secondary to fungal infection, ultimately leading to nail discoloration and/or dystrophy. It may present as superficial onychomycosis (SO; white or black), distal/lateral subungual onychomycosis (DLSO; Figure 16.1), proximal subungual onychomycosis (PSO), total dystrophic onychomycosis (TDO; Figure 16.2) or mixed type onychomycosis (Table 16.1) [3].

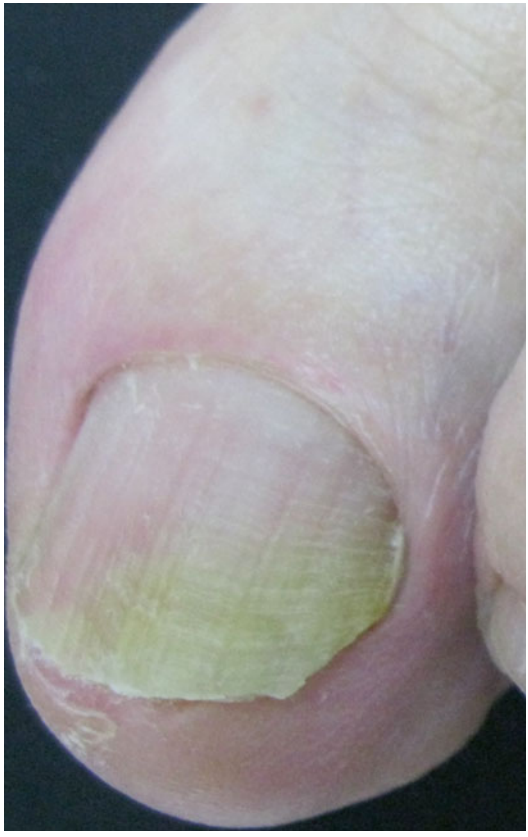

Figure 16.1 Distal/lateral subungual onychomycosis

In endonyx onychomycosis, there is diffuse opacification or graying of the toenail and lamellar splitting without characteristic hyperkeratosis or onycholysis [5].

While *Trichophyton rubrum* (*T. rubrum*) is the most common causative organism, non-dermatophyte molds and yeasts have been implicated as well (Table 16.2). In diabetic or immunocompromised individuals, atypical agents should be considered. Although more common in the elderly, appreciable rates of onychomycosis have been found in those under 18 years of age as well.

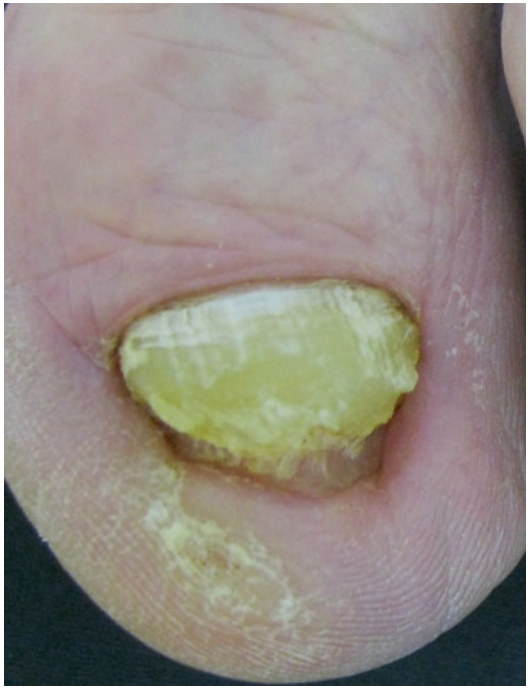

Figure 16.2 Total dystrophic onychomycosis

Unlike with other dermatologic conditions, the mechanism by which lasers are able to treat or improve the appearance of onychomycosis is unclear. Proposed mechanisms include direct inactivation of fungi by heat, the creation of reactive oxygen species, or selective photothermolysis, although a target chromophore has yet to be identified [16–18].

CO_2 Laser

The carbon dioxide (CO_2) laser system is ablative in nature and therefore can serve as a primary treatment for onychomycosis [1]. It may also serve as an adjunct to topical antifungal agents by providing a means of penetration through the nail plate to the nail bed where fungal growth originates [19]. Less invasive options, however, are currently available.

Table 16.1 Clinical presentation and commonly implicated organisms for each subtype [3, 4]

Subtype	Clinical presentation	Causative agent [3, 4]
Distal/lateral subungual	Hyperkeratosis, dyschromia, onycholysis.	*T. rubrum* (and other dermatophytes)
	Originating from distal and/or lateral nail edge.	*Scytalidium spp.*
		C. albicans
		Fusarium spp.
		S. brevicaulis
Proximal subungual	Striae, dyschromic patches, originating from proximal nail plate.	*T. rubrum*
	With or without paronychia.	*Fusarium spp.*
		Candida spp.
Superficial	Superficial white or black patches, originated from dorsal nail plate.	**White**:
	May progress ventrally through entire nail plate.	*T. mentagrophytes*
		T. rubrum
		Fusarium spp.
		Acremonium spp.
		Aspergillus spp.
		Black:
		T. rubrum
		Scytalidium spp.
Total dystrophic	Complete dyschromia and dystrophy of the nail plate.	*T. rubrum*
	Can be advanced form of other subtypes or primary disease in immunocompromised [3].	*C. albicans*
		Scytalidium spp.

(continued)

Table 16.1 (continued)

Subtype	Clinical presentation	Causative agent [3, 4]
Endonyx	Diffuse opacification of the nail without hyperkeratosis or onycholysis	*T. soudanense*
	Lamellar splitting of the nail plate [4].	*T. violaceum*

Table 16.2 Prevalence of various fungi based on special populations [6–15]

	Prevalence[a] (% of positive cultures)			
Organism	Overall [6–10]	Pediatric [11–13]	Diabetic [10, 14, 15]	Fingernail [6, 9, 12]
Dermatophytes	49.9–82.8	27.9–61.2	37–51.6	7.8–37.5
Yeast	10.8–47.4	6.3–34.7	10.4–56	62.5–88.7
Non-dermatophyte molds	2.7–21.2	1.4–4.3	13.7–14.8	0–15.4
Mixed	6.5	2.2–6.5	8.8	

[a]"Overall", "Pediatric" and "Diabetic" are in reference to toenail onychomycosis. "Fingernail" includes both pediatrics and adult populations

870/930 nm Diode

In one of the randomized controlled trials evaluating the efficacy of lasers for onychomycosis, both negative cultures and at least 3 mm of clear nail growth were reported in 39 % of nails 4 months after the last treatment [20]. A blinded panel, however, reported 77 % clinical improvement. Sessions consisted of treatment with the 870/930 nm first, followed by the 930 nm alone.

980 nm Diode

Currently, no peer-reviewed studies have been published on the efficacy of the 980 nm diode laser for onychomycosis; however, its mechanism is similar to the 870/930 nm diode.

Both systems are currently FDA-approved for the temporary increase of clear nail growth in patients with onychomycosis.

1,064 nm Nd:YAG

Several output modes are available for the Nd:YAG laser, including long- and short-pulsed and Q-switched modes, as well as 1,064, 940, 1,320, and 1,440 nm wavelengths. In addition, a potassium titanyl phosphate (KTP) filter allows for frequency doubling and thus 532 nm light. Due to its longer wavelength, the 1,064 nm Nd:YAG is thought to deeply penetrate tissue and target fungal overgrowth in the nail bed. The 532 nm Nd:YAG may also be better at targeting the fungal pigment xanthomegnin, which has a peak absorption between 406 and 555 nm [18, 21].

PDT

5-aminolevulinic acid (ALA) is the most commonly used photosensitizer in PDT for onychomycosis due to conversion of 5-ALA to protoporphyrin IX by fungi and yeast. Protoporphyrin IX possesses peak wavelength absorption between 630 and 700 nm, making it easily targeted by red light.

Indications

- Clinically- and mycologically-confirmed[1] onychomycosis, by:
  - Direct microscopy
  - Fungal culture

[1]Sensitivity and specificity can vary. Culture plus periodic acid-Schiff (PAS) stain is traditionally thought to be the most sensitive modality (94 %; PAS alone 85 % sensitive, no statistically significant difference), but results may take up to 6 weeks [22]. One study, however, showed that collection of subungual hyperkeratosis can lead to high diagnostic accuracy (97 %) without processing nail plates [23].

- Patient cannot tolerate or does not wish to undergo other treatment modalities, such as:
  - Topical lacquers/ointments
  - Surgery
  - Oral antifungals
- Able to maintain adequate hygiene in between treatments to prevent recurrence (avoid reusing socks, apply antifungal sprays to insides of shoes)

Contraindications

- Unable to tolerate other forms of light therapy, such as:
  - Patients with seizure disorders triggered by light
  - Patients with lupus erythematosus
  - Patients who have received or are currently receiving gold therapy
  - Patients with a light sensitivity disorder
  - Patients taking medication that increases sensitivity to light
- Pregnant (effects on fetus are unknown)
- Peripheral neuropathy[2]

Procedural Technique/Consideration

Pre-op Care

- It is important to rule out other causes that may result in dystrophic or discolored nails prior to treatment

[2]Relative contraindication. Patients with diabetes or a known peripheral neuropathy cannot provide feedback that temperatures are too high during treatment (laser modalities). To avoid burning, they should either be treated with lower amounts of energy than the normal population, gradually increasing at each session if they tolerated the previous dosage well, or the temperature of the nail should be monitored with live temperature readings.

Table 16.3 Conditions that may mimic onychomycosis [24]

Lichen planus
Atopic dermatitis
Psoriasis
Bacterial infections
Subungual skin cancer
Trauma
Congenital malalignment
Yellow-nail Syndrome
Median canalicular dystrophy
Pincer nail deformity

(Table 16.3). Nail samples for direct microscopy should be collected properly in order to facilitate diagnosis:

- DLSO: Debris should be collected from under the nail plate and nail bed. Sensitivity improves with proximity of infection and the use of a drill over curettage to collect sample [25].
- SO: Surface of the nail can be scraped with a scalpel.
- PSO: Sample should be taken from the proximal nail bed with drill, scalpel or curette [26].
- If whole nail clipping is obtained, grind in a nail micronizer before potassium hydroxide (KOH) preparation [27].
- Collect subungual debris if possible.

- Cultures should be obtained for identification of the fungal species [28]:
  - Cyclohexamide medium: isolates dermatophyte species.
  - Non-cyclohexamide medium: isolates yeasts and non-dermatophyte molds.
  - Chloramphenicol can be added to both mediums to eliminate bacterial growth.
  - The black mold, *Alternaria*, is a common contaminant [28].

- Discuss expectations with patients. Clear nail growth is not guaranteed. More than one session may be required, and re-infection is possible. It may also take several months to see an increase in clear nail growth.
- Extremely thickened nails may require pre-treatment with urea solution.
- For PDT: chemically avulse nail with urea, or pre-treat the nail with urea, prior to therapy.

Technical Considerations

- Consult laser manual for specific fluences, spot sizes, pulse durations and number of passes as these differ between laser systems.
- Generally, the great toenail will require the most energy for effective treatment. The remaining toenails and fingernails will typically require less than half of the energy that is required for the great toenail.
- A real-time temperature monitor may be used to ensure that excessive temperatures are not reached.

Post-op Care

- No wound care or dressings are necessary after treatment.
- Arrange open lines of communication should any adverse events occur.
- Patients should be encouraged to keep feet dry and to rotate shoes and socks (may reduce the chance of re-infection).

Complications

The reported incidence of complications following laser use for the treatment of onychomycosis is low, substantiating its role as a treatment modality for this condition. Side effects, however, may include:

- Pain, heat or tingling
- Temporary darkening under the nail [29]

Prevention and Management of Complications

One study evaluated the subjective pain evaluation following laser treatment for onychomycosis [30]. Approximately 26.4 % of patients experienced no pain, 45.8 % experienced mild pain, and 27.8 % experienced moderate pain. No patients reported severe or intolerable pain. Average temperatures of 50 °C were reached during treatment, dropping to approximately 40 °C after 1 min.

The use of temperature probes and/or predetermined dosage criteria can be helpful in preventing possible complications when using laser treatment for onychomycosis. This is especially helpful in diabetic patients and patients with peripheral neuropathy as they may not be able to provide verbal feedback that temperatures are intolerable.

Patients should also be made aware that temporary darkening under the nail may occur with laser treatment. Should any complications or adverse effects occur, physicians should make themselves available to address questions and concerns.

Conclusions

Despite the fact that many patients seek treatment for onychomycosis for cosmetic reasons, in the elderly, diabetic, and immunocompromised populations, serious sequelae such as infection may occur. It is important, therefore, to treat and prevent recurrences in these populations in order to avoid these complications. Current treatment options include topical lacquers and ointments, systemic anti-fungals, surgery, and laser therapy. As reported efficacy for topical lacquers and ointments are poor and many people cannot tolerate the invasiveness of surgery or the systemic side effects associated with oral antifungals, lasers are an ideal solution.

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Chapter 17
Intense Pulsed Light Therapy

Leyre A. Falto-Aizpurua, Christian R. Halvorson, and Robert Weiss

Abstract Intense pulsed light (IPL) systems are mostly used for improving the skin texture from aging damages. This technology works by emitting a pulsed, noncoherent, polychromatic light through a filter, which can be changed according to the desired target within the skin. The side effects of these devices have been reduced, allowing its use for a wide variety

L.A. Falto-Aizpurua, MD
Department of Dermatology and Cutaneous Surgery, University of Miami—Miller School of Medicine, 1475 NW 12th Avenue, 2nd Floor, Miami, FL 33136, USA
e-mail: lafalto@gmail.com

C.R. Halvorson, MD
Department of Dermatology, University of Maryland School of Medicine, 419 W Redwood Street, Suite 240, Baltimore, MD 21201, USA
e-mail: crhalvor@gmail.com

R. Weiss, MD FAAD, FACPh (✉)
Department of Dermatology, University of Maryland, 54 Scott Adam Road, Hunt Valley (Baltimore), MD 21030, USA

Laser Skin & Vein Institute, 54 Scott Adam Road, Hunt Valley (Baltimore), MD 21030, USA
e-mail: rweiss@mdlsv.com

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of clinical indications. Currently, IPL devices are a safe and efficient treatment option for non-ablative skin rejuvenation, hair removal, and the removal of pigmented and vascular lesions.

Keywords Intense pulsed light • IPL • Photorejuvenation • Photoepilation • Poikiloderma • Dyspigmentation • Acne • Telangiectasias

Introduction

Intense pulsed light (IPL) therapy is commonly used for the cosmetic improvement of the aging skin. In 1994, this device was first launched and promoted as a treatment option for leg telangectasias [1, 2] but had a limited utility due to the side effect profile. Throughout the years, technical modifications to this device have allowed it to be safer and easier to use, expanding its clinical use. Currently, IPL is a generally accepted treatment tool for non-ablative skin rejuvenation, photoepilation, and the treatment of pigmented and vascular lesions [1, 3–6]. It is regarded by some as the colloquial "jack-of-all-trades, master of none."

Background

This technology emits a pulsed, noncoherent, polychromatic light through a filter, which can be changed according to the desired target within the skin [1]. Devices contain a xenon-flash lamp powered by capacitor banks controlled by microprocessors, which can alter the pulse duration. The broad spectrum of a flash lamp allows energy from multiple wavelengths (500–1,200 nm) to be emitted [7]. Filters and parameters, such as fluence, pulse duration and pulse delay, can be adjusted by software to treat different targets, making it a versatile device.

General Concepts

- **Chromophore** It is destroyed by the heat generated upon energy absorption. This should occur with minimal damage to surrounding structures when using adequate parameters.
- **Filters** If changeable should be changed based on the target lesion's depth within the skin, absorption spectrum of the desired chromophore and the patient's skin type. Some devices require changing a particular delivery module.
- **Pulse duration** Should be equal to the thermal relaxation time (TRT) of the target [8], which is defined as the required time for a heated target to cool by 50 %. This dictates that smaller targets cool faster, requiring shorter pulses. For example, small collections of melanin within superficial pigmented lesions should be treated with short pulses, while deeper, larger melanin collections need longer ones. For vascular lesions, the pulse duration is approximately target size in millimeters squared. So for example, a 0.4 mm vessel would be treated with a 16 ms pulse.

Advantages

- Can target multiple chromophores simultaneously.
- Can treat vascular lesions with minimal risk of purpura when compared to older pulse dye laser (PDL) therapies, which only have very short pulse durations [1].
- Can treat large body areas in short treatment sessions given its large beam size and rapid pulse rate [9].

Disadvantages

- Bulky handpieces, making it difficult to treat certain areas of the face.
- Multiple treatment sessions might be required.

- Deeper lesions may be beyond the capability of the filtration or require too long a pulse, which can deliver too much infrared causing epidermal injury.
- Quality-switched lasers with nanosecond pulse durations provide greater selectivity for melanosomes and therefore higher efficacy for particular indications [10]. Newer picosecond lasers are now entering the arena for treatment of pigmentation.
- Given the wide range of treatment parameters, it can lead to undesirable adverse effects if utilized by inadequately trained providers and with changing pigmentation of patients based on seasonal tanning.

Indications

Treatment of Vascular Lesions

- Can efficiently treat facial and leg telangiectasias, poikiloderma of Civatte, hemangiomas, and venous and capillary malformations [11–14].
- Target: hemoglobin, which absorbs at 418, 542, 577 and 800–1,100 nm [15].
- Mechanism: Visible blood vessels are replaced with fibrous granulation tissue after vessel coagulation and destruction [16].
- Multiple sequential pulses or multiple filtrations (in some iterations) with appropriate delay times provide adequate heating of blood vessels without harming surrounding structures.

Facial Telangiectasias

- Small red facial telangiectasias can be treated with synchronized pulses. A first, short pulse should be used coupled with a second longer pulse. Duration and fluence should be gradually increased, with increasing vessel size [1].

- Bjerring et al. demonstrated that after 1–4 IPL treatment sessions, 79.2 % of patients achieved more than a 50 % reduction in the number of vessels, with 37.5 % achieving a 75–100 % reduction [17].
- Linear and spider telangectesias were treated in 140 patients by Retamar et al. with 67.1 % of patients having 80–100 % clearance [18].
- When compared to PDL, IPL was found to be equally safe and effective in treating facial telangiectasia in some studies [19].
- Adverse effects in the above mentioned studies were minimal. These included edema, erythema, and pain. Minimal hyperpigmentation that resolved within a month was reported in one patient. Purpura, hypertrophic or atrophic scars, or hypopigmentation were not reported [19].

Poikiloderma of Civatte

- This lesion is characterized by a reticulate dyspigmentation, telangiectasias, as well as epidermal atrophy.
- Target: melanin and hemoglobin [1, 3, 20].
- A study by Weiss et al. showed a 75–100 % improvement in 82 % of patients after 1–5 (usually 3) treatment sessions [3]. Similar results were obtained by Rusciani et al. [21].
- Adverse effects of the above mentioned studies were minimal. These included swelling and erythema (lasting 24–48 h), microcrusts, purpura (lasting a few days), unusual blister formation (in darker skin types) and small areas of persistent hypopigmentation [3].

Other Vascular Lesions

- Hemangiomas, port-wine stains, and non-facial telangiectasias can also be treated.
- Centrofacial hemangiomas: Angermeir showed a 75–100 % clearance rate in 45 patients [22, 23].
- Port-wine stains (PWS): Raulin et al. achieved 70–100 % clearance in 70 % of patients, with relatively few adverse

effects, which included superficial blister formation (8 %) and transient crusting (20 %). These were especially seen in those with purple PWS [14].

- Leg telangiectasia: multiple studies found clearance rates between 75 and 100 % depending on the size of the targeted vessel [24–26]. However, a study by Green et al. reported complete or almost complete clearance in only 9.5 % of patients (n = 72), with 50 % developing hyperpigmentation and 20 % hypopigmentation [27]. Due to conflicting results, IPL and laser treatment for leg telangiectasias should be reserved for resistant cases, very small vessels, or cases of telangiectatic matting after sclerotherapy [23, 28–30].

Treatment of Pigmented Lesions

- IPL is useful in the treatment if superficial pigmented lesions [5, 17, 31, 32]. Other lesions that can be treated are ephelides [33], post-toxic epidermal necrolysis hypermelanosis [34], aberrant Mongolian spots [35], pigmented actinic lichen planus [36], and lentigines associated with LEOPARD syndrome [37].
- Target: melanin. It has a broad absorption spectrum (250–1,200 nm) but has the greatest absorption at lower wavelengths and it decreases with higher wavelengths [3, 38].
- Filter: should be chosen based on the depth of the lesion [3] Lower cut-off filters along with shorter pulse durations are beneficial [39].
- Residual pigment can be treated with lower cut-off filters, higher fluences, and diminished skin surface cooling.
- Nevus spilus: Complete and sustained resolution after four treatments has been reported [31].
- Solar lentigines and macular melanocytic nevi: Single IPL treatments were performed, achieving pigment reduction in 96 % of patients; solar lentigines had an average clearance of 74.2 % and nevi, 66.3 % [17].

- Melasma: (there are no foolproof treatments for melasma)
  - 89 Chinese patients with Fitzpatrick skin types III–IV received 4 treatment sessions with 77.5 % of patients achieving 51–100 % improvement [32].
  - A study demonstrated that a single IPL treatment combined with triple combination topical therapy (hydroquinone 4 %, tretinoin 0.05 %, fluocinolone 0.01 %), was more effective than the use of topicals alone for refractory mixed and dermal melasma in patients with Fitzpatrick skin types II [40]. Of these patients, 3 with malar melasma and skin phototype IV, developed postinflammatory hyperpigmentation that resolved with the use of bleaching agents for 4–6 months.
- Complete elimination of facial dyspigmentation is rare with IPL alone, and alternate laser treatments, such as Q-switched devices, can be added to obtain best results [5].

Photoepilation

- Hair removal by IPL has been shown in numerous studies to be safe and effective [4, 41–43].
- Target: melanin within hair follicles (600–1,100 nm) [4, 44].
- Mechanism: Effective treatments require energy absorption and heat transfer from the hair matrix melanin to the stem cells in the bulge region of the hair follicle. This will produce collateral damage and eventual hair follicle destruction [9].
- Ideal candidates are light-skinned patients with dark hairs, as in darker-skinned patients, epidermal melanin competes with the hair follicle melanin for light absorption, decreasing treatment efficacy and increasing adverse effects [9].
- A report by Weiss et al., showed hair clearance to be 64 % after two treatments with a sustained hair reduction of 33 %, in patients with Fitzpatrick skin types of I–V [41].
- Long-term hair removal efficacy was found to be 76 % after a mean of 3.7 IPL treatments [4]. Transient superficial crusting was reported in 6 % of patients, and temporary

hyperpigmentation occurred in 9 %, but resolved within 12 weeks.
- Long-pulsed diode laser (LPDL) was compared to IPL for the treatment of hair removal in hirsute women, with IPL achieving best results, although not statistically significant [45].
- When compared to diode laser, it was found to be more effective, but the IPL was significantly less painful [46].

Photorejuvenation

- Target: multiple.
- Mechanism: A nonablative approach that improves the overall appearance of aging skin, possibly due to remodeling of collagen fibers and neocollagenesis [6].
- The entire face should be treated, with treatment sessions generally performed at 3–4 weeks intervals for a total of three to six treatments.
- IPL improved all aspects of photodamaged skin in 90 % of subjects with four treatments, and some up to six [47].
- Negishi et al. found greater than 60 % improvement in more than 80 % of patients after 5 or more treatments [48].
- Long-lasting results were obtained after 4 years of initial treatment with 83, 82 and 79 % improvement in skin texture, telangiectasia and pigmentation components, respectively [49].
- Hedelund et al. found that three IPL treatments were effective in improving skin texture, telangiectasias, and irregular pigmentation, but had no effect on rhytids [50].
- Topical 5-aminolevulinic acid combined with IPL may have superior photorejuvenative effects than IPL alone [51, 52].

Acne

- IPL may be used to treat acne and acne scars.
- Target: melanin and water, improving pigmentation, stimulating neocollagenesis, and destroying sebaceous glands [53, 54].

- 37 patients were treated with 4–6 IPL treatments, followed by two sessions of fractional carbon dioxide CO_2 laser [55]. Compared to baseline, IPL therapy reduced the inflammatory lesion and atrophic score, with even further improvement of the atrophic score with the fractional CO_2 laser. 80 % of patients rated their results as 'excellent' or 'good.'
- Photodynamic therapy with topical 5-aminolevulinic acid and IPL has also been shown to be an effective treatment for moderate to severe acne, and superior to IPL alone [56].

Contraindications

IPL should be avoided in:

- Women who are pregnant or are breastfeeding.
- Patients receiving systemic retinoids.
- Patients receiving photosensitizing medications.
- Patients suffering from a disease or genetic condition that results in photosensitivity [7].

Procedural Considerations

Pre-operative Care/Precautions

- Avoidance of tanning before therapy.
- Informed consent should be obtained for all patients. The risks, benefits, side-effect profile, and alternatives should be discussed.
- The area being treated should be clean and shaved if needed [7].
- Topical anesthesia is generally not required, but may be used if needed.
- Safety goggles and/or eye coverings should always be worn by the practitioner and patient.
- A 1–2 mm layer of cold ultrasound gel or aloe vera should be applied to the treatment area [1].
- A 10 % overlap between pulses is recommended.

- Positive clinical end points:
  - Vascular lesions: disappearance or a darker blue appearance of telangiectasias, as well as brightening or smudging of the lesions.
  - Pigmented lesions: will darken with effective therapy.
  - Hair removal: perifollicular edema and erythema.
- An initial or test pulse should be performed to determine the response to therapy. If adequate, start performing multiple passes at different angles.

Post-operative Care/Precautions

- Patients should be instructed to avoid sun and use sun protection.
- They should also be instructed to provide gentle skin care.
- Patients are normally followed-up and/or treated at 4–6 weeks interval.

Adverse Reactions/Complications

Common Side Effects [1]

- Pain: described either as a stinging, brief grease splatter, or electrical shock.
- Burning sensation: usually mild and lasted less than 10 min in 45 % of patients.
- Erythema: lasted several hours to up to 3 days. In full-face treatments, 25 % had mild cheek swelling or edema lasted 24–72 h.
- Dyspigmentation: hyper- or hypopigmentation lasting less than 2 months was described in 8–15 % of treated sites.
- Crusting: 2 % of patients developed scattered crusting in areas of increased pigmentation, and peeled off within 7 days.
- Purpura: was noted in isolated pulses in about 4 % of cases.

Serious Side Effects

- Blister formation[1]
- Permanent pigmentary alterations[1]
- Scarring[1]

Prevention of Management and Complications

- With the use of appropriate filters and parameters, selectiveness of treatment is achieved, minimizing collateral damage to surrounding structures.
- By using higher filters (550 or 560 nm) when treating poikiloderma in patients with significant dyspigmentation, major epidermal absorption is avoided, minimizing the possibility of excessive swelling and crusting [3].
- Gel use (water-based) is recommended to minimize epidermal damage by decreasing the refraction index of light to the skin. It also promotes a "heat-sink" effect and facilitates the gliding of the hand piece [1].
- Test pulsing is highly recommended as it helps determine the ideal parameters to provide best results with minimal side effects. Some signs that may indicate treatment parameters are too aggressive are: immediate purpura, excessive blanching, pronounced edema, blistering, graying, or excessive discomfort. Waiting 30 min after a test pulse is recommended to assess potential side effects.
- Performing multiple passes at different angles avoids footprinting of the crystal outline or what is sometimes referred to as zebra pigmentation.
- Darkly pigmented patients (Fitzpatrick skin types IV–VI) require lower fluences, longer wavelength filters, and longer pulse widths.
- Purpura most often results with use of a 515 filter or with too short pulse durations [1].

[1]Darker skin types being at greater risk.

Future Directions

IPL devices are versatile, non-invasive light-based systems that can successfully treat a wide range of skin conditions that continues to expand as technology improves [57]. It has gained popularity as a cosmetic and medical device, due to prevalence and decreased cost of ownership as well as increasing evidence supporting safety and efficacy when used by appropriate personnel. Unfortunately, non-selective thermal damage is always a risk that is increased when IPL therapy is provided by untrained or insufficiently trained practitioners. Therefore, a comprehensive understanding of mechanism, design and subtlety of different IPL devices, as well as parameters and indications is highly desirable in order to provide safe and successful treatments.

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Chapter 18
Photodynamic Therapy

Jessica A. Savas, Jennifer A. Ledon, Katlein França, and Keyvan Nouri

Abstract Photodynamic therapy (PDT) refers to the therapeutic use of a locally concentrated photosensitizing agent and subsequent light irradiation to produce reactive oxygen intermediates, specifically singlet oxygen species. The accumulation of the light-induced singlet oxygen in the target tissue causes selective damage to biologically important structures. PDT has an extensive history of use in oncology and has recently gained popularity in the management of dermatologic conditions, both malignant and benign. PDT has quickly become an attractive option for the non-invasive treatment of a variety of dermatologic indications due to a low incidence of adverse events and excellent cosmetic outcomes, even when treating large and/or multiple lesions. This chapter will discuss the currently supported indications as well as any known contraindications to PDT use in dermatology. Procedural techniques and pre- and post-operative considerations will

J.A. Savas, MD (✉) • J.A. Ledon, MD
K. França, MD, MS • K. Nouri, MD
Department of Dermatology and Cutaneous Surgery,
University of Miami—Miller School of Medicine,
1475 NW 12th Avenue, 2nd Floor, Miami, FL 33136, USA
e-mail: jsavas@med.miami.edu; jledon1@med.miami.edu;
k.franca@med.miami.edu; knouri@med.miami.edu;
knourimd@gmail.com

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also be addressed along with prevention and management of complications associated with the use of PDT.

Keywords Photodynamic therapy • Photosensitizer • Skin cancer • Actinic keratosis • Aminolevulinic acid • Treatment • Dermatology • Light • Laser

Introduction

- Photodynamic therapy (PDT) has an extensive history of use in oncology and has recently gained popularity in the management of dermatologic conditions, both malignant and benign.
- PDT has become an attractive option for the non-invasive treatment of a variety of dermatologic indications due to a low incidence of adverse events and excellent cosmetic outcomes, even when treating large and/or multiple lesions [1].
- Photodynamic therapy refers to the therapeutic use of a locally concentrated photosensitizing agent and subsequent light irradiation to produce reactive oxygen intermediates, specifically singlet oxygen species. The accumulation of the light-induced singlet oxygen in the target tissue causes selective damage to biologically important structures.
- The photosensitizing agents that are currently used are prodrugs that exploit the body's endogenous heme biosynthesis pathway for conversion into their active metabolite, protoporphyryin IX (PpIX).
- Early use of PDT was complicated by the long half-life of the systemic photosensitizing agents and the attendant prolonged photosensitivity experienced by patients.
- Over time, topical formulations have been developed and are particularly well suited for use in dermatology.
- Namely, 5-aminolevulinic acid (5-ALA) remains the most extensively studied topical photosensitizer and currently carries an FDA approval for the treatment of actinic keratosis (AK).
- While current evidence most strongly supports the use of topical PDT for the treatment of face and scalp AK's, Bowen's disease and superficial BCCs, the list of indications is rapidly expanding [2] (Table 18.1).

Table 18.1 Indications for topical PDT in dermatology [3]

Malignant and pre-malignant conditions	Actinic keratoses[a]
	Actinic chelitis
	Superficial basal cell carcinoma
	Superficial squamous cell carcinoma
	Field cancerization of the skin
	Bowen's disease
	Mammary and extra-mammary Paget's disease
	Erythroplasia of Queyrat
	Cutaneous T-cell lymphoma
	Kaposi's sarcoma
	Malignant melanoma
	Keratoacanthoma
	Gorlin syndrome
	Penile and vulvar intraepithelial neoplasia
	Langerhans cell histiocytosis
	Skin metastases

(continued)

Table 18.1 (continued)

Cosmetic and other potential indications	Acne vulgaris
	Sebaceous hyperplasia
	Hidradenitis suppuritiva
	Skin and nail mycoses
	Photorejuvination
	Fine rhytides
	Pigment changes
	Hair removal
	Erythrasma
	Molluscum contagiosum
	Rosacea
	Hailey-Hailey
	Darier disease
	Lichen planus
	Lichen sclerosus (genital and extragenital)
	Sarcoidosis
	Necrobiosis lipoidica
	Radiodermatitis

[a]Only indication that currently carries FDA approval

Background

Photosensitizers

- In dermatology, topically active agents are preferred over intravenously administered photosensitizers.
- Most research has been done with 5-aminolevulinic acid (ALA) and topical ALA-PDT currently carries FDA-approval for the treatment of AK's.
- An esterified preparation, methyl aminolevulinate (MAL), is also used for the treatment of AK's, Bowen's disease and superficial basal cell carcinomas (BCC).

- Studies investigating a potential difference in efficacy of ALA-PDT vs. MAL-PDT have been conducted; however, to date, neither has emerged significantly superior to the other, and both are currently recommended for use in topical PDT [4].
- Topical ALA-PDT for skin tumors involves the application of 20 % ALA in an oil-water emulsion, covered by an occlusive dressing [5].
- 20 % topical ALA preparations have been the most extensively studied for the treatment of Bowen's disease [6].
- Furthermore, no difference in efficacy has been noted between 10 and 30 % ALA preparations for the treatment of AK's [6].

Light Sources

- In order to achieve maximum efficacy and selectivity, the photosensitizer should display preferential absorption at the wavelength of visible light used.
- PpIX has its largest absorption peak at 410 nm (blue light) with lesser absorption peaks at 505, 540, 580, and 630 nm.
- Most light sources exploit the 630 nm wavelength (red light) to achieve greater tissue penetration [7].
- Both coherent and incoherent light sources have been used:
  - Coherent:
    - 630 nm argon pumped-dye lasers
    - 628 nm gold lasers
    - 595 nm pulsed dye laser
    - Diode lasers
  - Incoherent:
    - High pressure, broadband lamps

  Blue and red light sources are most commonly used.
  A blue fluorescent lamp that emits light at 417 nm is regularly used in conjunction with ALA-PDT for the treatment of AKs in the United States.

Table 18.2 Advantages of non-laser light sources for topical PDT

Inexpensive
Operator friendly
Requires little maintenance
Capable of irradiating large areas (ideal for acne, diffuse AK's, hair removal and other cosmetic indications)

Red light is preferred when treating Bowen's disease and BCC due to deeper penetration.
The use of white and green light has been reported as well for the treatment of facial and scalp AK's [8, 9].

  - Light-emitting diodes
  - Intense pulsed light systems

- Incoherent light sources generally represent the current gold standard for topical PDT offering several advantages over lasers (Table 18.2).
- At present, there is no single light delivery system that is considered ideal for every indication for topical PDT and each clinical scenario should be evaluated on a case-by-case basis [4].

Indications

- Age between 18 and 95 years [3].
- Skin types I–IV [3].
- Patients deemed poor surgical candidates.
- Patients who are unable to tolerate the associated adverse effects of traditional interventions (e.g. the inflammatory response produced by some topical immunomodulators).
- Patients who have failed previous attempts at cure with other topical therapies.
- Patients with lesions located in an anatomically or cosmetically sensitive areas, where surgical intervention may result in functional or aesthetic impairment.

- When size, site, and number of lesions would limit the utility/efficacy of traditional therapeutic interventions [3].
  - Lesions in unusual locations (e.g. digits, subungal, nipple)
  - Lesions that arise in the setting of poor wound healing (e.g. lower extremity, radiation dermatitis, epidermolysis bullosa) [3]
- In socio-economic situations that result in patient compliance issues
- PDT may prove to be particularly advantageous in the immunosuppressed where topical immunomodulators have demonstrated diminished effect [3].

Contraindications

- Patients on medications associated with photo-toxic reactions.
- Patients with photo-sensitive diseases.
- Patients who have a history of phototoxic or photoallergic reactions.
- Active infection in the area to be treated.
- Patients with a history of recurrent herpes simplex outbreaks in the area to be treated may be given antivirals prophylactically.
- Topical PDT is relatively contraindicated as monotherapy for high-risk lesions such as morpheaform subtype of BCC.

Pre-operative Considerations

- Complete a thorough history and physical examination.
- Establish diagnosis.
- Consider photography of lesions.
- Record number, size, and site of lesions.
- Lesional surface preparation prior to administration of the topical photosensitizing agent has been shown to contribute to increased efficacy of PDT treatment [3, 10].

- Lesional preparation with the aim of removing overlying crust or scale has been accomplished using any of the of the following methods:
  - Saline-soaked gauze
  - Glycolic acid scrub
  - Acetone scrub
  - 40 % Urea cream
  - Tape-stripping
  - Microdermabrasion
  - Curettage

Procedural Technique

- The photosensitizing agent should be applied to the affected area along with a 5 mm margin of clinically normal skin [4].
  - Anecdotally, practitioners may apply the topical agent to the entire face or scalp when multiple lesions are present as opposed to strictly adhering to the above guideline.
- An occlusive dressing should be placed to retain the photosensitizer cream as well as an additional bandage to minimize ambient light exposure during the incubation time [4].
  - The above only applies when using MAL; occlusive dressings should not be used with ALA preparations.
- Incubation Time:
  - Drug-to-light intervals (DLI) vary considerably depending on the photosensitizer and light source used as well as the primary lesion/condition being treated.
  - When utilizing ALA, DLIs of 3–48 h have been reported with 4–6 h being the most extensively studied [4].
  - Incubation times with MAL tend to be shorter than those recommended when using ALA with the DLI of 3–6 h supported by most recent evidence [10].
  - When treating superficial BCCs with MAL, in its licensed form, the protocol describes a drug-light interval of 3–6 h being administered for two sessions, 1 week apart [3].

- Remove excess photosensitizing cream after completion of the desired incubation time.
- Some authors recommend an optional Wood's light examination of the area exposed to the topical photosensitizer after the designated incubation time to confirm local PpIX accumulation [4].
- If topical anesthetic is used it should be applied after the excess photosensitizer has been removed and ideally, approximately 1 h prior to light irradiation [4].
- Light delivery
  - The light source and wavelength also varies depending on the lesion/condition being treated as well as the photosensitizer used.
  - The field of light irradiation should include the affected area as a well as a 5 mm border around each lesion [3].
  - For light dosimetry values for licensed indications, consult the illumination recommendations specific to the photosensitizer and brand/type of light delivery system used.

Post-operative Considerations

- Record the total light dose and intensity of illumination
- The patient should be advised to limit or completely avoid light/sun exposure for approximately 24–48 h after treatment.
- Patients should be followed regularly to assess for adverse reactions, determine if additional treatment sessions are required, and monitor for recurrence of lesions.
  - If a nodular BCC was treated with topical PDT as monotherapy, it is recommended that patients be evaluated at 1 year post-procedure for evidence of recurrence [11].
- For AK's, generally 1 treatment is administered however increased efficacy has been demonstrated when an additional treatment is administered anywhere from 1 week to 3 months after the first [12].

Complications

- Pain or discomfort experienced as "burning, stinging, or prickling" limited to the treated area [5, 13].
- Larger irradiation areas and sites characterized by extensive innervation, such as the head, hands, and perineum, are associated with more procedural-related pain [2].
- Immediately post-procedure, erythema and edema are commonly seen with erosion, crust formation and subsequent healing occurring within 2–6 weeks [5, 14–16].
- Generalized photosensitivity has NOT been reported after topical ALA-PDT.
- Hyper- or hypopigmentation has been reported but generally resolves within 6 months.
- Permanent hair loss has also been documented, although rare.
- Contact allergic dermatitis to the photosensitizer (ALA or MAL) has been reported.
- Recurrence of treated lesions is possible.

Prevention and Management of Complications

- Pain is generally self-limited however, occasionally it may persist for hours up to a few days.
- Some strategies utilized to reduce pain include:
  - Topical or injected local anesthetic prior to treatment
  - Premedication with benzodiazepines or systemic analgesia
  - Cool air
  - Spraying water on lesions during therapy
  - General anesthesia
- Avoid sun exposure for at least 24–48 h after treatment to avoid photosensitivity reactions and minimize the risk of pigmentary alteration.

Conclusions

- For facial and scalp AK's, Bowen's disease and superficial BCCs, PDT with ALA and methyl-ALA formulations show comparable efficacy to 5-fluorouracil, imiquimod and cryotherapy with superior cosmetic outcomes [4].
- Studies have also demonstrated the utility of PDT for the treatment of acne vulgaris as well as several other cosmetic indications.
- In the future, PDT may prove to be an important tool for chemo-prevention in solid organ transplant recipients.
- It is important to mention that there remains no consensus on the optimal treatment guidelines when utilizing PDT for specific dermatoses in regards to photosensitizing agent used, drug-to-light intervals, laser or light sources, and optimal wavelength. PDT protocols are currently under intense investigation to address these unknown variables; therefore the information presented in this chapter should serve merely as a guideline and practicing physicians should acknowledge that alterations in protocol might be necessary when considering individual patients and certain clinical scenarios.
- It would be prudent and is strongly recommended by these authors that the treating physician consult the current literature to determine the strength of recommendation and quality of evidence for the desired indication prior to recommending PDT to a patient for their dermatologic condition.

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Chapter 19
Lasers for Non-melanoma Skin Cancers

Jessica A. Savas, Jennifer A. Ledon, Katlein França, Anna H. Chacon, and Keyvan Nouri

Abstract According to the most recent incidence data, approximately 3.5 million cases of non-melanoma skin cancer (NMSC) are diagnosed each year, affecting 2.1 million people in the United States alone (Rogers et al., Arch Dermatol 146:283–287, 2010). Basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and squamous cell carcinoma in situ (SCCIS) represent the overwhelming majority of NMSCs, with BCC and its subtypes being the most common malignancy affecting Caucasians (Rogers et al., Arch Dermatol 146:283–287, 2010). Traditional treatments of NMSCs include standard excision, Mohs micrographic surgery, curettage and electrodessication (C&E), cryotherapy, radiotherapy, and topical cytotoxic therapy (e.g. fluorouracil). Some patients, especially those with multiple lesions, may not be amenable to several destructive or surgical interventions due to multiple comorbidities or fear of disfigurement, while others may

J.A. Savas, MD (✉) • J.A. Ledon, MD • K. França, MD, MS
A.H. Chacon, MD • K. Nouri, MD
Department of Dermatology and Cutaneous Surgery,
University of Miami—Miller School of Medicine,
1475 NW 12th Avenue, 2nd Floor, Miami, FL 33136, USA
e-mail: jsavas@med.miami.edu; jledon1@med.miami.edu;
k.franca@med.miami.edu; a.chacon@med.miami.edu,
annachaconmd@gmail.com; knouri@med.miami.edu,
knourimd@gmail.com

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be unable to tolerate the inflammatory side effects of topical preparations. A less invasive modality with fewer adverse effects and comparable efficacy is needed in certain patient populations, and to this end, lasers have shown great promise in carefully selected patients. This chapter will address the indications, procedural techniques, pre-operative and post-operative considerations as well as the prevention and management of complications when using lasers for the treatment of skin cancer.

Keywords Laser • Skin cancer • Basal cell carcinoma • Squamous cell carcinoma • Non-melanoma skin cancer • Treatment • Dermatology

Introduction

According to the most recent incidence data, approximately 3.5 million cases of non-melanoma skin cancer (NMSC) are diagnosed each year, affecting 2.1 million people in the United States alone [1]. Basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and squamous cell carcinoma in situ (SCCIS) represent the overwhelming majority of NMSCs, with BCC and its subtypes being the most common malignancy affecting Caucasians [1]. Traditional treatments of NMSCs include:

- Standard excision
- Mohs micrographic surgery
- Curettage and electrodessication (C&E)
- Cryotherapy
- Radiotherapy
- Topical cytotoxic therapy (e.g. fluorouracil)

Some patients, especially those with multiple lesions, may not be amenable to several destructive or surgical interventions due to multiple comorbidities or fear of disfigurement, while others may be unable to tolerate the inflammatory side

effects of topical preparations. A less invasive modality with fewer adverse effects and comparable efficacy is needed in certain patient populations, and to this end, lasers have shown great promise in carefully selected patients.

Background

- Lasers for the treatment of NMSC offer several potential advantages over traditional treatments including:
  - Convenience of an outpatient procedure
  - Low risk of bleeding and infection
  - No need for post-operative wound dressings or repair/reconstruction
  - Minimal if any downtime
  - Ability to treat multiple lesions in one office visit
  - Superior cosmetic results
- Superficial BCCs can be treated with the 595 nm pulsed dye laser (PDL) or the carbon dioxide (CO_2) laser [2–8].
- Squamous cell carcinoma and SCCIS have been successfully treated with CO_2 laser [5–8] (Table 19.1).
- Laser ablation with the CO_2 and erbium: yttrium-aluminum-garnet (Er:YAG) lasers followed by photodynamic therapy (PDT) has been investigated for the treatment of nodular BCCs [9, 10].
- The anti-tumor effects of laser irradiation are thought to be due to coagulatory necrosis, ablation, and hyperthermia [7].

Pulsed Dye Laser (PDL)

- The pulsed dye laser is a device primarily used for the treatment of vascular lesions such as port-wine stains, superficial hemangiomas, and telangiectasias.
- BCCs rely on a complex microvasculature system for growth that is composed of a vascular plexus of abnormally ectatic vessels [11, 12].

Table 19.1 Summary table of lesion type and anatomic location treated by each laser device

Laser	Type of lesion	Anatomic location
PDL	Small (<1.5 cm), superficial BCC	Trunk and extremities
CO_2 laser	Superficial BCC	Trunk, extremities, head, neck
	SCCIS	
	Nodular (if treated concomitantly with C&E)	
Alexandrite laser	Superficial BCCs	Upper extremities and anterior trunk
PDT + Er:YAG	Recurrent nodular BCCs	Head and neck
PDT + CO_2	Nodular and recurrent nodular BCCs	Face (including peri-orbital)

- It has been proposed that the selective destruction of tumor-associated vasculature results in prolonged ischemia and eventual destruction of the tumor.
- Clearance rates with the PDL vary according to wavelength used (595 nm > 585 nm) and size and histologic subtype of the BCC with small (<1.5 cm), superficial tumors on the trunk and extremities achieving clearance rates between 90 and 100 % [2–4, 13, 14].

Carbon Dioxide (CO_2) Laser

- The 10,600 nm wavelength CO_2 laser, when delivered in short bursts of high energy, can ablate to the mid-dermis and effectively remove skin cancers superficial to or confined within the papillary dermis [6].
- In healthy skin, one pass of the CO_2 laser achieves ablation of the epidermis while each subsequent pass ablates deeper levels of the papillary dermis [15].
- The CO_2 laser is superior to surgical excision in the following ways:

  - Production of a bloodless operative field as a result of hemostasis due to sealing of blood vessels.
  - Decreased peri- and post-operative pain due to the sealing of nerve endings.
  - An exceedingly low incidence of post-procedural infection due to sterilization of the treatment area by extreme heat produced by the laser.

- When used as monotherapy, the high-energy pulsed CO_2 laser can treat superficial BCCs as well as SCCIS, but is not suitable for nodular BCCs.
- When used in combination with C&E, one to two CO_2 laser passes can successfully treat superficial and nodular BCCs with complete histologic clearance and no recurrences [16].

Alexandrite

- The alexandrite laser, similar to the PDL, has been shown to target vascular lesions but offers the added advantage of deeper tissue penetration.
- While not extensively studied, one treatment of 18 BCCs on the trunk and extremities with the long-pulsed alexandrite laser was shown to significantly reduce the tumor burden in a patient with basal cell nevus syndrome (>250 BCCs) when all other treatment options proved to be impractical [17].

Laser + Photodynamic Therapy (PDT)

- Photodynamic therapy induces oxygen radical-dependent tissue damage through the utilization of a photosensitizing agent and subsequent light irradiation.
- The limiting factor for PDT use in the treatment of cutaneous malignancy is its inability to penetrate to depths beyond 2 mm, thus curbing its utility in tumors deeper than 2 mm.

- The Er:YAG and CO_2 lasers have been used to reduce tumor depth to less than 2 mm with subsequent PDT for the treatment of nodular basal cell carcinomas of the head and neck [9, 10].
- The combined treatment protocol provided greater efficacy and cosmetic results when compared to either laser or PDT alone [9].

Indications [18–20]

In biopsy-proven lesions of NMSC, the following are the patient-specific and lesion-specific indications for laser treatment:

Patient Characteristics

- Patients deemed poor surgical candidates (e.g. diabetics, smokers, or those with extensive vascular disease who have a diminished wound healing capacity).
- Patients with multiple NMSCs.
- Patients unable to tolerate the side effects of topical immunomodulators.
- Patients with syndromes characterized by the development of multiple NMSCs who will most likely require multiple interventions throughout their lifetime.

Lesion Characteristics

- Lesions located in an anatomically or cosmetically sensitive area, where intervention may result in functional or aesthetic impairment.
- Lesions on the lower extremity that are particularly prone to delayed wound healing and wound infection after creation of a surgical defect.
- Larger lesions (>1.5 cm in diameter) may benefit from adjuvant laser treatment to reduce tumor burden

before Mohs micrographic surgery, standard excision, or PDT.
- Smaller lesions (<1.5 cm in diameter) that are of the superficial subtype may be considered for monotherapy with the PDL.
- Clinically superficial BCCs and SCCIS can be reliably ablated with the CO_2 laser.
- Nodular BCCs are not suitable for ablation with the CO_2 laser

Contraindications

- Patients with darkly-complexioned skin (studies have only been conducted on patients with Fitzpatrick skin phototypes I–IV).
- Patients on drugs associated with photo-toxic reactions.
- Patients with photo-sensitive diseases.
- Patients who have a history of phototoxic or photoallergic reactions.
- Recurrent BCCs should not be treated with PDL but have been treated with variable success with the CO_2 laser, although the treatment of peri-ocular tumors using laser devices remains a highly controversial topic [5–8].
- Invasive BCCs or SCCs should not be treated with any laser or light device.
- Lesions on the head, neck, hands, feet, or genital areas should not be treated with the PDL.
- SCCIS that are highly keratotic, hyperplastic, or display significant follicular extension should not be treated with the CO_2 laser alone [5].

Pre-operative Care

- Lesion measurements should be recorded and photographs should be taken at the initial visit, each visit at which treatment is administered, and at subsequent follow-up visits.

- The lesion and margins of healthy tissue to be treated should be demarcated[1] to ensure a consistent treatment area if multiple sessions will be administered.
- Patients with a history of recurrent herpes simplex outbreaks in the area to be treated should be given prophylactic antiviral medication.
- Immediately prior to laser irradiation, the patient, treating physician, and all healthcare personnel present should put on appropriate eyewear that is protective against the specific wavelength of light being used.

Techniques

PDL

- The use of a dynamic cooling device to protect the epidermis when higher fluences are utilized is left to the discretion of the treating physician.
- No anesthesia is required.
- The treatment area consists of the lesion itself along with a 4 mm radius of normal skin.
- 10 % overlap should be used.
- One to two passes can be performed with no pulse stacking[2]
- Treatment sessions and intervals:
  - One treatment has been associated with a 56 % overall histologic clearance rate with a 100 % clearance rate for the superficial subtype of BCCs [13].

[1]One author reported the use of a Tegaderm template for each treatment site but the method of demarcation may vary depending on the discretion of the treating physician [3].

[2]One small pilot study compared 2 passes vs. 2 stacked pulses with a large spot size and lower fluence and found the stacked pulse setting to be superior to the 2 pass technique (did not reach statistical significance), suggesting a need for further studies to determine the optimal technique [4].

  - Four consecutive treatments at 2–4 week intervals has been associated with a 92–95 % clearance rate regardless of size (up to 17 mm) or subtype (superficial, nodular, and infiltrative) [2].

CO_2 Laser

- Local anesthesia should applied to the area to be treated
- The lesion and 4 mm of surrounding healthy tissue is treated with successive passes of the laser.
- After the first pass is administered, gauze soaked in saline solution should be used to remove vaporized debris. This process should be repeated in between all subsequent laser passes [6].
- If tumor can still be visualized as a slightly pinkish residue compared to the surrounding white dermis (Wheeland sign) [16], another pass should be performed.
- Passes are repeated until residual tumor is no longer visible,[3] which results in ablation to the lower dermis or subcutaneous tissue in most cases [5].
  - In general, approximately three passes are usually necessary to ablate superficial BCCs and SCCIS.

PDT + Laser

- Laser vaporization of the elevated nodular component of the lesion for tumor reduction with the Er:YAG or CO_2 laser.
- Cleanse the tumor with acetone.
- Photosensitizer is applied over the lesion along with a 1 cm margin around the visible edge of the lesion.
  - Topical methyl aminolevulinate (MAL) is the photosensitizer that has been studied for treatment of nodular BCCs [9, 10].

[3]Some authors suggest that after you have achieved visual clearance of the lesion, two additional passes should be performed to ensure complete ablation down to the deep dermis [5].

- The area is then covered with an occlusive bandage as well as a cotton bandage to prevent light penetration.
- Incubation time is 3 h.
- The bandage is removed and the lesion cleansed again.
- The lesion is then irradiated with a red light.
- The optimal number of treatment sessions has yet to be fully elucidated however authors have investigated the use of one combined laser-PDT session as well as a combined laser-PDT session followed by another PDT session with no laser treatment 1 week later. Both protocols have shown success but cannot be compared side-by-side as different laser devices were used [9, 10].

Post-operative Care

- The procedure is well-tolerated and generally no pain management is required post-procedurally.
- If anesthetic eye drops were used, the ocular conjunctiva should be washed with physiological saline after treatment.
- Regular gentle cleansing with soap and water is recommended to keep the treated area clean and dry.
- Hydration of the wound with petrolatum ointment may be recommended.
    - If PDT + laser is used, topical antibiotic ointment can be used for 5 days post-procedure [10].
- All patients should be counseled on sun avoidance.
- Close follow-up visits should be scheduled to inspect the treated area and assess for signs of infection or complication.
- Indefinite, regular and close follow-up is also required to monitor for recurrence of lesions.

Complications

PDL

- Blistering, itching, hypo-/hyperpigmentation, scarring and post-operative erythema and purpura have been reported.

CO_2

- Erythema and pinpoint bleeding of the treated lesion is expected.

Alexandrite

- Blisters in the treated areas that crusted over and healed with erythematous thin scars.

PDT + Laser

- Slight hypopigmentation.
- Mild discomfort during the PDT portion of treatment.
- Prolonged photosensitivity after PDT is expected.

Prevention and Management of Complications

- If soreness or pain is experienced after the procedure, a non-steroidal anti-inflammatory can be used for symptomatic relief.
  - Pain experienced during PDT was overcome with the use of electric fans, local anesthetic, water sprays, jellyperm pads, and diversion techniques [10].

- If hyper- or hypopigmentation occurs, reiteration of the importance of sun avoidance before and after the laser procedure as well as reassurance is appropriate, as this complication generally resolves with time
- If hypertrophic scarring occurs, standard intralesional treatment can be administered
- If signs of infection are noted at follow-up, either topical or oral antibiotics may be considered depending on the nature/severity of the infection
- Erythema or purpura is an expected response after treatment with the PDL and generally resolves within 10 days. Patient reassurance is all that is required.

Conclusions

- Overall, BCCs respond better to laser irradiation when compared to SCCs.
- The PDL and the Alexandrite laser have been shown to effectively reduce tumor burden in patients with large or multiple BCCs.
- PDL may be effective as a primary modality for the treatment of patients with small, superficial BCCs.
- The CO_2 laser can reliably ablate clinically superficial BCCs when lased to the mid-dermis or deeper, while nodular BCCs are not at all suitable for ablation with the CO_2 laser [5].
- Preliminary data shows that PDT with prior laser ablation has demonstrated promising clinical efficacy and favorable aesthetic outcomes.
- More studies with long-term follow-up are needed to determine the optimal laser parameters, number of treatment sessions, treatment intervals, and wavelength needed to achieve high clearance rates with a low incidence of recurrence for BCCs, SCCs, and SCCISs.
- It is important to note that the current literature only reflects small trials and case reports/series on the safety and efficacy of lasers for the treatment of NMSCs and the

decision to treat patients with this largely experimental modality should be considered on a case-by-case basis, using strict selection criteria that takes into account both patient and lesion characteristics.

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Chapter 20
Light-Emitting Diode Phototherapy

R. Glen Calderhead and Tokuya Omi

Abstract

- Phototherapy is the process of using light as a therapeutic modality. In contrast to photosurgery, phototherapy induces its effect without producing significant heat damage to the target tissue.
- The light-emitting diode (LED) is a solid state semiconductor chip which emits light when an electric current is applied to it, and LED-based systems represent one type of phototherapy source that has a variety of clinical applications.
- Laser energy entered the arena in 1960 with Maiman's ruby laser, and attenuated laser beams were used for phototherapeutic purposes as low level laser therapy (LLLT) in the late 1960s, pioneered by the late Endre Mester and colleagues.

R.G. Calderhead, MSc, PhD, DrMedSci, FRSM (✉)
VP, Medicoscientific Affairs,
Clinical Research Facility, Clinique L,
219 Sowon-ro, Haengshin-dong, Doegyang-gu, Goyang City,
Goyang-shi, Gyeonggi-do 412-223, South Korea
e-mail: docrgc1213@gmail.com

T. Omi, MD, PhD
Department of Dermatology, Queen's Square Medical Center,
2-3-5 Minatomirai, Yokohama, Japan
e-mail: t.omi@queens-sq.or.jp

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- Light-emitting diodes (LEDs) were then tried as a phototherapeutic source, but were mostly inefficient due to their wide divergence, limited and unstable output powers and a wide waveband which limited target specificity.
- The advent of the "NASA LED" in 1998 changed this, when Whelan and colleagues developed an LED that was many orders of magnitude more powerful than existing LEDs with a stable output power, and, most importantly, a quasimonochromatic beam. They thus offered an excellent new phototherapy source with biological target-specific wavelengths. The acronym 'LLLT' is thus still used, but with the readily available clinically useful LEDs being widely reported in a large variety of indications, LLLT now stands for low level LIGHT therapy so that LED phototherapy is part of the LLLT family.
- A large body of low level laser therapy literature exists where the systems were either laser diode (LD)-based systems at specific wavelengths or the 633 nm helium:neon (He:Ne) laser. Taking these previously reported data into consideration, phototherapeutic LED-based systems were built based on the same effective wavelengths, but incorporating the inherent advantages of LEDs: namely a very efficient light source; able to be mounted in large planar arrays to treat large areas of the body in a hands-free manner; and comparatively inexpensive compared even with LDs thereby helping to minimize cost to the clinician and patient.
- LED phototherapy has now been well-reported in many clinical fields where it is used to:
  - accelerate and enhance wound healing in acute and chronic wounds of all etiologies
  - control inflammation and erythema
  - speed up the healing of bone damage, even for slow union fractures
  - attenuate and control acute and chronic pain of all types
  - improve results of any aspect of aesthetic and cosmetic surgery

  - rejuvenate photodamaged skin
  - provide prophylaxis against hypertrophic scar formation
  - attenuate hyperactive melanocytes in acquired-type pigmentary disorders
  - treat circulatory disorders such as Raynaud's disease, vasculogenic ulcers and diabetic foot

- This chapter will focus on the photobiological basics behind LED phototherapy and examine the mechanisms which have currently been elucidated, as well as providing some basic studies underlying the success of LED phototherapy in many fields. The potential user, however, should carefully ascertain the specific qualities of any LED system in regard to the true wavelength, active irradiated area and certified irradiance or power density. Furthermore, the user must match the wavelength with the desired target to ensure efficient absorption, because, as the first law of photobiology points out, without absorption there can be no reaction.
- In conclusion, LED phototherapy at appropriate wavelengths is safe and effective, easy to apply, pain- and side effect-free and well tolerated by patients of all ages.

Keywords Quasimonochromaticity • Photobioactivation • Mitochondria • Cytochrome-c oxidase • Systemic effect • Wound healing

Introduction

"*Nihil novi sub sole*" ('there is nothing new under the sun') can be found in the fourth century Vulgate Bible, and it certainly applies to the use of light energy to achieve a measurable clinical effect of some kind in living tissue in a non-invasive manner, but without heating tissue or causing any significant skin damage. The idea of using light as therapy is not a new idea. In fact, the first use of phototherapy can be dated back to ancient Egypt, where the sun

was used a therapeutic source of light [1]. Heliotherapy, phototherapy with the sun, persisted through the Greek and Roman civilizations and can actually still occasionally be seen today as a suggested cure for certain skin diseases such as psoriasis [2]. However, the sun can be a fickle light source, and is not available at night. It was Nobel Laureate Nils Finsen who developed the first electrically-powered phototherapy light source at the turn of the twentieth Century, and his arc lamp was used in the cure of a number of skin conditions including lupus erythematosus [3]. The laser first appeared in 1960, Maiman's ruby laser, with therapeutic as distinct to surgical indications reported in 1968, and the first truly clinically useful LED was developed in 1998.

What Is Phototherapy

Phototherapy is the application of some form of light energy to achieve a clinical effect in an athermal and atraumatic manner. It has also been called low level laser therapy (LLLT) [4], or more recently, low level light therapy with the same acronym of LLLT. The reader should note that in LLLT, the 'level' referred to has nothing at all to do with the light source, so when people talk about using a 'low level laser' (or low level light), they're mistaken! In LLLT, the 'level' is the level of reaction induced in the tissue by the light source. The level is 'low', i.e., below the damage threshold of the cell, and is used for a therapeutic rather than a surgical effect, hence 'low level light therapy'. A 20 W CO_2 laser defocused to a 10 cm diameter spot has an irradiance of just over 250 mW/cm^2: this is an LLLT power density, and will produce no heat or damage in the target tissue. If the level of photon stimulation exceeds the damage threshold of the cell, then the treatment is classified under photosurgery, or high level light therapy (HLLT), with sufficient energy eventually resulting in cell death. This is illustrated in Fig. 20.1

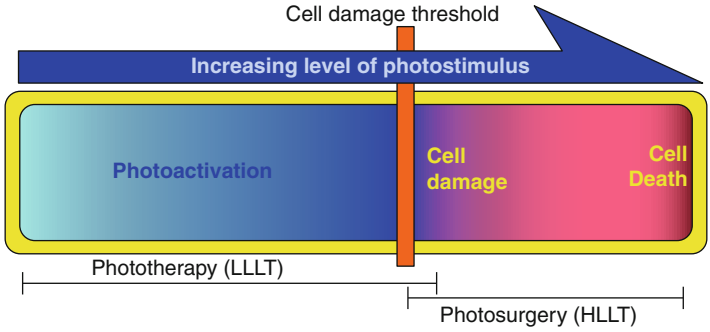


FIGURE 20.1 Schematic depicting a cell showing the cell damage threshold. As the light stimulus increases in magnitude, the cell becomes photoactivated with no energy lost through heat or damage. The maximum point of photoactivation is just before the damage threshold is reached. Once the damage threshold is passed, the degree of damage to the cell increases concomitantly with the incident light energy through a photothermal reaction until finally the cell survival threshold is passed and cell death occurs. Note there is a little grey area between the phototherapy and photosurgery components just beyond the damage threshold. In this zone, although slightly damaged, the cell is still alive and capable of some activity: this would correspond to the early stages of protein denaturation

Why Use LEDs?

Power and Quasimonochromaticity

If the authors had been asked this question 15 years or so ago, they would now be chuckling quietly, because LEDs were simply a very bright, cheap and cheerful light source, creating colorful christmas lights and highly visible traffic signals but with little or no therapeutic benefit. This did not stop some manufacturers from putting together so-called 'cluster probes' with a number of old-generation LEDs which more often than not surrounded, or were interspersed with, laser diodes (LDs). The reported efficacy of these probes was most probably

down to the presence of the LDs, which were delivering coherent light energy with photon intensities many times those of the LEDs.

The work at the NASA-associated Space Medicine Laboratory by Harry Whelan and colleagues signaled a new generation of LEDs in 1998, the 'NASA LED' [5], which was very swiftly shown by the same group to have beneficial clinical effects in wound healing [6]. The NASA LED was several orders of magnitude more powerful than the previous generation of LEDs, had stable output powers, and delivered the vast majority of its photons at a rated wavelength rather than a waveband, in other words, it was quasimonochromatic. Finally it was possible to source a 633 nm LED rather than simply a 'red' LED. Many cellular and subcellular targets are very wavelength specific: quasimonochromaticity was therefore a powerful advantage of the new-generation LED.

Efficiency

LEDs require a very little electrical energy to produce a great deal of light, and are therefore a very economical and efficient electricity-to-light converter, offering rates around and over 85 %, whereas the most efficient lasers are around 10 %. There is no filament, and no discharge tube, so there is virtually no energy lost as heat from the LED itself.

Clinical Practicality

A number of LEDs can be mounted on multiple articulated panels to treat a large area of the human body in one single session, and in a hands-free manner. This makes LED-based systems clinic-friendly and therapist-non intensive. The articulation of the panels allows them to be adjusted to treat both flat and contoured areas of the body, ensuring uniform distance from the LEDs to the target tissue.

Light-Tissue Interaction

Importance of Wavelength

As already stated above, the first law of photobiology demands that absorption must take place before any reaction can be expected. The one single factor which determines absorption in a biological target is the **wavelength** of the incident photons. Not only that, the wavelength also decrees the depth to which the light energy will intrinsically penetrate into tissue. Following reports from Karu and others [7], it has been shown that there is a 'window' waveband within which light energy will penetrate well into tissue. This extends from around 610 nm to around 1,700 nm, after which water absorption gradually limits penetration. The shorter visible light wavelengths are preferentially absorbed in the competing chromophores of epidermal melanin and dermal blood, so that limits their penetration capacity. Figure 20.2 illustrates schematically the penetration of light into tissue based on data from Smith's illustration of the penetration of 'white' light through a human hand in vivo [8]. The deepest penetrating wavelength is from 820 to 840 nm, because this is at the bottom of the water absorption curve. 1,064 nm, the wavelength of the Nd:YAG, is often erroneously stated to be the best penetrating wavelength, but even at 1,064 nm water absorption is a limiting factor.

Waveband and Primary Response

The basic reaction at a cellular level in LED phototherapy is photoreception, followed by signal transduction and amplification and finally the photoresponse [7]. The waveband within which the light energy falls, namely visible and near-infrared (near-IR), determines the target's primary response to photon absorption.

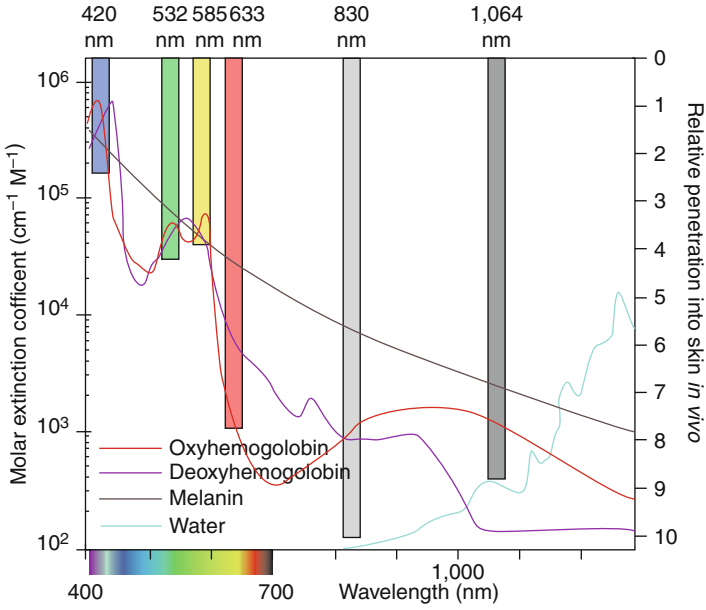


FIGURE 20.2 Relative depth of penetration into living tissue of a variety of visible light and near IR wavelengths (right-hand axis) overlying the absorption spectra of the biological chromophores: blood, melanin and water. These can explain why the shorter visible light wavelengths from blue to yellow cannot penetrate very deeply into tissue. Using LEDs at these wavelengths will therefore limit penetration to the epidermis and very superficial dermis. At only 48 nm more than 585 nm, penetration at 633 nm is increased by about 3.5 orders of magnitude allowing visible red light at that wavelength to penetrate well into the skin, reaching and passing through the subdermal fatty layer. Deepest penetration is at the bottom of the water absorption curve (820–840 nm), as seen by the 830 nm example. 830 nm is capable of penetrating some centimeters into tissue with appropriate photon intensity. At 1,064 nm, the wavelength of the Nd:YAG laser, the water absorption curve starts to rise so water becomes an important chromophore and penetration of 1,064 nm light energy into tissue (over 75 % water content) is slightly limited by water absorption

Visible Light

- Visible light penetrates through the cell membrane
- Preferential absorption occurs in organelles within the cell.
- For the red wavelengths, especially 633 nm, the primary photoacceptor, or chromophore, is cytochrome-c oxidase (COX) which is the terminal enzyme of the mitochondrial respiratory chain [9], mitochondria being the adenosine triphosphate (ATP) factories of the cell.
- ATP is the basic fuel for the human metabolism.
- The light energy is transferred to the COX and initiates a primary photochemical cascade which results in the production of ATP, and also the powerful signaling components, calcium ions (CA^{++}) and protons (H^{+}) [10].
- Increased intracellular levels of ATP, Ca^{++} and H^{+} kick-start the membrane transport mechanisms such as the sodium-potassium (Na^{+}/K^{+}-ATPase) pump.
- Excellulation of these components occurs. This raises their extracellular levels, and they can then activate nearby unirradiated cells. This is known as the bystander theory [11], and can account for the systemic effect of LLLT whereby unirradiated areas of the body receive indirect benefit from the irradiated area.

Near-Infrared Light

- On the other hand, cell membranes are not transparent to near IR light.
- Near IR light is primarily absorbed in the cell membrane where the primary response is photophysical, not photochemical, due to changes in the rotational and vibrational state of the membrane molecules.
- Na^{+}/K^{+}-ATPase membrane transport mechanism is immediately initiated.
- Mitochondria are called upon to produce more ATP to meet the increased energy requirement of the cell.
- The same ATP production cascade as for visible light is thus induced, but as a secondary response to the primary photophysical reaction in the cell membrane.

Despite the difference in primary response between visible and near-IR light, the end result is the same, namely a photoactivated cell. When cells are in a photoactivated state one or more of three things can happen:

- If the cell is damaged or compromised, it will repair itself, or be repaired.
- If the cell has a function, e.g., collagen and elastin synthesis by fibroblasts, it will perform that function more efficiently.
- If proliferation is required, the cell will proliferate.

Validation Through Basic and Clinical Research

LLLT and Skin Cells

Including the laser phototherapy-related literature, a very large number of papers has been published which validate the photoactivation of cells by a variety of wavelengths, both in vitro and in vivo. Since most laser diode (LD)-based experiments involved a defocused beam to encompass the target vessel containing the cells in an appropriate medium, the incident irradiance can be arguably equated to LED energy at appropriate irradiances and distances, although the photon intensity of even a defocused LD is still greater than that of an LED-based system. This can be compensated for by an increased dose (J/cm^2) through longer irradiation times.

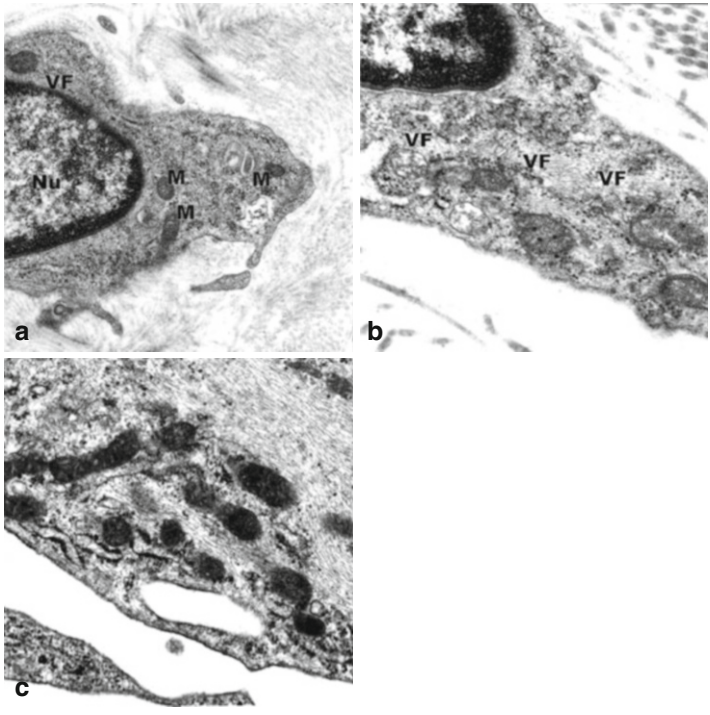
From the data of over 30 years of LLLT, two wavelengths have been highlighted as having the greatest effect on the action mechanism of skin cells, including epidermal keratinocytes, and fibroblasts, mast cells, macrophages and neutrophils in the dermis: 633 nm in the visible red, and 830 nm in the near-IR [12]. With the current ability to source LEDs at almost any specific wavelength in the visible red and near-IR wavebands, other wavelengths are emerging as potential candidates for LED phototherapy, but 633 and 830 nm remain those most reported on.

Fibroblasts and Collagen

Omi and colleagues examined the effect of 633 nm LED phototherapy on human skin in vivo [13]. Subjects (n = 8) had punch biopsies taken from an arm on day zero before treatment, and the same arm of the subjects was treated three times at 126 J/cm^2/session on day zero, 2 and 4, with subsequent biopsies taken from the treated arm on day 2 before treatment, and then again on days 4 before treatment and finally on 6 (48 h after the final treatment). Specimens were routinely processed for electron microscopy in ultrathin slices stained with uranyl acetate/lead citrate and double stained with oolong tea extract for vimentin [14], vimentin being one of the building blocks of collagen through copolymerization in the Golgi complex with desmin. Figure 20.3a shows a transmission electron photomicrograph of a fibroblast in unirradiated tissue at baseline, with normal morphology. Mitochondria were noted, with small pockets of vimentin fibrils, and many vimentin granules seen as small black dots. Note that vimentin fibrils are required for copolymerization, rather than the granular vimentin. At 48 h after the first treatment (Fig. 20.3b), there were more mitochondria seen in every field, more vimentin fibrils and fewer vimentin granules. Furthermore, chromatin was seen to have accumulated at the nuclear membrane, suggestive of preparation for ribosomal mRNA signaling. In Fig. 20.3c, 48 h after the final irradiation, a dramatic change was seen in fibroblast morphology and activity.

There were significantly many more mitochondria which were electrodense showing high ATP activity, including so-called giant mitochondria, with very few vimentin granules and a mass of vimentin fibrils. These findings suggested that the fibroblast was photoactivated, and was entering a highly fibroplasic state with imminent enhanced collagen production. Lee and colleagues, in a split-face, controlled and double-blinded study with 127 subjects [15], examined the effects of LED phototherapy on skin rejuvenation using 633 nm alone, 830 nm alone and 830 nm followed by 633 nm compared with sham-irradiated control. Punch biopsies were

taken from the irradiated and unirradiated sides of the face at 2 weeks after the final session (8 sessions over 4 weeks) and examined with light and transmission electron microscopy. Figure 20.4 shows enhanced collagenesis in an 830 nm-irradiated specimen compared with the contralateral unirradiated side in the same patient, and Fig. 20.5 shows the same for elastin, both sets of specimens being taken from 830 nm-irradiated subjects. In addition to the light microscopic findings, transmission electron microscopy at 2 weeks after the final session showed plump, active fibroblasts in 830 nm irradiated tissue, surrounded by well-organized collagen fiber bundles, compared with rather anemic-looking fibroblasts in the contralateral unirradiated tissue with poorly organized collagen. As for the degree of collagenesis



and elastinogenesis, the 830 nm group was superior to the combination group, statistically so for skin elasticity, and the combination group was in turn superior to the 633 nm group. All three groups were statistically significantly superior to both the unirradiated side of the face and the sham-irradiated control group.

Mast Cells

Calderhead and colleagues explored the role of 830 nm LED phototherapy in the activation of mast cell degranulation in the skin of normal healthy individuals (eight subjects), *in vivo* [16]. A single session of 830 nm LED phototherapy was given

FIGURE 20.3 Effect of 633 nm LED phototherapy on fibroblasts *in vivo* (see text for experimental details) as shown by transmission electron microscopy (TEM). (**a**) Photomicrograph of normal tissue at baseline, preirradiation. Part of a fibroblast displaying normal architecture is seen with the nucleus (*Nu*) containing chromatin to the left of the image. Mitochondria (*M*) can be seen in the cytosol to the right. A small pocket of vimentin fibrils (*VF*) is seen just above the nucleus. Multiple small black dots exist in the cytosol: these are vimentin granules stained by the oolong tea extract (TEM, magnification ×12,000). (**b**) Specimen at a higher magnification taken from an irradiated arm 48 h after a single irradiation (633 nm, 126 J/cm^2). The number of mitochondria has increased considerably, and there are large amounts of vimentin fibrils (*VF*) in the cytosol, converted from vimentin granules, the number of which has dropped. The chromatin has apparently located next to the nuclear membrane (*top left*) suggesting the cell is preparing for ribosomal mRNA signaling (TEM, magnification ×30,000). (**c**) At 48 h after three irradiation sessions, a dramatic change has occurred in the fibroblast architecture. Hardly any vimentin granules can be seen, and the cytosol is full of vimentin fibers. Mitochondria have significantly increased in number, including a so-called giant mitochondrion, and are electrodense showing high ATP synthesis activity. The cell is now highly fibroplasic (TEM, magnification ×30,000. All photomicrographs courtesy of T Omi MD PhD)

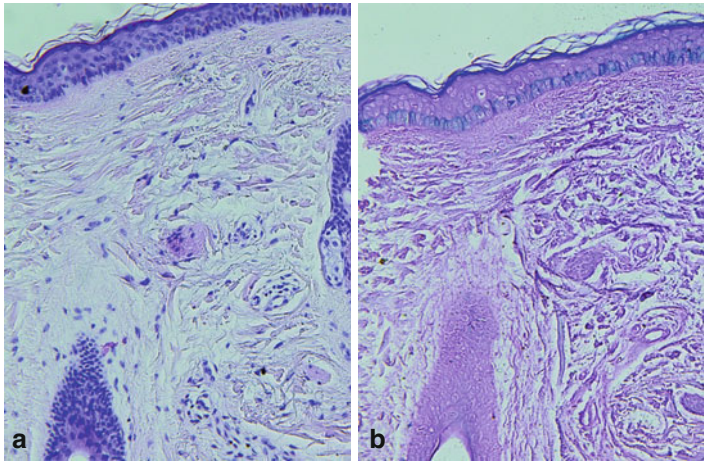


FIGURE 20.4 Effect of 830 nm LED-LLLT on collagen synthesis. (**a**) Specimen from the unirradiated side of a patient's face in the 830 nm-treated group. Dermal collagen is poorly organized with many interstitial spaces. (**b**) At 2 weeks after the final LED phototherapy session in this specimen from the 830 nm LED- irradiated side of the same patient, a much younger-looking dermal matrix is seen. Collagen fibers and bundles have increased and better organized down into the mid-reticular dermis, with much smaller interstitial spaces. The Grenz layer at the dermoepidermal junction is linearly organized and thicker, with a more cellularly active-looking epidermis (Skin, hematoxylin and eosin, original magnification ×200. Microphotography courtesy of SY Celine Lee, MD)

on one forearm, the other serving as an unirradiated control. Punch biopsies were taken from the irradiated arm at baseline and 48 h post-irradiation, and from the unirradiated arm at the 48 h point, and examined with transmission electron microscopy. In addition, an independent count of mast cells, macrophages and neutrophils per field was conducted in eight fields per subject.

No morphological change was seen in the unirradiated arm at 48 h post irradiation compared with baseline, with no increase in cell count. In the irradiated arm, mast cell degranulation was induced, with at least 50 % of the granules being

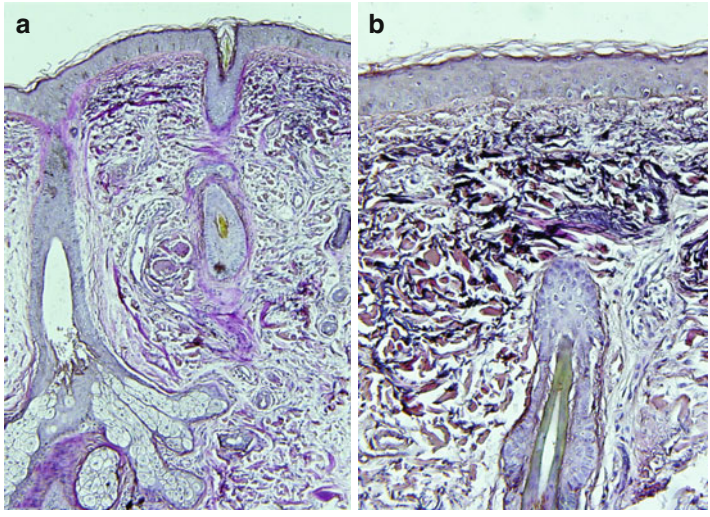


FIGURE 20.5 Effect of 830 nm LED-LLLT on elastin synthesis. (**a**) Specimen from the unirradiated side of a patient's face in the 830 nm-treated group. Elastic fibers are haphazardly organized and sparse, especially in the deeper dermis and in the Grenz layer. (**b**) At 2 weeks after the final LED phototherapy session in this specimen from the 830 nm LED- irradiated side of the same patient, the elastic fibers have increased in number and density, and are better-organized, even in the deeper dermis. A profusion of fine, linearly organized elastic fibers is seen in the Grenz layer. Note also the thicker epidermis (Skin, Verhoeff-van Giessen stain, original magnification ×200. Microphotography courtesy of SY Celine Lee, MD)

excellulated into the matrix. As a result, a mild inflammatory response was noted as if the tissue had been wounded, but the morphology was otherwise normal. The cell counts of all cells of interest, the major wound healing cells, were significantly higher in the irradiated arm.

The authors proposed that this creation of a 'quasi-wound' was the first stage of photoinducing the wound healing cycle, resulting in the neocollagenesis and elastinogenesis necessary for good skin rejuvenation and additionally suggesting an important role of the mast cell in 830 nm LED phototherapy for wound healing.

Macrophages and Neutrophils

The literature also contains good evidence that phototherapy at certain wavelengths activates macrophages and increases their ability to synthesize mediators of wound repair. Low incident doses of visible red and near-IR coherent and non-coherent light energy increased the phagocytic activity of macrophages through enhanced chemotaxis and internalization [17, 18], but at the same time significantly increased the production of fibroblast growth factor (FGF). As for neutrophils, *in vitro* irradiation with 830 nm [19, 20] and other wavelengths including 633 nm [20] significantly increased their ability to identify, move to and engulf targets, and then destroy them more effectively through enhanced respiratory burst activity. Furthermore, release of trophic factors was also enhanced following irradiation with low incident doses of light energy.

The Systemic Effect of LED Phototherapy

The earliest proof that phototherapy of one area would induce effects in a distant unirradiated area came from the pivotal study in the early 1970s by the late Endre Mester on torpid crural ulcers with a treatment-resistant history of at least 6 months, whereby treatment with a HeNe laser brought about healing of the irradiated ulcers in the vast majority of the 1,000-plus patients in 3–4 weeks [21].

Subsequently, the ulcers on the contralateral limb also started to heal even though they had not been treated directly with the 633 nm LLLT. More recently, a very convincing controlled study with 830 nm LED phototherapy in an animal model showed significantly more rapid healing of standardized wounds on the dorsum of the LED-irradiated animals compared with the wounds on the backs of the unirradiated controls [22], with the LED energy being restricted to the abdomen of the irradiated animals. In other words, an indirect, systemic effect of LED phototherapy was clearly demonstrated.

Dosimetry

Because of the wide range of wavelengths used in LED phototherapy, and given the fact that the photons in each wavelength have both a different inherent level of energy with longer wavelengths having a lower electron volts (eV) value than shorter ones and different principal targets, any thoughts on dosimetry must be rather general. One can, of course, look to the literature where a rather bewildering range of doses is given, but very often all parameters are incomplete. Knowing the dose in J/cm^2 is important, but as that parameter is composed of both the intensity in W/cm^2 (or mW/cm^2) and the exposure time in seconds, a dose of 30 J/cm^2 could be 300 mW/cm^2 for 100 s, 30 W/cm^2 for 1 s or 300 W/cm^2 for 0.1 s. These sets of parameters would produce, respectively, very little heat if any, quite a bit of heat and a great deal of heat in the target tissue with only the first set approximating an LLLT-like effect, but all three having the same dose. Another three variables to be considered are the size of the LED active area, (treatment head), the angle of divergence of the LEDs and the distance between the head and the target tissue. The clinician has to look at the recommendations of the manufacturer, and trust that the manufacturer has performed due diligence with dose-ranging studies and hopefully had some corroborative literature published on the clinical application of their system.

Here are some examples from the literature in which all the parameters were given and can therefore be used as a basis for thinking about the ideal dose. In the study mentioned above by Lee et al. which compared 633 and 830 nm LED-LLLT for skin rejuvenation, and showed efficacy of these wavelengths at a histological and ultrastructural level [15], the dose for the 633 nm component was 96 J/cm^2 with an intensity of 80 mW/cm^2 over 20 min. For the 830 nm component, the dose was 60 J/cm^2 comprising an intensity of 50 mW/cm^2 over 20 min. The same dose of 96 J/cm^2 for 633 nm energy was also advocated by Lee and colleagues in their article already cited above on the combination of 415 nm visible blue and 633 nm

for the successful light-only treatment of active acne [11], with a dose of 48 J/cm^2 for the 415 nm component (40 mW/cm^2 for 20 min). The article cited above showing the systemic effect of 830 nm LED-LLLT on wound healing also used 60 J/cm^2 (100 mW/cm^2 for 10 min). The literature would suggest for 830 nm LED-LLLT that the effective range lies between 40 and 80 J/cm^2, with a fair body of evidence pointing to 60 J/cm^2.

Phototherapy systems from different manufacturers are, however, different, and in the absence of strong and validated recommendations from the manufacturer regarding the correct parameters, the clinician or therapist will very often have to conduct their own dose-ranging studies to arrive empirically at the ideal dose for that particular system.

Conclusions

- It is impossible in this short article to summarize the entire body of literature on phototherapy with LEDs and defocused laser diode sources, but the authors believe that we have adequately demonstrated that LLLT using LEDs is a fast-emerging and truly viable alternative to the proven efficacy with laser diode-based LLLT, employing the wavelengths already proven and tested with the latter.
- LED phototherapy can be applied by a trained therapist or nurse, freeing up the clinician for other duties, is easy to apply, pain- and side-effect free and is tolerated well by patients of all ages. The current article has not even mentioned the effect of LED-LLLT on blood flow, but that is more appropriate for the section elsewhere in this book on lasers and light in wound healing, so please refer to that section for information on this important aspect of LED phototherapy.
- A recent review article by Kim and Calderhead made a convincing argument that LED-LLLT was indeed effective [23], and as more and more of the many ongoing controlled and clinical studies come to an end and the data are collated, the authors are sure that LED phototherapy will take its rightful place in a large variety of indications.

- Although the stand-alone indications of LED phototherapy are interesting, perhaps even more exciting is the enormous potential of LED phototherapy as an adjunct to any kind of surgical procedure or post-trauma to obtain faster relief from pain, edema and erythema, and enhanced, more rapid wound healing. However, and there is always a 'however' with LLLT, a great deal depends on the quality of the LEDs in the following order of importance: the wavelength must be correct for the target, with the LEDs emitting a very narrow band around the rated wavelength e.g., within ±5 nm or so; the irradiance must be adequate; and the dose sufficient. Provided these conditions are met, LED phototherapy WILL work, and work well.

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Chapter 21
Lasers and Lights in Wound Healing

R. Glen Calderhead and Boncheol Leo Goo

Abstract Those who pioneered the use of surgical lasers as a therapeutic modality were the first to report that patients undergoing laser surgery experienced less post-surgical pain and inflammation as compared with the traditional cold scalpel. Moreover, these early adopters of surgical lasers reported that wound healing was not compromised after laser surgery. This was finally found to be due to the "L" of LASER, namely light, because in addition to the surgical effect of the incident light energy, a series of other effects with descending photothermal activity occurred simultaneously as the photon intensity propagating through the tissue decreased, finally arriving at the phototherapeutic zone (Mester et al. Acta Chir Acad Sci Hung 9:349–57, 1968). Thus, incident light energy was suggested as a potential link between lasers and wound healing.

R.G. Calderhead, MS, MSc, PhD, DrMedSci, FRSM (✉)
VP, Medicoscientific Affairs,
Clinical Research Facility, Clinique L,
219 Sowon-ro, Haengshin-dong, Doegyang-gu,
Goyang City, Goyang-shi, Gyeonggi-do 412-223, South Korea
e-mail: docrgc1213@gmail.com

B.L. Goo, MD
Medical Director, Clinique L Dermatology,
219 Sowon-Ro, Haengshin-dong, Doegyang-gu,
Goyang City, Gyeonggi, 412-223, South Korea
e-mail: boncheolgoo@lutronic.com

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Background

Those who pioneered the use of surgical lasers as a therapeutic modality were the first to report that patients undergoing laser surgery experienced less post-surgical pain and inflammation as compared with the traditional cold scalpel. Moreover, these early adopters of surgical lasers reported that wound healing was not compromised after laser surgery. This was finally found to be due to the "L" of LASER, namely light, because in addition to the surgical effect of the incident light energy, a series of other effects with descending photothermal activity occurred simultaneously as the photon intensity propagating through the tissue decreased, finally arriving at the photo-therapeutic zone [1]. Thus, incident light energy was suggested as a potential link between lasers and wound healing.

Rationale and Application

- As noted above, the impact zone in tissue of almost all surgical laser beams has a phototherapeutic zone at the beam periphery in which the cells are athermally and atraumatically photoactivated—leading to quicker and more efficient wound repair.
- Endre Mester was the first to report that stand-alone low levels of incident laser energy (HeNe laser, 632.8 nm) promoted healing of long-term torpid crural ulcers in a large patient population.
- Defocused Nd:YAG and CO_2 surgical lasers were also used as an early source of phototherapy to potentiate wound repair.
- Laser diode-based systems became popular for wound healing with low level laser therapy (LLLT) in the late 1980s.

Key Cells and the Role of the Circulatory System

- Keratinocytes, mast cells, macrophages, neutrophils, fibroblasts and endotheliocytes have all been shown to play a major role in normal wound healing. LLLT is able to increase the wound repair activity of these cells. Because these cells are found at different depths within the skin, the wavelength of light applied to the targeted tissue plays an important role in which of these cells become photoactivated.
- LLLT increases local—and even systemic—blood flow, leading to better perfusion of the targeted tissue. Early and adequate perfusion has been shown to favor better wound healing. This facilitates the delivery of oxygen and nutrition to the wound, and results in an optimal wound healing environment.

Enter the LED

- From the turn of the twenty-first Century, new generation light-emitting didoes (LEDs) became an important light source for wound healing and other applications. Low level laser therapy was renamed low level LIGHT therapy (same acronym, LLLT).
- LEDs are efficient light generators, relatively inexpensive and can be mounted in large hinged panel arrays to treat areas on flat or contoured tissue in a hands-free manner. The best LEDs for use as a therapeutic modality offer extremely narrow band light (quasi-monochromaticity), enabling wavelength-specific cellular photoactivation.

Fractional Laser Technology Improves Wound Healing

Fractionation of an ablative or nonablative surgical laser beam into microbeams offered reduced downtime and improved wound healing.

Phototherapy and Wound Healing

- The role of phototherapy using low incident doses of laser energy and LED energy in wound healing in soft tissue, bone and burn wounds has been well-proven. The key to achieving good results is dependent upon the selection of an appropriate wavelength and irradiance.
- Phototherapy following any wound, surgical or traumatic, should be applied as a matter of course to accelerate the wound healing process, and as prophylaxis against hypertrophic scar formation.

Introduction

It did not take long following Maiman's successful development of the ruby laser in 1960 for other laser systems to be constructed based on different media. In the first 4 years after the ruby laser was introduced, many other lasers were introduced: the helium neon (HeNe) and neodymium:yttrium aluminum garnet (Nd:YAG) lasers in 1961; the argon (Ar) laser and diode lasers (visible red and near infrared) in 1962; and the carbon dioxide (CO_2) laser in 1964. Ophthalmology was the first medical specialty to show the potential of the ruby and argon lasers as a therapeutic modality. This was followed by pigment-specific applications in dermatology. The focused CO_2 laser with its high affinity to water was quickly recognized as a true surgical system, and the light scalpel was broadly investigated in all surgical fields including otorhinolaryngology and neurosurgery. The CO_2 was very popular as the "light knife", because, as it incised tissue, it coagulated and cauterized the wound edges, sealing small blood vessels and allowing for a comparatively dry field.

Laser Surgery Versus Conventional Surgery

The early adopters of surgical lasers were quick to report the very interesting postoperative effects Compared with the conventional scalpel, CO_2 laser surgery produced less postoperative pain and inflammation, with good wound

healing and an aesthetically-pleasing scar. It was first thought that it was the thermal aspect of the light-tissue interaction which was responsible for this, but comparison between procedures with the laser and the electrocautery knife disproved that, the latter producing a pure electrothermal reaction in tissue, but being more painful postoperatively with more inflammation than the laser. Finally, the element responsible for these beneficial effects was isolated to the "L" of 'laser', the light itself. Endre Mester of Semmelweis University was the first to investigate dedicated systems delivering low incident doses of laser energy in the pioneering days of phototherapy [1], and wound healing was one of his major papers in 1971 in which he demonstrated that the HeNe laser, at very low incident power levels, was successfully used to treat non-healing crural ulcers in 78 % of 1,120 patients: only 85 (7.6 %) patients failed to respond at all [2].

Advent of "LLLT"

Although Mester continued his studies, including wound healing with the HeNe and defocused surgical lasers, it was not until 1980 that a serious interest was taken in laser therapy elsewhere. The 4th annual meeting of the International Society for Lasers in Surgery and Medicine (ISLSM) in 1981 was held in Tokyo at which Prof Mester was a keynote speaker, and at that meeting there was the first session dedicated to what was called "low power laser" which included defocused surgical systems such as the Nd:YAG laser and the very first of the gallium aluminum arsenide (Ga:Al:As) laser diode-based systems [3]. In 1988, Ohshiro and Calderhead published "*Low Level Laser Therapy, a Practical Introduction*" (John Wiley & Sons, Chichester, UK) which introduced Calderhead's terminology of 'low level laser therapy' (LLLT). The wavelength which featured strongly in many of the examples, including wound healing, was 830 nm from Ga:Al:As diode lasers and that has gone on to become a pivotal wavelength in the phototherapy field associated with wound healing. At first, despite the growing body of evidence from other countries including Japan, China, Russia and the UK, there was a great deal of

skepticism in United States mainstream medicine regarding LLLT, and it was often branded "hocus pocus" by such leading laser clinicians as the late Professor Leon Goldman. In 1991, however, there was a 'Biostimulation' session for the first time at the annual meeting of the American Society for Lasers in Surgery and Medicine (ASLMS) at which several good papers were presented on the clinical and basic research aspects of the use of low incident levels of light, so LLLT had started to gain at least some acceptance in the USA. This culminated in US Food and Drug Administration (FDA) clearance of an LLLT device for the treatment of carpal tunnel syndrome in 2002.

"NASA LED"

In the late 1990s, the NASA Space Medicine Laboratory—under the direction of Professor Harry Whelan—was engineering a new generation of light-emitting diode (LED) that was to be used for growing plants in space. The new generation LED aimed to achieve stable output powers that were orders of magnitude greater than existing LEDs—better optics on the chip envelope, and an extremely narrow-band output because the LEDs were specifically targeting chlorophyll, i.e., quasichromaticity. In 1998, the 'NASA LED' was introduced, and became a new and really interesting phototherapeutic source [4]. In just a couple of years, Whelan and colleagues showed its efficacy for wound healing [5]. Since that time, LED phototherapy has become a solid player in the wound-healing arena, in addition to laser therapy.

Light-Skin Interaction

Basic Reactions

The skin is a complex mixture of different substances each with different refractive indices and other optical attributes, and the light-tissue interaction is equally complex. When light

is shone on a target it can interact with that target in a number of different ways depending on the target's chemical and physical attributes. Light can be: reflected off a target, transmitted through the target, scattered by the target, or absorbed in the target. All of these light-tissue interactions happen together when light is incident on the skin. A portion of incident light energy is reflected off the surface of the stratum corneum: the greater the incident angle, the greater the percentage that is reflected. Similarly, at longer wavelengths, a higher percentage of light is reflected. In the near-infrared spectrum, this can be as high as 12–15 %. That is why a light source should be held as perpendicular to the target tissue as possible during treatment.

Because of the inhomogeneous nature of the dermal matrix, a lot of scattering of incident light occurs: scattering is higher in the red waveband (600–700 nm) than in the shorter wavebands and is particularly high in the near-IR (700–2,000 nm). Both forward and back-scattering occur: this explains why, for near-IR light energy, the photon intensity is often higher beneath the surface of the skin in the dermis than at the epidermal surface itself. Together with scatter, transmission occurs, driving the light energy into the tissue. The incident photons are ultimately absorbed in whatever chromophore is appropriate for the wavelength of the light, and pass their photon energy to the absorbing cell.

No Absorption, No Reaction!

The goal of the use of lasers and light in wound healing is to obtain some kind of clinical effect to enhance the wound healing process, but this can only happen if the light is absorbed in the target cells or their organelles. The first law of photobiology—the Grotthuss-Draper Law—clearly states that without absorption, there can be no reaction. Therefore, absorption of radiant energy is the most important of the basic light-target interactions, followed by penetration of the light with sufficient photon intensity to reach that target.

Importance of Wavelength

The one single parameter of light that assures both absorption and the intrinsic depth to which that light can penetrate is its wavelength—not the incident power of the light. (Please see Chap. 20 in this handbook on LED phototherapy for a detailed discussion on the relationship among wavelength, absorption and penetration). Light penetrates living biological tissues most efficiently in the window between 610 nm and 1,700 nm. The shorter visible light wavelengths, blue, green, yellow and even orange, have specific biological chromophores which limit penetration to the epidermis and superficial dermis, namely epidermal melanin and dermal blood. On the other hand, for the near-IR spectrum (beyond 1,700 nm) water is the main chromophore, and water absorption rises steeply after 1,700 nm. From 700 nm to around 1,700 nm penetration is very efficient with the deepest penetration being seen between 820 and 840 nm, the bottom of the water absorption curve: this accounts for the popularity of the 830 nm wavelength when aiming for therapeutic effects throughout the skin, right down to the subdermal layers and beyond.

Laser Surgery and Laser Therapy: Two Sides of the Same Coin

Consider Fig. 21.1, which shows a schematic of the impact of a surgical laser beam in tissue on the left, and the thermally-dependent reactions listed on the right, plus a zone of athermal activity at the periphery of the beam. Figure 21.2 shows a typical histological specimen of skin following a surgical CO_2 laser impact, demonstrating clearly demarcation between the decreasing photothermal effects, down to normal-looking skin architecture. It is important to remember that not all of the photons incident on tissue in a laser 'shot' are absorbed in the initial reaction, and a wave of light energy of lower photon intensities can spread out and down into the tissue until finally the photon density is low enough not to generate a thermal effect when the photons are absorbed by the skin cells in the periphery of the beam. The degree of

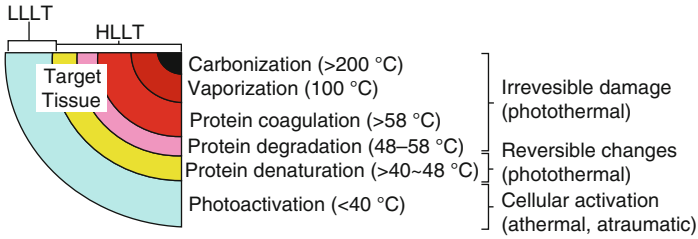

FIGURE 21.1 Typical surgical laser impact on tissue Illustration showing schematically a typical surgical laser impact on tissue with the total range of thermally-mediated reactions and the all-important athermal and atraumatic photoactivation zone at the periphery of the beam. The photoactivated cells in this zone will have a potentially beneficial effect on post-treatment pain, inflammation and wound healing

this phototherapeutic reaction—called "simultaneous low level light therapy"—and the size of the photoactivation zone which occurs concomitantly with the photosurgical effects will depend on the wavelength, and on such parameters as the beam mode (continuous wave, long-pulsed or Q-switched) and incident power density: however, even in Q-switched laser beams, some residual photons will still provide a narrow periphery of photoactivated tissue. It is this photoactivated tissue which bestows the lower postoperative pain and less erythema associated with laser versus conventional surgery through assisting with the wound healing process in the necrotic and damaged tissues. Photosurgery and phototherapy can therefore be called two sides of the same coin. For a more detailed discussion on phototherapy and its associated reactions, please see the chapter on LED phototherapy elsewhere in this handbook.

The Wound Healing Process and the Role of LLLT

Understanding the stages and development of the wound healing process is important when thinking how and when to apply phototherapy to accelerate the process. Wounds may

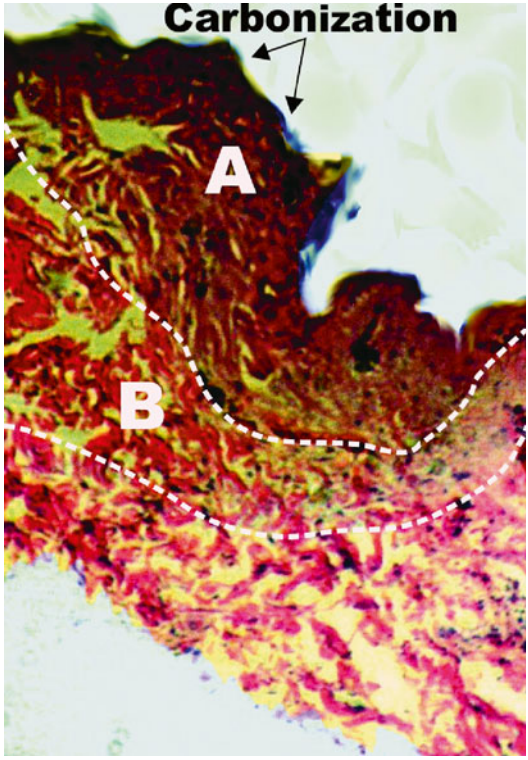

FIGURE 21.2 Hematoxylin and eosin stain (original magnification × 100) of a surgical CO_2 laser impact on human skin (continuous wave, 4 W, 2 mm, 300 ms: irradiance 117 W/cm^2). The epidermis has been totally vaporized together with the superficial dermis. Some carbonization can be seen at the impact. *Zone A* consists of fully coagulated necrotic tissue. The tissue in *zone B* shows partial coagulation, becoming more like normal tissue towards the periphery (protein degradation and protein denaturation). The tissue beyond *zone B* has normal architecture, and comprises the photoactivated zone (Photomicrograph courtesy of Mario A Trelles MD, PhD)

be traumatic, or they may be iatrogenic, i.e., postsurgical. Following wounding, there are three recognized phases of wound healing: the inflammatory phase, from the actual wounding until around day 3–5; the proliferative or regenerative phase, from around day 3–21; and the remodeling or the maturation phase from 3 to 26 weeks or more post-wound. The border between the phases is indistinct and there is some cross-over activity for a day or two up to a week, but each phase is characterized by the presence, or absence, of specific cell-types and inflammatory mediators.

Inflammation

Inflammation is often erroneously thought of as a 'bad' thing: in fact, inflammation is absolutely required before the wound can progress to proliferation. It is *uncontrolled* or prolonged inflammation that is to be avoided. For example, the overuse of steroids to 'control' inflammation is associated with a prolonged course and poor wound healing [6].

- **Inflammatory stage cells** During the inflammatory phase, the skin cells of interest are, in numerical order, the mast cells, macrophages and neutrophils which peak around day 1–2 and then decline back to their pre-wound levels [7]. The granular mast cells are stimulated to degranulate rapidly, releasing a cocktail of anticoagulants, and potent pro- and anti-inflammatory substances in addition to some trophic factors and signaling compounds to bring in more reparative cells. Some of these substances also help mediate the release of platelet-derived growth factor from free platelets in the wound area. The inflammatory substances help to peak the inflammatory response, and the anti inflammatory substances to quench it. Macrophages are recruited into the area to clean up the debris associated with the wound which are a source of irritation, but as they work phagocytosing dead cells and denatured connective

tissue they release fibroblast growth factor (FGF) into the dermal matrix, leaving a favorable environment for the fibroblasts in the proliferative phase. They can also release transforming growth factor (TGFα) (alpha) which is associated with epithelial regeneration. Neutrophils are the first line of defense of the body against invading pathogens which they phagocytose and kill through oxidative burst activity. Neutrophils have additionally been associated with the release of TGFβ (beta), an important factor which can accelerate tissue regeneration.

- **Phototherapy and Inflammatory Cells** Low incident doses of light energy have been proved to activate all three types of inflammatory cell both in vitro and in vivo. Many visible light wavelengths will affect the cells in vitro, with the end terminal of mitochondrial respiratory chain as the primary photoacceptor [8], but the penetration characteristics through biological tissue of visible light restrict the use of the shorter visible light wavelengths in vivo up to around 610 nm due to the presence of epidermal melanin and dermal blood (for a detailed explanation, please refer to the chapter elsewhere in this handbook on LED phototherapy). Visible red light at 630 nm and beyond penetrated very deeply into tissue, and the deepest penetration is in the near-infrared (near-IR) at 820–840 nm. The wavelengths which have proved to increase the action potential of the inflammatory stage cells are 633 nm (HeNe laser and LEDs), 830 nm (diode laser and LEDs) and 1,064 nm (defocused continuous wave Nd:YAG). 10,600 nm has also shown efficacy (defocused CO_2). The use of the defocused surgical laser beams illustrates to the reader why the term 'low power laser' is totally inaccurate: a 'high power' 20 W CO_2 can slice through tissue like a hot knife through butter to create a wound when focused to a 100 μm spot (irradiance or power density of 254 kW/cm^2). On the other hand, when the same output power is defocused to a 10 cm spot which could treat, for example, a crural ulcer, the irradiance is around 254 mW/cm^2, a therapeutic irradiance which is capable of LLLT for healing wounds, but a 20 W CO_2 is not a "low power" laser!

- **Mast Cells** 830 nm LED phototherapy has been shown in vivo in human subjects to activate mast cells to degranulate by as much as 50 % only 48 h after a single irradiation, without any wound [9], although a wound or an allergic reaction is usually required to initiate this degranulation process. In addition, cell counts showed significantly increased numbers of macrophages and neutrophils in the irradiated compared with unirradiated control tissue.
- **Neutrophils** When photoactivated, neutrophils detect their target, migrate to the target, and internalize it more quickly and with a significantly higher degree of oxidative burst [10]. In a study on chemotherapy-induced oral mucositis in children treated with 830 nm diode laser phototherapy, the pain and healing time were significantly reduced compared with retrospective controls. The authors suggested that the near-infrared photoactivation of neutrophils and T-cells played a key role in controlling the excessive inflammatory response, a result of immunoincompetence induced by the chemotherapy, and in enhancing the proliferative stage of wound healing [11]. In two controlled studies with animal models that examined the effects of LLLT on wound healing it was shown that sites treated with LLLT healed faster than untreated controls. Interestingly, the LLLT-treated wounds had significantly fewer neutrophils at 7 days post-wound as compared with the controls. This illustrates the quenching action of LLLT on the inflammatory stage of wound healing with normalization of the presence of the inflammatory cells [12, 13].
- **Macrophages** LLLT activates macrophages in vitro to move to their target, engulf it and internalize it faster [14] and at the same time to release more than ten-fold the amount of FGF compared with unirradiated controls [15]. In a paper by Mârţu and colleagues referenced above [13], not only neutrophils but also macrophages were returning to their normal number at 7 days post-wound following LLLT in an *in vivo* animal model showing normalization of the regenerating wound.

Proliferation

In the proliferative phase, wound damage in the epidermis and dermis is repaired through epithelialization and regeneration of the connective tissues making up the dermal matrix, respectively.

- **Epithelialization** Epithelialization takes place from the epidermis at the margins of the wound, and also from the epidermal remnants invaginating any pilosebaceous units remaining in the wound. Mitosis, separation and differentiation are induced in the mother keratinocytes in the epidermal stratum basale. The new epithelium gradually forms over the granulation tissue in the wound bed, and under the protective crust which will have formed over the wound. For this reason, crusts should never be forcibly removed, but allowed to drop off naturally. Epidermal keratinocytes are known to be activated by both 633 and 830 nm so that epithelialization post-wounding can occur faster with LLLT at appropriate wavelengths. A preclinical study showed that LLLT induced the creation of new keratinocytes in incisional wounds in an *in vivo* animal model [16]. It is accepted that no or little visible scar will be seen if epithelialization of a wound can be complete in 10–12 days. This means that a wound the full thickness of the dermis, but very narrow (<4 mm wide) and a very shallow but wide wound can both heal by primary intention, i.e., by epithelialization with or without surgical approximation. Wider and deeper wounds, if left unapproximated, heal by secondary intention, i.e., granulation tissue formation is not covered by epithelium within the 12-day time limit, resulting in a broader scar.
- **Connective Tissue Regeneration** The major cells involved in this process are the fibroblast and the endotheliocyte. Fibroblasts are responsible for synthesizing collagen and elastin, plus replenishing the glycosaminoglycans, and endotheliocytes clump together to form new blood vessels from which bud existing vessels in the process known as neovascularization. New vessel formation is very important

in a wound to supply the fibroblasts and other cells with oxygen and nutrition. One of their first tasks is manufacturing the granulation tissue over the wound, composed of an immature form of collagen (type III) and very small blood vessels. The fibroblasts in the dermis first produce procollagen within the cell that is transformed to tropocollagen outside the cell. The tropocollagen forms collagen fibrils which in turn are cross-linked with hydrogen bonds to form collagen fibers which then form collagen bundles. Collagen give skin its shear strength, due to the comparatively random orientation of the fibers and strong cross-linking within the bundles.

- **Light-Fibroblast Interaction** Fibroblasts respond well *in vitro* to most wavelengths of visible right, but particularly to light in the red waveband around 633 nm, the wavelength of the HeNe laser with which a great deal of the initial work on fibroblasts was carried out. In vivo they respond well to red light, because the shorter visible wavelengths do not penetrate very deeply into living biological tissue and so do not reach the main target fibroblasts in the deeper dermis. Fibroblasts also respond well in vivo to infrared light, which has only comparatively recently been illustrated. For an illustrated example of how 633 nm LED induces fibroplasia in fibroblasts *in vivo* [17], please refer to the sister chapter elsewhere in this book on LED phototherapy. Figure 21.3 illustrates the effect of 830 nm LED phototherapy on human fibroblasts in vivo. Figure 21.3a shows a fibroblast in a transmission electron photomicrograph from the unirradiated (control) side of a patient's face who participated in a split-face trial to assess the efficacy of LED phototherapy in skin rejuvenation, from a specimen taken 2 weeks after the treatment had finished [18]. The fibroblast is tired-looking with scant cytoplasm, surrounded by irregularly oriented and sparse collagen fibers. The fibroblast in Fig. 21.3b, on the other hand, is from the contralateral side of the same patient's face irradiated with 830 nm LED, 60 J/cm^2, biopsied at the same time as Fig. 21.3a. The fibroblast is plump and active with

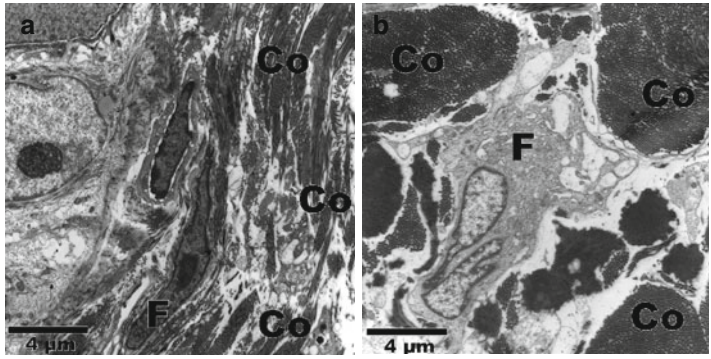

Figure 21.3 Effect of 830 nm LED-LLLT on human fibroblasts in vivo. (**a**) Transmission electron microscopy of a specimen from the unirradiated side of a subject's face shows a thin and rather anemic-looking fibroblast with poor cytoplasm (*F*) surrounded by sparse and poorly-organized collagen fibers (*Co*). (**b**) SEM photomicrograph taken from the contralateral side of the same patient's face, 2 weeks after 830 nm LED phototherapy for skin rejuvenation, This fibroblast (*F*) is plump with abundant cytoplasm, and is surrounded by well-organized collagen fibers linked into bundles (Scale bar 4 µm for both: photomicrography courtesy of SY Celine Lee MD: see also Ref. [18])

an abundant cytoplasm, surrounded by well-organized bundles of collagen fibers. The authors of this trial also subjected specimens to immunohistochemistry to test for matrix metalloproteinase (MMP 1 & 2) and also for tissue inhibitor of MMP (TIMP) 1 & 2 at 48 h after the final treatment. No MMP activity was seen, but a significant increase in TIMP activity was seen after LED phototherapy in the irradiated sides compared with the unirradiated sides [18]. This showed a protective effect of LED phototherapy against breakdown of young collagen fibers by MMPs, which is very important in the early phases of wound healing to ensure good wound closure and tissue strength (Fig. 21.4).

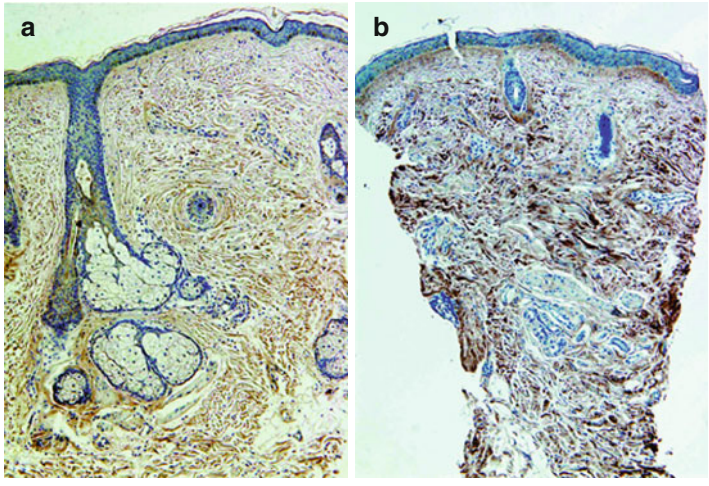

FIGURE 21.4 Protective effect for new collagen 830 nm LED LLLT positively affects tissue inhibitor of matrix metalloproteinase 1(TIMP 1) in treated tissue. (**a**) Specimen from the unirradiated side of a subject's face immunohistochemically stained for TIMP 1 with an anti-TIMP 1 antibody showing very faint TIMP 1 activity (brown staining). (**b**) Specimen with same staining from the contralateral side of the same patient's face treated with 830 nm LED phototherapy showing dense brown staining indicating high TIMP 1 activity (Original magnification × 100. Photomicrography courtesy of SY Celine Lee MD: see also Ref. [18])

No studies have been done on the specific phototherapy effects on endotheliocytes, but neovascularization has been proved in an ischemic flap rat model after phototherapy, in a recent study by Cury et al. with both visible red and near IR phototherapy [19].

Remodeling (Maturation)

The final stage of remodeling is the longest, taking anywhere from some months to a year or more. It is an extremely

important stage, and accounts for the continued improvement seen in the condition of wounds and their surrounding tissue long after the wound has actually healed. This is because the mass of collagen fibers which was swiftly but somewhat haphazardly laid down in the proliferative phase is remodeled to achieve greatest strength without haphazard bulk. At the beginning of this phase there are now too many fibroblasts in the matrix.

- **Fibroblasts remain to maintain the matrix** Some of the fibroblasts remain as they are and continue to maintain the extracellular matrix (ECM) through synthesizing collagen and elastin to renew the elastic fiber component in the ECM. Elastin fibers allow skin to reform when it has deformed, and a good layout of elastic fibers fights gravity in the face, halting the downward migration of facial tissues and also strengthens wounds by increasing their cohesiveness and strength. 830 nm phototherapy was shown to significantly increase elastin fiber deposition and actual skin elasticity in photoaged skin [18]. In addition, the fibroblasts also constantly renew the glycosaminoglycans, or ground substance, ensuring a well-lubricated matrix and plumped-up dermis and providing a transport mechanism for extravascular oxygen to reach the working cells.
- **Fibroblasts transform to Fibrocytes** Some fibroblasts are prompted to dedifferentiate into quiescent fibrocytes, a kind of unipotent stem cell which is capable of re-differentiation into a healthy young fibroblast, thereby helping to renew the stem cell pool to help keep the matrix younger and maintain this condition for longer.
- **Fibroblasts transform to myofibroblasts** The remaining fibroblasts transform into myofibroblasts and as '*myo*' means 'muscle', the myofibroblast is simply a fibroblast with muscles. The muscles are located in feathery tufts at either end of the elongated fibroblasts, and contain barbs which hook onto collagen fibers. The myofibroblast is then programmed to contract, pulling the collagen fibers into better and tighter alignment so that the dermal matrix will attain full strength through better alignment of its collagen

bundles. Once the process is complete, the myofibroblasts enter apoptosis, programmed cell death, and die. 633 nm LLLT enhanced the remodeling or transected tendons in the rabbit model [20], and near-IR LLLT was proven to accelerate the transformation from fibroblasts into myofibroblasts, also in the rabbit model, thereby enhancing the remodeling process [21]. In both sets of experiments, the LLLT- treated tendons were macroscopically thinner but significantly stronger than unirradiated tenotomized tendons.

Role of the Vascular System

Inflammatory and reparative cells need oxygen and nutrition to fulfill their various tasks, and this is provided from the extracellular matrix via the blood supply. If the blood supply is insufficient, cells and tissues are starved of oxygen and ischemia occurs which is extremely detrimental to wound healing. A good blood supply and replacement of damaged vessels through neovascularization are both essential for good wound healing. Low incident doses of 830 nm were shown to significantly increase the blood supply through neovascularization of the rat skin in an in vivo model [22]. Three groups were compared: an unirradiated control group, a sham irradiated group and the 830 nm irradiated group: 830 nm was applied twice per week for 4 weeks. Figure 21.5 compares transilluminated 830 nm sham-irradiated skin 2 weeks after the final treatment with skin from an irradiated animal. The difference in the density of blood vessels is clear. Flap survival is an important consideration for the plastic surgeon, and 830 nm LLLT was shown to increase the survival rate of axial pattern flaps in a rat model [23]. The perfusion of the irradiated flaps was significantly better than the unirradiated flaps as assessed with speckle Doppler flowmetry, and perfusion remained high for some time after a single treatment (Fig. 21.6). The authors concluded that 830 nm LLLT significantly increased blood flow rate and volume in irradiated flaps, paving the way for significantly better survival.

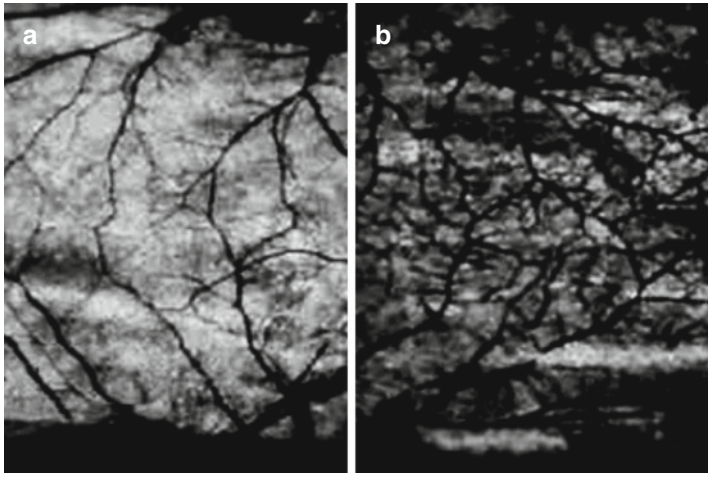

FIGURE 21.5 Excised and transilluminated rat skin immediately ex vivo (Original magnification × 3). (**a**) Sham irradiated specimen. (**b**) 830 nm phototherapy specimen showing rich vascular network. See the text for treatment and timing details (Photomicrography courtesy of Junichiro Kubota MD, PhD)

In a recent prospective study in 30 patients with diabetic foot and leg, a combination of 633 nm and near-IR LLLT significantly increased blood flow in the affected limbs, and prevented complications [24].

The Systemic Effect of LLLT in Wound Healing

It has been well illustrated that irradiation of one part of the body with low intensities of laser or LED energy will cause a systemic effect which can affect other unirradiated areas. The earliest proof was in the 1971 torpid ulcer trial cited above by Mester. The irradiated ulcers healed within some weeks in 78 % of the 1,120 patients with long-term bilateral torpid ulcers: what really surprised readers was that the unirradiated contralateral leg ulcers also healed in the majority of these patients some weeks later, despite not having been treated directly [2]. A recent systemic controlled wound healing study in an animal

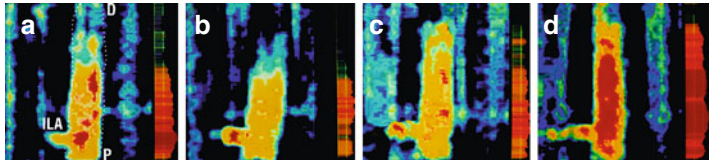

FIGURE 21.6 Laser Doppler speckle flowmetry images of flaps on the back of a rat model of the iliolumbar flap, unirradiated (control) or irradiated with 830 nm LLLT (60 J/cm^2). (**a**) Unirradiated animal just after raising the flap, shown by the *dotted white outline*. ILA is the iliolumbar artery, and P and D represent the proximal and distal ends of the flap, respectively. Note the colored scale on the right of the panel: this represents the comparative degree of perfusion: red represents excellent blood flow, decreasing to *dark blue/black*. (**b**) Same animal as in Fig. 21.4a, 90 min after the flap was raised. Perfusion in the distal end of the flap is extremely poor. (**c**) 830 nm LLLT-irradiated animal, just after raising the flap: the flap was immediately irradiated with the near-IR nm energy. (**d**) Same animal as in Fig. 21.4c, 90 min post irradiation. Perfusion throughout the majority of the flap is excellent. Compare the right-hand perfusion scale for Fig. 21.4b, d. The effect of the single LLLT session on the blood supply to the flap thus continued for at least 90 min (Speckle laser flowmetry images courtesy of Junichiro Kubota MD, PhD)

model involved creating identical wounds with a fractional CO_2 laser on the shaved dorsa of the animals [25]. One group underwent 830 nm LLLT to their abdomen; the control group were treated in exactly the same manner but without the irradiation. At 7 days after the wounding, all of the indirectly irradiated animals were nearly (>75 %) or completely healed, whereas in the control group no animal showed complete healing, and some were still less than 50 % healed ($p<0.001$).

Surgical Lasers and Wound Healing

Defocused surgical lasers have shown efficacy in wound healing, such as the CO_2 laser [26] and the Nd:YAG laser [3]. However, the introduction of fractional laser technology without defocusing, whereby laser energy was fractionated

into precise microbeams, offered significantly faster wound healing than the conventional total ablative approach and is thus worthy of mention in this chapter. Fractional technology was originally designed to bridge the gap between the successful, but very uncomfortable full-face ablative laser applications and the unsuccessful attempts at nonablative laser skin rejuvenation. The former produced excellent results and can still be considered especially for severely photoaged skin, but is associated with extreme discomfort post-procedure and a long downtime; whereas the latter was associated with virtually no downtime, but by and large no results. Both nonablative and ablative fractional lasers have been developed, but the latter have proved more effective in more severely photoaged skin and scar revision. The concept was to fractionate the laser energy of a single 'shot' over many microbeams, around 100 μm in diameter or more, but leaving a large percentage of the skin in the treated area completely untreated, and therefore able to help with speedy wound healing of the microablative zones. Figure 21.7 shows histological specimens immediately after treatment with a fractional CO_2 laser, then at 48 h and finally at 2 weeks post-treatment with absolutely normalized epidermal and dermal morphology, a tighter, younger-looking dermis and better organized epidermis, especially the stratum corneum.

Types of Wounds

Wounds that can be treated with LLLT basically comprise any wound at all, whether it is a surgical wound or a traumatic wound following an accident of some kind. LED phototherapy with its hands-free and noncontact approach means that burn wounds and infected wounds can be treated with possibility of contamination, or a surgical wound following emergency or elective surgery. The aesthetic surgeon should find LLLT particularly useful, especially with the new-generation LED phototherapy systems that work in a hands-free manner, which makes them very operator-friendly and nonintensive in addition to being contact-free.

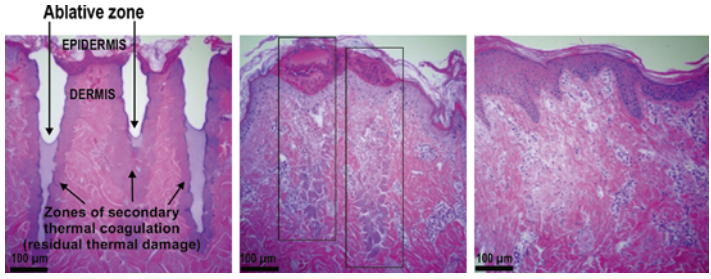

FIGURE 21.7 The evolution of speedy wound healing following fractional ablative CO_2 resurfacing. (*Left panel*): Immediately post fractional ablative laser resurfacing. The microablative columns (MACs) are clearly seen extending through the epidermis into the dermis. Each MAC is surrounded first by a zone of secondary thermal damage: this will kick-start the wound healing process. Note the normal epidermis and dermis between the MACs: this will help speed up the wound healing process even faster. (*Middle panel*): At only 48 h post-treatment, epithelialization is almost 100 % complete. The MACS have gone, replaced by zones of dermal repair with an inflammatory infiltrate. (*Right panel*): Two weeks after treatment the dermis is well-ordered and completely repaired with tight new collage fibers, especially in the Grenz layer just under the dermoepidermal junction. The epidermis is highly cellular with excellent rete peg formation, and a smooth stratum corneum: this is young skin (Human skin, hematoxylin & eosin, scale bars all 100 µm. Photomicrographs courtesy of Boncheol Leo Goo, MD)

There could be pages of examples, but as a single powerful example where LED phototherapy both hastened wound healing and ameliorated side effects in clinical practice, a controlled study by Trelles and colleagues took 50 females undergoing full face ablative resurfacing with the combined Er:YAG and CO_2 lasers, and divided then into 2 age- and characteristic-matched groups of 25 [27]. One group had LED phototherapy after their treatment (immediately after, then 24 and 72 h after, followed by two treatments per week for 3 weeks, separated by at least 2 days). Time to complete full epithelialization was noted in both groups, as well as the

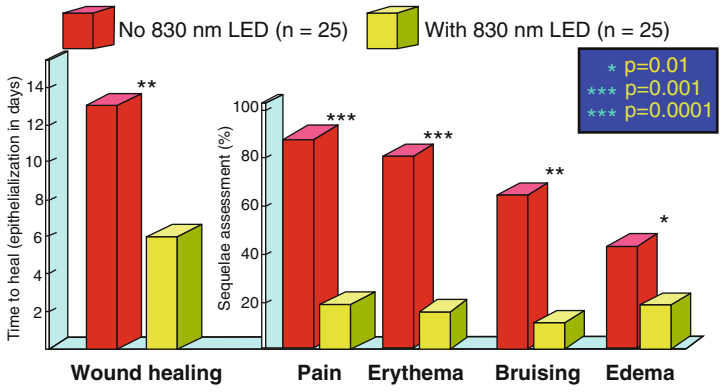

FIGURE 21.8 Comparison between the speed of wound healing, pain, erythema, bruising and edema A graph depicting the comparison between the speed of wound healing, pain, erythema, bruising and edema in a controlled study on the use of 830 nm LED phototherapy following full face ablative laser resurfacing (Adapted from data in Ref. [27])

incidence of pain, erythema, bruising and edema. The data were tabulated and compared. Wound healing in the LED group was better than half that in the unirradiated control group, and all side effects were significantly reduced in the LED-treated group (Fig. 21.8). At a 6-month assessment point, an independent panel of three dermatologists scored the LED treated group significantly higher for overall skin condition compared with the control group (personal communication from Mario Trelles MD PhD). Figure 21.9 shows a typical example of a patient before and only 5 weeks after full-face ablative laser resurfacing, adjunctively treated with 830 nm LED phototherapy. For the full-face ablative laser approach, LED phototherapy was therefore able to dramatically reduce the long downtime associated with this technique making that approach more attractive again for surgeons, and for patients with a severely photoaged face.

A word needs to be added here regarding the use of LLLT on dressed wounds. If the dressing is semiopaque, such as a thick cocoon of gauze, then it will diffuse the incident light to such an extent that not much will reach the wound. However,

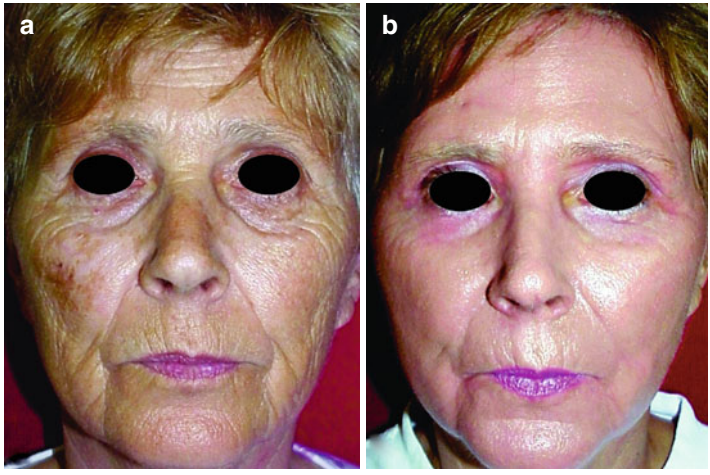

FIGURE 21.9 A 65-year-old female with severe solar-mediated photoaging (loved skiing) at baseline (**a**, **b**) only 5 weeks after full face ablative resurfacing with a combination Er:YAG and CO_2 laser, followed by 830 nm LED phototherapy. Full-face ablative laser resurfacing has been associated with several weeks to even months of erythema. The addition of LED phototherapy helped to deliver the excellent result associated with full face resurfacing in severely photoaged skin while effectively ameliorating the usual downtime (Photography courtesy of Mario A Trelles MD, PhD)

if adjacent areas to the wound are uncovered, these can be irradiated and the bystander cell effect plus the systemic effect will indirectly benefit the actual wound. Semi-transparent thin dressings on the other hand, such as DUKAL™, Dynarex View Guard™ and Tegaderm™ will allow much more incident light to reach the target tissue, although the energy will be somewhat diffracted and a little diffused.

Conclusions

- Both laser energy at sufficiently low intensity and energy from LED systems have beneficial effects on wound healing through accelerating the overall process, controlling

post-wound pain and erythema and offering prophylaxis against hypertrophic scarring.

- LED phototherapy offers a noncontact approach, ideal for treating burn injuries and infected wounds.
- Not all phototherapy will work, although even small amounts of light are theoretically capable of inducing cellular reactions: very importantly the irradiance (power density in mW/cm^2 – W/cm^2) must be high enough to achieve a viable clinical effect, but not so high that a photothermal reaction occurs to bring skin temperature to over 40 °C: this would potentially create more damage than induce healing.
- Appropriate selection of wavelength is critical. Optimal light penetration and absorption by the target chromophore must be within the waveband of 610–1,700 nm.
- Visible light causes a primary photochemical reaction whereas near-IR energy induces a primary photophysical reaction in target cells. However the result is the same: a photoactivated cell to work harder and better during the entire wound healing process.
- Phototherapy should be delivered as soon as possible after any wound—traumatic or surgical. Typically, the wound is retreated with phototherapy at 24 and 72 h post-wound. Phototherapy should be continued with two treatments per week separated by an interval of at least 2 days. This regimen can be continued for 3 weeks, depending on the severity of the wound.
- Wound healing with defocused lasers, laser therapy systems and LED sources is easy and painless to apply, is effective and side effect-free, and is well-tolerated by the overwhelming majority patients.

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Chapter 22
The Use of Lasers and Light Treatment for Hair Growth and Hair Transplantation

Nicole E. Rogers

Abstract Laser light presents a non-invasive treatment option for patients with hair loss. In this chapter, we examine data for the use of ultraviolet, fractionated, and low-level light therapy (LLLT) for the treatment of male and female pattern hair loss, as well as alopecia areata and cicatricial alopecias. Mechanisms for laser-induced hair growth include localized vasodilation and skin wounding. More data about ideal dosing and treatment parameters is still needed.

Keywords Hair loss • Hair growth • Low-Level Light Therapy (Llt) • Minoxidil • Finasteride • Laser • Hypertrichosis • Alopecia

Background

The treatment of hair loss can be challenging both for patients and for physicians. This is because there is just one FDA-approved medication for women (topical minoxidil) and two FDA-approved medications for men (topical

N.E. Rogers, MD, FAAD
Department of Dermatology, Tulane University School of Medicine, 701 Metairie Road, Ste 2A205, Metairie, LA 70005, USA
e-mail: nicolerogers11@gmail.com

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FIGURE 22.1 FDA-approved medications for male and female pattern hair loss include topical minoxidil (men and women) and oral finasteride (men only)

minoxidil and 1 mg oral finasteride) (Fig. 22.1). Hair transplantation can provide a much more dramatic effect in terms of relocating hairs from denser parts of the scalp to thinning areas (Fig. 22.2a, b), but not all patients are candidates for such a procedure. They may be limited by the amount of density in the donor area, have unrealistic expectations, or not be able to afford the procedure. Thus, the potential role of lasers in treating hair loss has been greeted with both welcome and caution simultaneously.

The use of lasers in the treatment of hair loss has been discovered through mostly accidental means. First, Hungarian researcher Endre Mester observed that applying low- level laser therapy (LLLT) to the backs of shaven mice could help regrow the hair more quickly [1]. Subsequently, lasers used in dermatology for purposes of hair removal were found to cause a paradoxical hair growth. This has been observed primarily in women with dark skin types or ethnic skin, and at low fluences

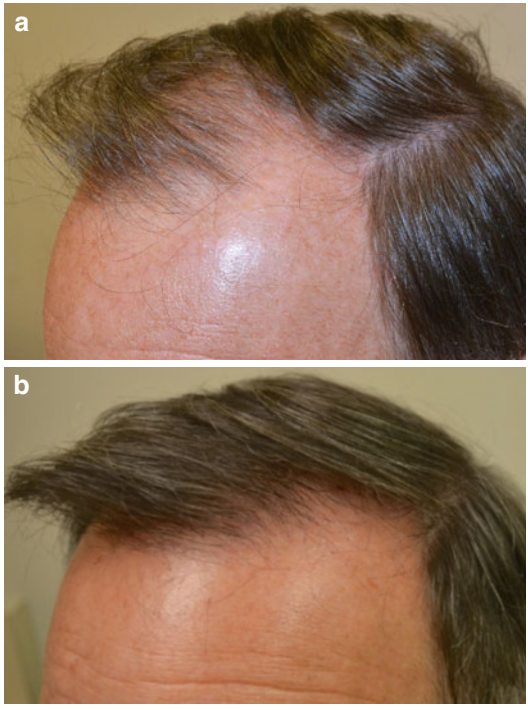

FIGURE 22.2 (**a**) 55 year-old male, before hair transplant surgery. (**b**) Same patient 26 weeks after receiving 1,400 1–4 hair follicular unit grafts

[2]. Table 22.1 summarizes various cases of such hair growth with the corresponding light source and patient population.

One possible mechanism by which light could affect hair is via photo-relaxation, proposed by Nobel-prize-winning Dr. Robert Furchgott a half-century ago. Dr. Furchgott observed that the smooth muscle of rabbit aorta vasodilated when exposed to ultraviolet light [10]. His assistant had observed strips of intestinal tissue (located near a window) alternately contract and relax as he cast a shadow over it or allowed the sun to shine on it, respectively. Years later, Dr. Furchgott

Table 22.1 Reports of paradoxical hypertrichosis [3–9]

Light source	Wavelength	Incidence
Long-pulsed NdYag	755 nm	3/489 patients [3]
Diode laser	810 nm	1/1 [4]
Intense-pulsed light	650–1,200 nm	5/49 patients [5, 6]
		51/991 patients [7]
		57/543 patients [8]
IPL & LP NdYag	755–1,200 nm	30/750 patients [9]

identified that UV light activates the release of nitric oxide from the vascular smooth muscle cells [11]. This photo-activated vasodilation may translate to an increased blood supply for nearby hair follicles.

There is also the observation that wounding can result in the regeneration of hair follicles. This was observed by Kligman and Strauss over 50 years ago after dermabrasion resulted in regeneration of hair follicles and sebaceous glands of the face [12]. Cotsarelis and colleagues showed that Wnt-dependent signaling after wounding can result in hair follicle neogenesis [13]. Recently, 1,550 nm fractionated carbon dioxide laser therapy was observed to result in induction of *de novo* hair regeneration in scars [14]. Three patients developed terminal hair growth after 1–3 treatments with the laser.

Overview of Laser Mechanisms

- LASER is an acronym for **l**ight **a**mplification by **s**timulated **e**mission of **r**adiation [15].
- Many forms of laser technology have evolved over the years. In this chapter we will limit our description of lasers to those that have been applied toward the treatment of hair loss or in the use of hair transplantation.
- Table 22.2 summarizes the various parameters of each form of laser technology to be included here.

Table 22.2 Lasers used for hair growth

Laser	Wavelength	Application
LLLT	600–700 nm	AGA[a]
		Alopecia areata
		Chemo-induced alopecia
		Wound healing post HT
Narrow-band UVB	311 nm	Alopecia areata
UVA/PUVA	320–400 nm	Alopecia areata
Excimer laser	308 nm	Cicatricial alopecia
Fractionated laser	1,550 nm	AGA
Ablative lasers	CO_2	Creation of graft sites in HT

[a]FDA-510 K-cleared for this application in humans

Lasers for Androgenetic Alopecia (AGA)

- The laser technology most commonly being applied toward treatment of androgenetic alopecia (male and female pattern hair loss) is low-level light therapy.
- This 'cold laser' technology employs the use of low-fluence red light at wavelengths of 655 nm for the stimulation of hair growth (Fig. 22.3).
- A number of devices exist on the market, but the data is somewhat limited. Presently we have just two multi-centre, sham device-controlled trials demonstrating a statistically significant difference between treatment groups.
- The first, published by the manufacturers of the HairMax LaserComb (Lexington International, Boca Raton FL) tested the device in 110 male patients spread across several U.S. treatment centers [16]. Subjects were treated for 15 min three times weekly with either the laser or sham device, over a 24-week period. At the conclusion, there was a significantly greater increase in mean terminal hair density in treated subjects than in the sham device group (Figs. 22.4 and 22.5).

FIGURE 22.3 Application of low-level light therapy to the scalp for hair loss

- More recently, the Oaze (a helmet-type device emitting 630–660 nm red light) was tested in 40 Korean patients in two research centers [17]. Scalp tattooing was performed, and after 24 weeks of using the device for 18 min daily, phototrichogram and global assessments were performed. The phototrichogram showed a significant difference in hair density and hair thickness. However subject global assessment and subjective satisfaction were not significantly different. The authors believed that this discrepancy was probably because a change in global appearance required a greater accumulation of microscopic change than was achieved with this device.
- A smaller study was conducted by the author using a hood-type device to emit LLLT on patients with AGA [18]. In this study, just eight patients were enrolled. Microscopic analysis demonstrated an increase in the percentage of terminal hairs and a decrease in the percentage of vellus hairs, but the results were not statistically significant. As in the prior case, no global improvement could be appreciated by blinded investigators.
- In 2011, the 1,550 nm fractionated erbium-glass laser was used for the treatment of female pattern hair loss [19]. Twenty-eight South Korean females were enrolled and underwent 10 treatments at 2-week intervals. The authors demonstrated statistically significant increases in hair density (from 100 to 157 hairs per cm^2) and hair shaft

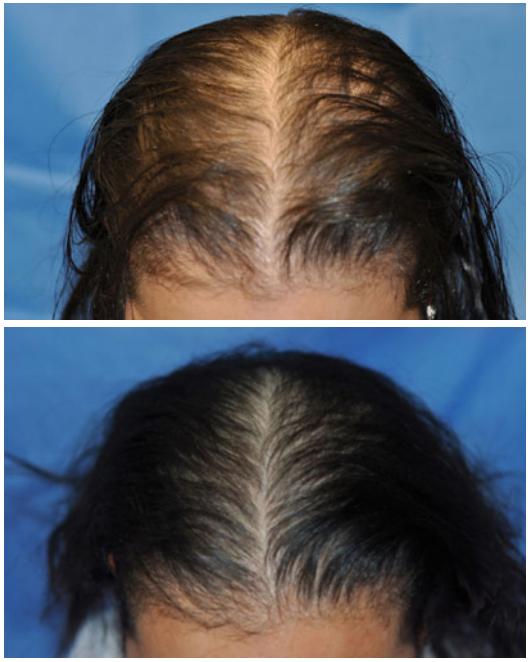

FIGURE 22.4 Female before and months after using the Hairmax Lasercomb (Photos courtesy of Lexington International, Inc.)

thickness (from 58 to 77 μm). The authors propose that the microscopic zones of injury created by the laser could serve as a stimulus for hair follicle neogenesis, as published by Ito et al. [13]. Little is known about the duration of these results after cessation of laser therapy.

Lasers for Alopecia Areata

- Alopecia areata is an autoimmune form of hair loss resulting in the loss of immune privilege surrounding the hair follicle.
- On histology, there is infiltration of the hair bulb with CD4 and CD8 T-cells.

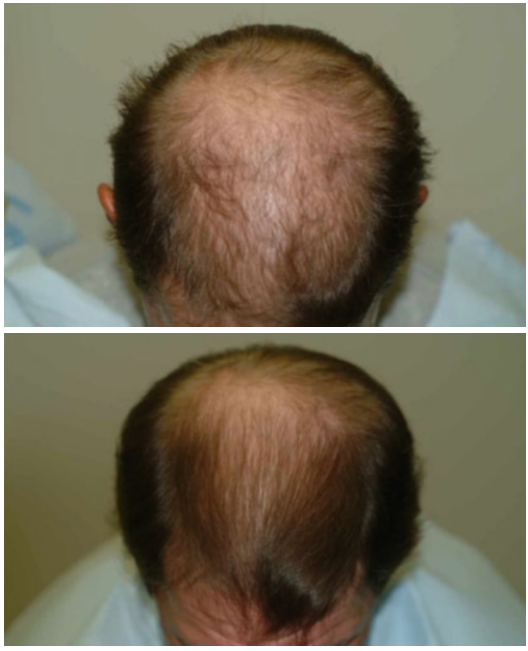

FIGURE 22.5 Male before and months after using Hairmax Lasercomb (Photos courtesy of Lexington International, Inc.)

- First-line treatments are topical or intralesional steroid injections.
- Presently, no lasers are FDA-approved for this application. Their success in treating the condition varies, and most studies are limited by small sample size.
- The use of PUVA has been mostly abandoned because early studies showed little improvement over spontaneous regrowth, and had the added risk of skin cancer development [20, 21].
- Interestingly, the fractionated laser technology was quite effective in one case report (n = 1) [22] and a series of 2/3 ophiasis patients [23].
- Perhaps the most effective light treatment for alopecia areata is the 308 nm excimer laser, with several slightly larger studies showing good results [24–26].

- The efficacy of LLLT in treating alopecia areata is uncertain. The author has used LLLT for very young patients (as an alternative to intralesional or topical steroids) with mixed results.
- In one study, sixteen patients with a total of 34 resistant patches were treated with a low-level (150 W) pulsed infrared diode laser (904 nm) weekly for 6–12 months [27]. Regrowth was seen in 32 of 35 patches, with continued growth after discontinuing the laser.
- Two mouse models have been conducted with mixed results.
  - In the first, twelve mice with heat-shock induced AA were randomized into treatment and sham-device control groups. They were treated with the HairMax Lasercomb (655 nm, 150 W) for 20 s, three times per week for 6 weeks [28]. The laser-treated mice showed an increase in the number of anagen hair follicles on histology. The sham-treated mice had hair follicles in the telogen phase with no hair shaft.
  - In the second study, aged mice with either natural-onset alopecia universalis (AU) or grafted-induced AU were treated in a similar fashion [29]. In this study, there was no regrowth in either the sham or laser treated groups.

Lasers for Chemotherapy-Induced Alopecia

- Low-level light therapy has also been investigated for the ability to regrow hair after chemotherapy-induced alopecia.
- Rat models were treated with cyclophosphamide, etoposide, or a combination of cyclophosphamide and doxorubicin and hair loss resulted 7–10 days later [30]. Investigators found that the rats treated with the HairMax LaserComb regrew hair a full 5 days earlier than rats undergoing sham laser treatment.
- Similar results have been observed in humans treated with topical minoxidil continuously throughout their chemotherapy regimens [31].

Lasers for Cicatricial Alopecia

- Cicatricial or scarring alopecias are a form of permanent hair loss resulting from trauma or from chronic inflammatory conditions such as lichen planopilaris (LPP), frontal fibrosing alopecia (FFA), or central centrifugal cicatricial alopecia (CCCA), to name a few. Their complete description and treatment is beyond the scope of this chapter.
- However, some have proposed applying the anti-inflammatory effects of light therapy on these inflammatory scalp conditions.
- In one study, 13 patients with LPP were treated with the 308 nm xenon chloride excimer laser [32]. A statistically significant number of patients had decreased erythema, pain, pruritus, and hyperkeratosis.

Lasers in Hair Transplantation

- In the early 1990s, there was interest in using laser light sources to create recipient sites for hair transplantation.
- The perceived advantages were less bleeding, greater density of recipient site creation, and less compression on adjacent grafts [33, 34].
- A number of different lasers were tried, including the Ultrapulse CO_2 (Coherent Medical Group, Palo Alto, CA) the Silktouch CO_2 (Sharplan Lasers Inc, Allendale, NJ) and the Erbium-Yag.
- However, the application of lasers for this purpose was ultimately abandoned due mostly to the collateral thermal damage created adjacent to the recipient sites.
- Laser-assisted graft sites had greater superficial de-epithelialization (with more prolonged crusting and erythema) and a higher incidence of graft fallout. One

explanation for this was that as the laser sealed off any bleeding from the dermis, this reduced the 'biological glue' available to hold the grafts in place [35].
- The most successful results were observed using low wattage for creation of small (1–3 hairs) grafts [36].
- Larger grafts with correspondingly deeper and larger laser-assisted sites showed poorer growth.
- Table 22.3 compares the advantages and disadvantages of laser-assisted hair transplantation with standard steel-punch recipient site creation.

Future Directions

Although CO_2 lasers were not embraced for recipient site creation, many hair loss specialists are using low-level light therapy in combination with other hair loss medications or for use after hair transplant surgery. The role of LLLT in enhancing wound healing has been well established [37], and most hair restoration surgeons agree that it has some role in the treatment of hair loss [38]. Many hair specialists either sell hand-held devices or perform in-office low-level light therapy during the postoperative period. This may be considered adjuvant treatment along with topical minoxidil to help maximize total growth of transplanted follicles [39].

There is still a great deal of research to be done examining ideal laser treatment parameters, including wavelength, energy density, duration and frequency. The variety of laser hoods, caps, combs, and brushes also indicates that we still have not identified the optimal method of light delivery. How well does the light penetrate the scalp if it must get through layers of hair first? Would the use of pulsing or fiber optics help increase the penetration and efficacy of this light? Many questions remain to be answered.

Table 22.3 Advantages and disadvantages of laser-assisted hair transplantation

	Laser-assisted recipient site creation	**Steel-punch recipient site creation**
Advantages	Less bleeding	Less collateral thermal damage
	Shorter operative time	No laser experience required
	Fewer epidermal cysts	Greater ability to control graft site angle
	No vasoconstrictors required	
	OK for smaller (1–3 hair grafts)	
	Vaporization of bald scalp leads to less graft compression	
Disadvantages	Cost of laser	Need vasoconstrictive medications
	Laser experience needed	
	Greater postoperative crusting and erythema	
	Telogen effluvium 2nd to collateral thermal damage	
	Risk of graft fallout with larger (4–5 hair) FU-grafts	
	Greater difficulty controlling angle of recipient sites	
	Risk of hypopigmentation	

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Chapter 23
Devices for Weight Loss and Fatty Tissue

Andrew A. Nelson

Abstract Traditional methods for body shaping and weight loss include diet, exercise, and invasive liposuction. In the last several years, multiple novel non-invasive devices for body shaping and fat sculpting have been developed. These technologies include: manual massage, laser, ultrasound, radiofrequency, and cold exposure. These devices have become increasingly popular, as patients desire simple, safe, non-invasive methods to remove and reshape unwanted fat.

Keywords Non-invasive fat reduction • Body sculpting • Cryolipolysis • Radiofrequency • Focused ultrasound

Background

- It is important to first determine if your patient is a good candidate for non-invasive fat reduction and body sculpting.

A.A. Nelson, MD
Department of Dermatology, Tufts University,
Private Practice Nelson Dermatology, 350 Sixth Street South,
St. Petersburg, FL 33701, USA
e-mail: andrew.nelson.md@gmail.com

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- Body mass index (BMI) = person's weight in kilograms divided by the square of their height in meters. This is the traditional method for classifying patient's weight status.
- Obese patients (BMI > 30) are not good candidates for non-invasive fat sculpting, and may require referral to bariatric center for surgical treatment options.
- The best candidates for non-invasive treatments have a normal BMI (18.5–24.9), with small, localized "problem areas" of excess fat, such as the "muffin top" (abdomen), "love handles" (flanks), and back fat pads.
- In general, patients typically experience modest improvement in the appearance of fat and cellulite with these treatments.
- As the results may be modest, it is important to document specific measurements such as thigh circumference, waist circumference, skin fold thickness, visual assessment, as well as obtain high quality before and after photographs to determine procedure efficacy.
- Many different technologies are available, including manual massage, laser devices, ultrasound devices, radiofrequency devices, and cryolipolysis (cold exposure). Each technology has associated risks and benefits.

Specific Technologies

Manual massage—Endermologie (LPG Systems, Valence, France)

Indications

- FDA (U. S. Food and Drug Administration) cleared for treatment of cellulite [1].

Contraindications

- No significant contraindications

Procedural Technique

- Device is rolled across the skin, combining positive and negative pressure from a vacuum system created between the two rollers to physically manipulate ("knead") the patient's skin.
- Thought to stimulate blood and lymphatic flow, thereby improving the appearance of cellulite [1].
- Likely requires ongoing treatment (one to two times per week) to maintain modest improvement in appearance of cellulite [1].

Complications

- Bruising of treatment area may occur due to high pressure gradient

Prevention and Management of Complications

- Avoid treatment in patients prone to easy bruising.
- May not be an ideal treatment for patients who cannot undergo weekly or biweekly treatment sessions.

Ultrasound Technology

Historically, ultrasound technologies were incorporated into invasive liposuction procedures to allow for easier more effective treatments, known as ultrasound assisted liposuction (UAL). More recently, high intensity focused ultrasound (HIFU) has been utilized to specifically target adipocytes transcutaneously, allowing for safe, effective and non-invasive ultrasound treatments for fat.

Indications

- The LipoSonix device (Medicis Technologies Corp, Scottsdale, AZ) is currently FDA cleared for non-invasive waist circumference reduction [2]. The UltraShapes device

(Syneron Medical Ltd., Irvine, CA) was recently FDA cleared for non-invasive reduction of abdominal circumference via fat cell destruction.

Contraindications

- HIFU technologies should not be used in pregnant or breastfeeding patients.
- There must be at least 1 cm of subcutaneous fat below the depth level of the treatment in order for the treatment to be safely performed [2].

Procedural Technique

- HIFU focuses ultrasound energy into the subcutaneous layer; the LipoSonix device for instance, focuses energy exactly 1.3 cm below the surface of the skin. The ultrasound energy creates a rapid temperature increase, to approximately 56° while sparing the surrounding dermis and epidermis. Macrophages then break down the heated adipocytes and they are gradually eliminated from the body over the next 2–3 months [2].
- The HIFU handpiece is passed over the treatment area, requiring approximately 1 h for the full treatment to be performed.
- Typically one treatment is necessary to improve adipose tissue.
- Currently, the LipoSonix device is approved for treatment of the abdomen and flanks. In other countries, the devices have also been used for treatment of the hips and thighs.
- The UltraShapes device also utilizes pulsed focused ultrasound energy that precisely targets subcutaneous fat. However, the UltraShape device uses a purely mechanical effect to destroy the fat cells without inducing thermal heating. This may help to spare the surrounding tissue from unintended treatment effects. Currently, the UltraShape device is FDA cleared for reduction of abdominal fat (approved 2014), but has been utilized in other countries for several years.

Complications

- Pain syndromes have been reported following treatment [3].
- Bruising and edema are common [3].

Prevention and Management of Complications

- Avoid use in patients who do not have sufficient subcutaneous fat, as this could lead to inappropriate heating of underlying muscular layers.
- Avoid use in patients with history of hernias.

Radiofrequency Devices

- Radiofrequency devices utilize sinusoidal, alternating current (AC), which is passed through tissue; this current causes ionic flow and molecular friction, leading to heat [4].
- Adipocytes have high tissue resistance as well as low heat transfer coefficients. They can therefore be easily heated by RF technology and the heat generated will stay relatively localized to the targeted adipocytes [4].
- Several different manufacturers produce RF devices which have been reported to improve the appearance of subcutaneous fat.
- RF devices may have an added benefit of also heating the dermis, resulting in skin tightening in the treatment area.
- The VelaShape (Syneron Medical Ltd, Irvine, CA) device combine physical manipulation of the area, with RF energy, and broadband light (700–2,000 nm) to treat fat.
- A novel radiofrequency device (BodyFX, Invasix Inc, Richmond Hill, Canada) combines controlled radiofrequency heating with high voltage ultrashort electrical pulses to target and reduce adipose tissue.

Indications

- Currently, radiofrequency has not yet been approved by the FDA for fat removal.

- Some RF technologies have been FDA cleared for skin tightening and rejuvenation.

Contraindications

- There is a theoretical interaction between RF devices and patients with implanted cardiac pacemakers and defibrillators, due to electromagnetic interference.
- RF should not be used in pregnant or breastfeeding patients.

Procedural Technique

- RF devices are typically passed over the treatment area to warm the subcutaneous fat and dermis. As many of the devices utilize a vacuum component, the treatment area must be able to be elevated and pinched.
- No specific pre or post-operative care is necessary.
- Depending on the exact technology, the treatment could last between 20 and 60 min.
- A series of four to eight treatments is often necessary to reduce subcutaneous fat and tighten skin.
- The results gradually appear over the next several weeks following the treatment.

Complications

- Bruising and edema are common, likely related to the vacuum function of the devices.
- Warm sensations (due to heat) and pain syndromes can be associated with the treatment.

Prevention and Management of Complications

- Avoid overheating the treatment area, as this may cause pain.

- Avoid use in patients who do not have sufficient subcutaneous fat, as this could lead to inappropriate heating of underlying muscular layers.

Laser Devices

- Historically, lasers were combined with invasive liposuction techniques to improve efficacy, a process known as laser assisted liposuction (LAL).
- More recently, laser technologies have been developed to non-invasively improve the appearance of fat and cellulite.
- Most of the current laser devices do not target fat or adipocytes specifically. Rather, they heat the deep dermis and the diffusion of heat away from the deep dermis may have some effect on adipocytes.
- Laser devices that heat the dermis may lead to collagen remodeling and improve the appearance of cellulite.

Indications

- Zerona (Erchonia, McKinney, TX) is a low level laser device incorporating multiple divergent beams of 635 nm wavelength. It is FDA cleared for the reduction of circumference of the hips, waist, and thighs [5].
- The TriActive device (Cynosure Inc, Bedford, MA) combines deep tissue massage with a low intensity diode laser (808 nm). It is FDA cleared for the treatment of cellulite [6].
- The VelaShape (Syneron Medical Ltd, Irvine, CA) device, as discussed in the radiofrequency section, combine physical manipulation, bipolar RF energy, and broadband infrared light (700–2,000 nm). It is FDA cleared for the temporary reduction in the appearance of cellulite, and for temporary reduction of thigh circumferences [6].
- The SmoothShapes device (Eleme Medical, Merrimack, NH), combines two different wavelengths of laser (a 915 nm diode wavelength to liquefy fat and a 650 nm wavelength to improve fat membrane permeability) as

well as physical manipulation. It is FDA cleared for temporary reduction in the appearance of cellulite [7].

Contraindications

- These devices should not be utilized in pregnant or breastfeeding patients.
- These devices should not be used in patients with a history of scarring from laser treatments.

Procedural Technique

- The exact technique for the treatment depends on the specific technology.
- The Zerona low level light treatment does not require physical manipulation of the area, as the beams are placed away from the patient's body. Clinically significant reduction in waist circumference and cosmetic improvement has been observed following a series of eight treatments [5].
- Laser devices incorporating physical manipulation of the tissue require passing a handpiece over the treatment area.
- Multiple treatments (6–8 treatments) are typically necessary to achieve clinical improvement. Treatments range from 20 to 40 min typically.
- The improvement, particularly in the appearance of cellulite, may be temporary and require ongoing treatments.

Complications

- Bruising and edema have been reported in laser devices incorporating vacuum and physical manipulation of the tissue.

Prevention and Management of Complications

- Avoid use in patients with history of scarring from previous laser treatments.

- If patient has a history of easy bruising, consider avoiding laser treatments which incorporate a vacuum or physical manipulation modality.
- May not be an ideal treatment option for patients who do not wish to undergo a series of treatments.

Cryolipolysis

- Cold exposure has long been known to affect adipocytes, affectionately known as popsicle panniculits in children.
- Cryolipolysis or CoolSculpting (Zeltiq Aesthetics, Pleasanton, CA) utilizes controlled cold exposure "energy extraction" to selectively cool fat and cause adipocyte apoptosis [8].

Indications

- Cryolipolysis is FDA cleared for non-invasive reduction of fat.

Contraindications

- Obese patients.
- Pregnant patients.

Procedural Technique

- Typical treatment areas for cryolipolysis include: the flank "love handle", the back "back fat pads" or the abdomen "muffin top."
- A coupling sheet is initially placed on the treatment area. The CoolSculpting device is then applied to the area.
- A vacuum is generated to pull the treatment area up into the space between the two cooling plates. New applicators have recently been developed which allow the treatment to be performed on "flat" fat that does not require the treatment area to be elevated by the vacuum device. The treatment cycle and cold exposure then begins.

- A treatment cycle lasts approximately 60 min, at the conclusion of which the device automatically terminates the treatment.
- At the conclusion of the treatment, the physician may then massage the area gently to break up any crystallized adipocytes and lead to a more efficacious treatment.
- The clinical improvement then gradually occurs over the next 2–4 months.

Complications

- Immediately following the treatment, the skin appears cool, firm and erythematous.
- Bruising, as well as transient altered sensation, numbness or even pain can occur.
- Very rarely, there can be a pain syndrome characterized by significant pain requiring analgesics [8].
- Recently there have been observations of paradoxical fat hypertrophy; this is thought to be extremely rare and the pathogenesis has not been determined.

Prevention and Management of Complications

- Avoid use in patients with history of pain syndromes.
- Analgesics may be required for severe pain syndromes.

Future Directions

- The field of non-invasive body contouring and fat reduction is new and rapidly expanding.
- Well done, blinded, placebo controlled trials are necessary to establish the exact efficacy of many of these devices.
- Head to head trials would be ideal to determine the safest and most efficacious technologies. Unfortunately, these have currently not yet been performed with most of the devices.
- Lasers with new specific wavelengths targeting adipocytes are being developed, and may represent the next step in fat treatment.

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Chapter 24
Lasers for Ethnic Skin

Heather Woolery-Lloyd, Davina Tolbert, and Neh Onumah

Abstract The use of lasers in skin of color continues to grow with advancing technologies. At the same time, patients with skin of color often require special consideration when receiving laser, light and energy based procedures. These patients are especially vulnerable because any significant trauma can cause temporary or permanent pigmentary changes and scarring. For the clinician, laser procedures in patients with

H. Woolery-Lloyd, MD (✉)
Department of Dermatology and Cutaneous Surgery,
University of Miami, Miller School of Medicine,
1295 NW 14th Street, South Building, Suite K,
Miami, FL 33135, USA
e-mail: woolerylloyd@yahoo.com

D. Tolbert, MPH
Skin of All Color, LLC, 339 Princeton-Hightstown Road,
East Windsor, NJ 08512, USA

Public Health Sciences, University of Miami,
1120 NW 14th Street, CRB 1027, Miami, FL 33126, USA
e-mail: dvtolbert@gmail.com

N. Onumah, MD
Skin of All Color, LLC,
339 Princeton-Hightstown Road, East Windsor, NJ 08512, USA
e-mail: nehonumah@yahoo.com

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skin of color can therefore be challenging. Due to enhanced technology and recent advances, the demand to seek laser procedures to address these patients' cosmetic concerns has reached new heights. Patients with skin of color have various motivations and goals including attaining an even skin tone, removing unwanted hair, and/or reducing the signs of aging. The American Society of Plastic and Reconstructive Surgery's annual survey revealed that cosmetic procedures among minority patients increased from 12 % of all cosmetically treated patients in 1992 to 21 % in 2012. Close to 15 million aesthetic procedures were performed in the US in 2012. Of these patients, 7 % were African American, 8 % were Hispanic, 5 % were Asian, and 2 % were other non-Caucasian.

Keywords Lasers • Ethnic skin • Skin of color • Light devices • Darker skin types

Introduction

The use of lasers in skin of color continues to grow with advancing technologies. At the same time, patients with skin of color often require special consideration when receiving laser, light and energy based procedures. These patients are especially vulnerable because any significant trauma can cause temporary or permanent pigmentary changes and scarring. For the clinician, laser procedures in patients with skin of color can therefore be challenging. Due to enhanced technology and recent advances, the demand to seek laser procedures to address these patients' cosmetic concerns has reached new heights. Patients with skin of color have various motivations and goals including attaining an even skin tone, removing unwanted hair, and/or reducing the signs of aging. The American Society of Plastic and Reconstructive Surgery's annual survey revealed that cosmetic procedures among skin of color patients increased from 12 % of all cosmetically treated patients in 1992 to 21 % in 2012. Close to 15 million aesthetic procedures were performed in the US in 2012. Of these patients, 7 % were African American, 8 %

were Hispanic, 5 % were Asian, and 2 % were other non-Caucasian [1, 2].

Laser Assisted Hair Reduction

Introduction

Laser assisted hair reduction is one of the most common cosmetic procedures performed in patients with ethnic skin. It is one of the safest laser procedures in ethnic skin when the correct device and settings are utilized. The two lasers that have been studied extensively in ethnic skin are the diode laser and the Nd:YAG. The diode laser can be safely used in Skin Type IV and some patients with Skin Type V. The Nd:YAG laser can be safely used in Skin Types IV, V, and VI. The long-pulsed Nd:YAG is the safest hair reduction laser for ethnic skin [3, 4].

Indications

- Unwanted hair on face and body

Contraindications

- Significant recent sun exposure
- Recently tanned skin
- Skin with self-tanner, tattoos, permanent makeup in affected areas

Procedural Technique

Pre-op

- Shave hair prior to treatment to reduce excessive heat and smoke during procedure

- All laser devices require a cooling system to cool the epidermis (contact cooling or cryogen cooling)
- Advise patient to avoid plucking and waxing 2–4 weeks before treatment
- Pretreatment with hydroquinone is not necessary but hydroquinone can be used to treat post inflammatory hyperpigmentation that occurs from chronic plucking

Procedural

- Utilize close fitting goggles when treating hair on the face
- Avoid double pulsing
- Utilize 20 % overlap

Post-op

- Cooling is essential in ethnic skin and ice packs should be applied after all treatments to minimize side effects
- Avoid waxing and plucking between treatments
- Avoid excessive sun exposure
- Wear sunscreen

Complications

- Dyschromia is rare due to the exceptional safety profile of laser assisted hair reduction in skin of color with the long pulsed Nd:YAG [5]
- Hyper and hypopigmentation may occur infrequently with the diode laser at higher settings [5]
- Paradoxical hypertrichosis [6]

Prevention and Management of Complications

- Cooling during the procedure is mandatory
- Post cooling with ice packs can prevent most complications

- Using longer pulse widths delivers energy more slowly to avoid excessive heat in the epidermis
- Increase energies in small increments at successive visits
- Ask about any persistent erythema from previous treatment. If there was persistent erythema do not increase settings at future visits
- In Skin Type VI, applying ice packs during the procedure can minimize pain due to cooling of the epidermis

Intense Pulsed Light

Introduction

Intense Pulsed Light (IPL) can be safely performed in ethnic skin. It has been studied in Asian skin and is limited to carefully selected patients with Skin Type IV. The risk of significant and permanent pigmentary changes is much higher in Skin Types V and VI. Studies have demonstrated the efficacy of IPL in Asian patients with Skin Type IV [7].

Indications

- Photorejuvenation [7]
- IPL combined with topical 5-aminolevulinic acid (ALA-PDT) for improvement in inflammatory acne on the skin [8]
- Unwanted hair

Contraindications

- Skin Types V and VI
- Photosensitivity
- Active Dermatosis

Procedural Technique/Considerations

Pre-op

- Strict sun avoidance in ethnic skin is essential to avoid unwanted side effects when treating patients with IPL
- Pretreatment with hydroquinone may be helpful to minimize side effects

Procedural

- Apply a cold gel to minimize excessive epidermal heating
- Utilize close fitting goggles when treating the face
- Utilize minimal overlap
- Immediate darkening of epidermal pigment can be observed

Post-op

- Advise patient to expect darkening of lentigos and subsequent peeling over 7–10 days
- Strict sun avoidance
- Sun protection is especially important with IPL in Skin Type IV

Complications

- Hyperpigmentation
- Hypopigmentation is difficult to treat and can occur in darker skin types
- Transient edema
- Transient erythema

Prevention and Management of Complications

- Topical steroid cream and an oral anti-inflammatory agent may be administered for significant edema and erythema
- Careful patient selection is essential to minimize side effects

Light Emitting Diode

Introduction

Light Emitting Diodes (LEDs) offer advancement in visible spectrum, monochromatic light therapy for photoaged skin. Typically, LEDs in devices are arrayed in panels with each LED emitting visible light in a ±10–20 nm band around the dominant emitted wavelength. Energy output is less than 25 W, representing a fluence of about 0.1 J/cm^2. These devices act by targeting stimulation of fibroblast mitochondrial metabolic activity. In addition concomitant up-regulation of procollagen and down-regulation of matrix metalloproteinase I have been demonstrated [9]. Although there are limited studies on LED in ethnic skin, based on the mechanism of action, these devices should be and are generally considered safe in skin of color.

Indications

- Photorejuvenation
- Acne [10]

Contraindications

- Photo-allergic

Procedural Technique/Considerations

Pre-op

- Cleanse skin
- Apply ALA if treating acne

Procedural

- Treatment times vary (average time 20 min)

Post-op

- Strict sun avoidance if treated with ALA

Complications

- Complications are rare when blue or red light are used alone
- There is a risk of hyperpigmentation when blue light is combined with ALA for acne in Skin Types V and VI

Prevention and Management of Complications

- Strict sun avoidance after blue light/ALA treatments

Infrared Skin Tightening

Introduction

Infrared Tightening devices are designed to thermally induce immediate collagen contraction (with water as the target chromophore), followed by the induction of collagen remodeling and the synthesis of new collagen. The procedure is associated with minimal downtime and is safe to use on all skin types [11]. Although, an immediate tightening effect is achieved; the full effect is observed 6 months after the last treatment. Liberal use of gel appears to improve patient tolerability. In all skin types, multiple sessions (3–5) are needed for best results. Response rates are variable and can be influenced by patient selection [12].

Indications

- Skin Tightening [13, 14]
- Safe in Skin Types IV, V, VI

Contraindications

- Active dermatosis
- Other factors that might inhibit or compromise healing and dermal collagen remodeling

Procedural Technique

Pre-op

- Cleanse skin
- Apply cold gel

Procedural

- Observe for significant erythema and edema
- Adjust energy according to patient pain level
- Use caution over bony prominences

Post-op

- Avoid tight abrasive clothing immediately after treatment
- Repeat treatments at 4–6 week intervals

Complications

- Minimal pain and edema
- Blistering is rare but has been reported in cases where minimal gel was used

Prevention and Management of Complications

- Reapply gel throughout procedure to minimize pain and improve tolerance

Ultrasound Tightening

Introduction

Intense ultrasound (IUS) is an energy that can propagate through tissue up to several millimeters. Ultrasound waves induce a vibration in the molecules of a target tissue during propagation, and the thermoviscous losses in the medium lead to tissue heating. When the beam is directed in a firm focus of the skin tissue at a certain depth, it produces a thermal coagulative necrosis, leaving the superficial layers unaffected. This type of intense ultrasound device has been developed specifically for treating facial soft tissues and targeting the superficial musculoaponeurotic system (SMAS), a continuous fibrous network composed of collagen and elastic fibers that envelopes the muscles of facial expression and extends superficially to connect with the dermis [15, 16].

Indications

- Skin Tightening

Contraindications

- Active dermatosis
- Other factors that might inhibit or compromise healing and dermal collagen remodeling
- Metal prosthesis in the treated area

Procedural Technique

Pre-op

- Cleanse skin
- Apply cold gel

Procedural

- Observe for significant erythema and edema
- Use caution over bony prominences

Post-op

- Avoid tight abrasive clothing immediately after treatment
- One repeat treatment after 4–6 weeks is sometimes indicated

Complications

- Mild Erythema
- Persistent edema is rare but can last several weeks

Prevention and Management of Complications

- Reapply gel throughout procedure to minimize pain and improve tolerance

Future Directions

In summary, there is an increasing demand for the use of lasers in patients with skin of color. Given the recent advances in technology, the array of lasers that are safe for use in darker skin types continues to grow. Laser hair removal, non-ablative lasers and lights, and skin tightening are just a few applications that are safe and effective. At the same time, treating pigmentary disorders with lasers remains a challenge. As the laser armamentarium continues to grow, it is essential that clinicians are well informed on risks, benefits, technique and patient selection. It is also important to choose devices that have been studied and have demonstrated safety in this population. With this approach clinicians can achieve the best possible clinical outcome with the least unwanted side effects when utilizing lasers in patients with skin of color.

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Chapter 25
Reflectance Confocal Microscopy Enables the Non-invasive Diagnosis and Management of Skin Tumors

Salvador González, Concepción Parrado, and Jesús Cuevas

Abstract Reflectance-mode confocal microscopy (RCM) is a novel, laser-based technique that enables a non-invasive diagnosis of the skin. Despite a relatively lack of depth, its use is taking off due to its ease of use, reproducibility and lack of invasiveness. Good correlation with the gold standard in diagnosis of skin diseases, which is conventional histology, validates the technique. Recent reports have focused on this

S. González, MD, PhD (✉)
Dermatology Service, Ramon y Cajal Hospital (Consultant),
Memorial Sloan-Kettering Cancer Center,
160 E 53rd Street, New York 10022, NY, USA
e-mail: gonzals6@mskcc.org

C. Parrado, MD, PhD
Department of Histology and Pathology,
University of Málaga, Campus de Teatinos,
Malaga 29071, Spain
e-mail: cparrado@uma.es

J. Cuevas, MD, PhD
Pathology Department, Guadalajara University Hospital,
University of Alcalá, Alcalá de Henares (Madrid) 28871, Spain
e-mail: jcuevas@sescam.org

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crucial aspect for different pathologies as well as non-diseased, physiological skin. Particular attention has been pointed to the diagnosis of different types of cancer, e.g. squamous and basal cell carcinoma and melanoma. In vivo assays have revealed that RCM displays good sensitivity and accuracy for the diagnosis of BCC and melanoma. Furthermore, RCM has also been used to delimit the edges of suspected tumors before surgery and also to image the response of the skin to different treatments. This review summarizes the current state of the art in terms of available RCM units, diagnosis both in vivo and ex vivo and current applications of the technique.

Keywords Reflectance-mode confocal microscopy • Non-invasive imaging • In-vivo microscopy • Skin Tumors • High-esolution monitoring

Introduction

A major goal in dermatology is the non-invasive assessment of different types of skin lesions, e.g. psoriasis, dermatitis, nevi, etc. This is also important in the diagnosis and procedural decisions regarding skin cancer. In the latter, it is crucial to determine unequivocally the margins of the lesion before surgery. An important additional benefit of non-invasive examination is that it enables efficient, repetitive assessment, which helps establishing responsiveness to treatment or post-surgical evolution.

Non-invasive techniques for observation of the skin can be divided into sound-based, e.g. ultrasound and echo-based scanning; and image-based, e.g. magnetic resonance and optical coherence tomography, dermoscopy, and confocal microscopy. Both approaches share the same limitation, which is penetration beyond the upper layers of the skin, i.e. the epidermis and superficial layers of the dermis.

Many reviews have addressed some of these techniques in detail, including their application in dermatology [1–5]. Here,

we summarize the state-of-the-art of reflectance confocal microscopy (RCM). RCM derives from a very simple premise, which is that, when illuminated with infra-red photons, some skin structures, particularly those containing melanin, appear as bright structures, whereas others, such as normal epithelial nuclei, are dark. Stacks of images from the skin are collected using a handheld lens system. Therefore, this approach enables real-time imaging of the skin based on contrast differences, which is an excellent method to determine abnormalities and changes in the morphological makeup of the skin. In addition, its non-invasive nature makes the exploration conveniently quick and pain-free, and it enables repetitive examinations of the same area to monitor changes over time. Recent years have witnessed a manifold increase in the use of this technique by several dermatology groups vested in clinical and basic research, which is rapidly enabling the establishment of tight correlations between the current gold standard in diagnosis of skin disease, i.e. biopsy- and staining-based histology, and this microscopy modality, particularly in cancer.

The Technological Foundation of Reflectance Confocal Microscopy

Confocal scanning microscopy was originally described by Marvin Minsky the mid-fifties [6], but its full in vivo use required many more years of development. Tandem scanning confocal microscopy appeared in the 1980s, and one of its major applications has been to obtain serial tissue images in vivo [7–9]. Later, it was employed to obtain high resolution, in vivo images of human skin [10], spearheading the development and application of microscopy-based approaches in the diagnosis of different skin maladies.

A particular application of confocal microscopy to the study of the skin is reflectance confocal microscopy (RCM). In RCM, a laser beam is focused on the sample, which is normally translucent, i.e. it permits a certain degree of light to

pass through. Due to the different absorption properties of the skin "objects" (cells and extracellular matrix), some absorb the laser photons, whereas others reflect them back. The reflected photons are led into a mechanical pinhole that discards out-of-focus photons (this is the general principle of confocal microscopy). Line scanning of the laser beam and photon collection and translation into an electrical signal using a photomultiplier enables the reconstruction of the sample as images of the planes perpendicular to the laser (sectioning).

Photon reflection is due to two major causes: one is the intrinsic refractive index variability of the tissue; the other is size of the skin objects that are close to the wavelength of the photons from the light source, e.g., melanosomes [11].

Usually, RCM lasers generate photons of the IR range (800–1,064 nm, with a maximum at ~830 nm). Since the aim of this approach is to image in a non-invasive manner, low power (<30 mW) is required. In addition, photons with these properties are well-suited for skin imaging as they bear high transmittance [12], which in turn decreases lateral resolution. A balance has been struck with conditions that enable a depth <250 μm, which is still enough to obtain good quality images of the upper reticular dermis [11].

Technically, the laser beam passes through a beam splitter on its way to the sample and traverses a dual function scanning/focusing lens mounted on a contact device. This is a rather elaborate setup that aims to decrease the effect of sample motion, which is unavoidable since the images are obtained from live patients. Its major function, though, is to minimize the sudden shift in refractive index between the lens and the sample (skin) that causes spherical aberrations. For this purpose, the contact device contains a liquid reservoir that surrounds the lens. It is filled with immersion oil with a refractive index of 1.33/1.34, which is the refractive index of the skin. In practical terms, most RCM devices mount a 30× lens with a numerical aperture ~0.9 that results in a XY resolution of ~1 μm and a Z-resolution ~3–5 μm [11].

Allowing for some discontinuity due to the relatively low Z resolution, the images obtained (60–80 images in Z) may be mounted to generate three-dimensional maps, which provides unprecedented visualization capability in vivo.

From the Workbench to the Bedside: Clinical Use of RCM in Dermatology

The RCM applications bearing more promise in dermatology are diagnosis, treatment follow-up and pre-surgical demarcation of pathological borders. These are outlined in the following sections.

Diagnosis

In order to use RCM for pathological diagnosis, the baseline, i.e. the appearance of normal skin in this technique, needs to be established. The following paragraphs describe the main features of normal skin as visualized using RCM. It is important to underline that normal skin varies in appearance by RCM depending on skin phototype and tanning level, age and anatomic location [13]. In general, darker skin tones appear brighter by RCM due to increased pigmentation, which means more reflecting skin structures.

The most external layer, the stratum corneum, appears as groups of large, bright (10–30 μm thick) de-nucleated polygonal corneocytes separated by dark folds. The next layer is the stratum granulosum (25–35 μm in thickness), which contains 2–4 layers of cells with dark central round-shaped nuclei and brightly granulated cytoplasms. The next layer is the stratum spinosum, which is 15–25 μm wide and mainly appears as cells arranged in a honeycomb pattern. Next is the basal layer (7–12 μm thick). Basal cells contain large melanin aggregates that appear as bright objects in RCM. Also, single bright ovals are melanocytes and are melanin-containing keratinocytes [14].

The dermo-epidermal junction (DEJ) appears as a collection of rings of bright structures clustered around dark cores, which correspond to dermal papillae. Blood flow at the centre of the papillae can be seen as motion in consecutive time-lapse series [11]. Next are the outer layers of the dermis, specifically the papillary dermis. RCM reveals a web of fibres containing central thin blood vessels and thick collagen elastin bundles. Eccrine ducts are located at this layer and are visualized as bright rings with a dark core that meander across the thickness of this layer and entering the upper epidermal layers. Also, hair shafts are also at this layer. They look like dark ovals surrounded by bright cells delineating their perimeter.

Once we have established the general features of normal skin as seen using RCM, we will now describe the documented use of RCM in diagnosis of different skin tumours.

Non-pigmented, Non-melanocytic Skin Tumours

RCM has been used to satisfactorily diagnose several types of skin diseases implicating either abnormal growth (neoplasm) or architectural organization.

Actinic Keratoses

Actinic keratoses (AKs) are frequent pre-malignant skin disorders that often precede squamous cell carcinoma (SCC). At epidermal level, RCM reveals superficial disruption of stratum corneum, irregular hyperkeratosis with parakeratosis. Keratinocytes, meanly at the spinosum layer, are abnormally shaped with large nuclei and disorganized [15, 16] displaying an atypical honeycombed pattern (Fig. 25.1a, b). Visualization of dermal compartment by RCM reveals round blood vessels (Fig. 25.1c) and thick, bright bundles consistent with sun-induced elastosis. Using RCM, it is difficult to distinguish hypertrophic AK from established in situ SCC, although subtle changes can be observed to identify novel lesions [17, 18].

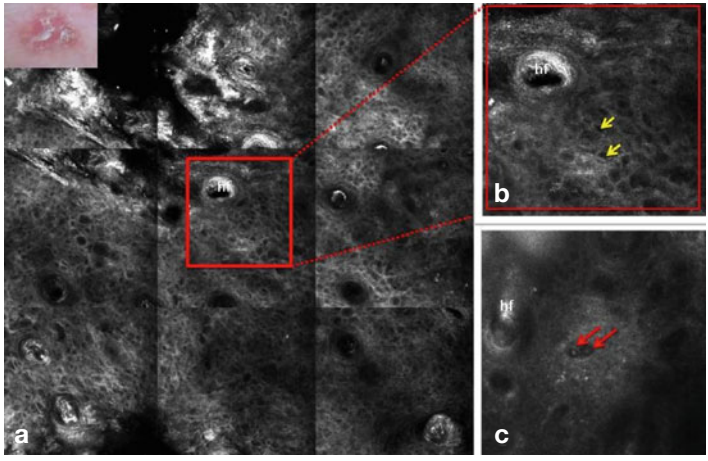

FIGURE 25.1 Actinic keratosis. Dermoscopy reveals the presence of scales and other non-specific features. (**a**) RCM mosaic (1.5 × 1.5 mm) of the stratum spinosum that reveals numerous pilosebaceous units (*hf*) with atypical honeycombed pattern. (**b**) Higher magnification of the skin area (0.3 × 0.3 mm) located with in the red square seen in the mosaic a. It reveals architectural disarray with an atypical honeycombed pattern. Atypical keratinocytes are seen as polygonal cells of different shapes and sizes with central dark nuclei and bright cytoplasms (*yellow arrows*). (**c**) RCM image (0.3 × 0.3 mm) of the dermoepidermal junction level from exactly the same area (image **b**) shows dilated round blood vessels (*red arrows*)

Squamous Cell Carcinoma (SCC)

AK often evolves into squamous cell carcinoma. RCM reveals severe dysplastic, pleomorphic keratinocytes and architecturally, disorganized, atypical honeycombed, or even disarranged pattern of the stratum spinosum as well as the stratum granulosum. At a dermal level, other abnormal structures can be observed, e.g. neovascularisation with blood vessels traversing through the dermal papillae perpendicular to the skin surface and keratin deposits seen as intradermal bright structures [15, 19]. RCM is not ideally suited for diagnosis of SCC, since the architectural distortion that affects

the DEJ makes it quite difficult to explore it which is fundamental to distinguish superficially invasive SCC from in situ SCC (Bowen's disease) [20].

Basal Cell Carcinoma

Basal Cell Carcinomas (BCCs) are the most common skin cancers, and RCM has been extensively used to visualize their main features; these include groups ("islands") of similarly shaped, tightly packed aggregates of elongated cancer (basaloid) cells with nuclei oriented along the longitudinal axis [21]. These basaloid islands display peripheral palisading and lobulated shape (Fig. 25.2). Also, epidermal layers overlaying de tumours may display atypical honeycombed pattern (Fig. 25.2a) as a consequence of actinic damage or reactive to the tumour. Inflammation is also detected by strong motion and blood vessels of enlarged diameter. Since BCC are well-characterized, a collection of five morphological criteria has been established: (i) actinic damage of the epidermis above the lesion; (ii) areas of bright cancer cells with elongated basaloid nuclei; (iii) polarized nuclei forming a "palisade" (Fig. 25.2c); (iv) increased dermal vasculature with enlarged blood vessels (Fig. 25.2b) and visible leukocyte motion; (v) presence of inflammatory infiltrate [22]. Clear identification of two or more of these five RCM features in a sample has 100 % sensitivity, where four or more of these have a specificity of 95.7 % and a sensitivity of 82.9 % [22], constituting an excellent asset for BCC diagnosis. A recent study has described the use of automated algorithms that take into account these parameters, with excellent specificity and sensitivity [23].

Mycosis Fungoides

Preliminary use of RCM to diagnose mycosis fungoides (MF) reveals differences in terms of the type of MF. In patch- type MF, RCM reveals dim papillary rings at the DEJ, which correspond to lymphocyte infiltrates into the basal cell layer

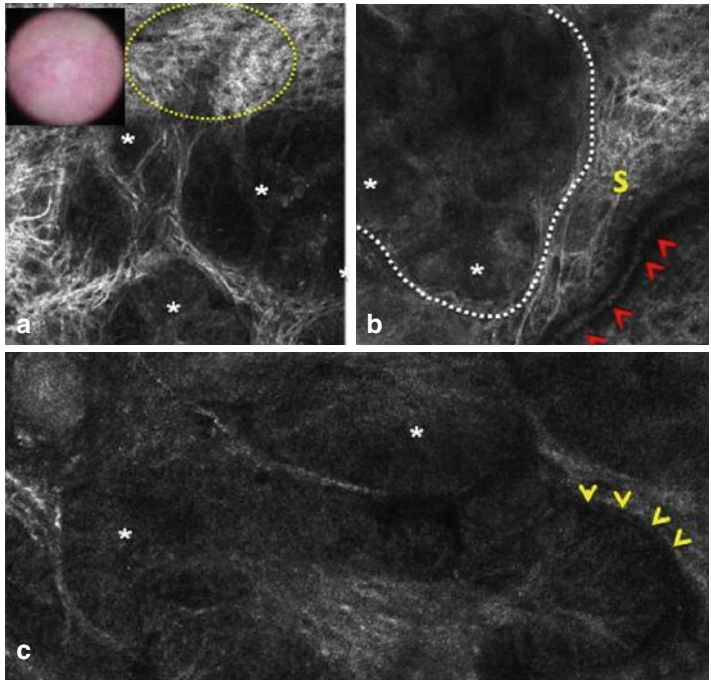

FIGURE 25.2 Basal Cell Carcinoma. Dermoscopy reveals a pearly papule with arborizing vessels and a shiny surface. (**a**) RCM image (0.5×0.5 mm) shows several low-refractility cellular accumulations compared to the surrounding stroma, forming "dark silhouettes" that correspond to tumor islands (*asterisks*) and in the superior area discrete atypical honeycombed epidermal pattern (*dashed yellow line*). (**b**) RCM image (0.5×0.5 mm) shows several low-refractility cellular accumulations (*white dashed line*) compared to the surrounding stroma (*s*), forming "dark silhouettes" (*asterisks*) and elongated blood vessels (*red arrowheads*). (**c**) RCM image (0.25×0.5 mm) shows "dark silhouettes" (*asterisks*) with peripheral palisading (*yellow arrowheads*)

or melanocyte apoptosis. In plaque- type MF, dim cells appear in the stratum spinosum, corresponding to infiltrating leukocytes. Pautrier microabscesses are visualized as dark,

"empty" spaces in the epidermis. Finally, tumor-type MF display similar findings to plaque-type, but obvious lack of Pautrier microabscess-like "empty" spaces [24, 25]

Pigmented, Non-melanocytic Skin Tumours

Seborrheic Keratosis

Seborrheic Keratosis (SK) is a frequent benign hyperplasia. It often appears as brown plaques that evolve into dark, wart-looking lesions. RCM visualizes it as bright, tortuous structures with dark spaces showing occasional bright clusters, which correspond to keratin deposits. The stratum spinosum displays an accumulation of brighter-than-usual basaloid cells. In heavily pigmented SK, the stratum spinosum is arranged following a cobblestone pattern formed by bright, polygonal cells that are pigmented keratinocytes. The DEJ appears elongated and distorted (Fig. 25.3), often sided by bright keratinocytes. Melanophages often appear inside the papillary rings of the dermis.

Dermatofibroma

Dermatofibroma (DF) is a benign histiocytic tumor, more common in young females out of childhood. RCM reveals a roughly normal epidermis. The dermis in the central area of the dermatofibroma is fibrotic (Fig. 25.4) as revealed by bright collagen bundles [26]. The depth of the lesion, including spindly fibroblasts, histiocytes and sclerotic stroma in the reticular dermis makes RCM a less-than-ideal tool for its diagnosis.

Pigmented Basal Cell Carcinoma

Pigmented BCC is a subtype of BCC, which occasionally may be confused with melanoma [27, 28]. It is important for its diagnosis that its RCM features are those of BCC, not melanoma. Melanin distribution is heterogeneous including melanocytes within the tumour islands and melanophages in the papillary dermis.

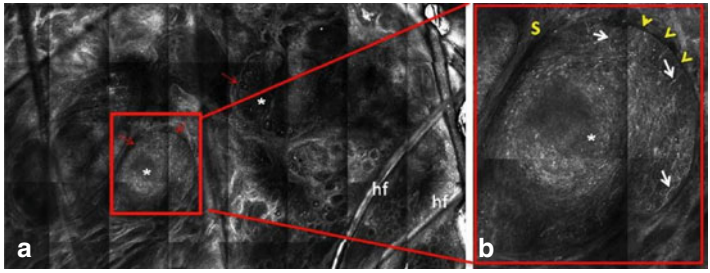

FIGURE 25.3 Spotty pigmented basal cell carcinoma. Dermoscopy reveals the absence of a pigmented network and presence of blue-gray globules. (**a**) RCM mosaic (2 × 4 mm) at the level of the upper dermis revealing tumor nodules (*asterisks*) of weak to moderate refractility. Within tumor nodules, dark stroma delineates individual tumor lobules; and occasionally, peritumoral cleft-like dark spaces are seen (*red arrow*). Of note, hairfollicles (hf) are also seen. (**b**) RCM submosaic (0.75 × 0.75 mm) of the area with in the red square located in previous one (mosaic a) shows a defined lobulated tumor island (*asterisk*) speckled with brightly refractile dots, granular structures and dendrites (*White arrows*). Subtle peripheral palisading of nuclei (*yellow arrowheads*), extensive peritumoral dark cleft-like spaces, and refractile surrounding stroma (*s*) are seen

Melanocytic Tumours

Melanocytic Nevi

Nevi appear as clusters of bright, round cells with central nuclei that correspond to nevomelanocytes [14, 29]. In benign cases, the epidermis is brighter than usual, but no architectural disarray is observed except occasional bright cells, which correspond to spare nevomelanocytes. Junctional nevi display single melanocyte proliferation with single refractile polygonal cells outlining the DEJ revealing a ringed/reticulated pattern (Fig. 25.5). It is not infrequent to observe nests located at the crestae's tip showing-up a meshwork pattern as a consequence of junctional enlargement between the papillae. No atypical melanocytes are seen. Intradermal nevi show groups ("nests") of nevomelanocytes revealing a "clod" pattern. Dermal nesting may appear as compact dense or dense (Fig. 25.6) and sparse nets [30, 31]. Combination of

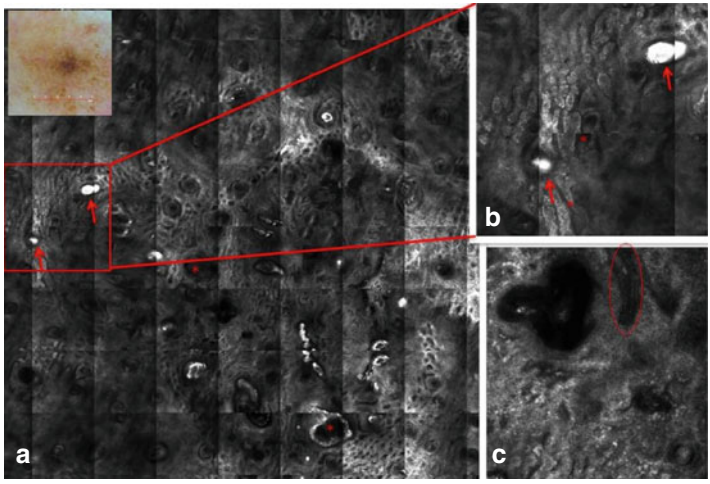

FIGURE 25.4 Seborrheic Keratoses. Dermoscopy reveals a star-shaped lesion with sharply circumscribed and moth-eaten edges, also containing a central hyperpigmented area with millium-like cists. (**a**) RCM mosaic (5.5 × 5.5 mm) at the level of the DEJ shows a demarcated lesion with dark rounded areas (*red asterisks*) corre- sponding to comedo-like openings and well-defined, intensely bright, rounded areas (*red arrows*) corresponding to millium cysts. Red square outlines the confocal image that is magnified in image. (**b**) RCM image (0.5 × 0.5 mm) within the mosaic A displaying irregular dermal papillae in size and shape with curved, invaginated borders (*asterisks*). Millium cysts (*red arrows*) are also observed. (**c**) RCM image (0.5 × 0.5 mm) revealing a typical hairpin vessel (*red dashed line*)

junctional (ringed, meshwork) (Figs. 25.7 and 25.8) and intradermal (clod) (Fig. 25.6) pattern is frequent, showing a presence central of clods (dermal nests) in the majority of nevi.

Dysplastic Nevi

Dysplastic nevi at the DEJ appear distorted. With RCM, interesting aspects such as bridging [32] and atypical melanocytes [14, 29] can be detected. Atypical melanocytes ("dysplastic") appear as dim, large cells with eccentric nuclei [30] that, despite their epithelial morphology, display dendritic projections; accumulations of cell-free melanin, often referred to as "melanin dust" can be

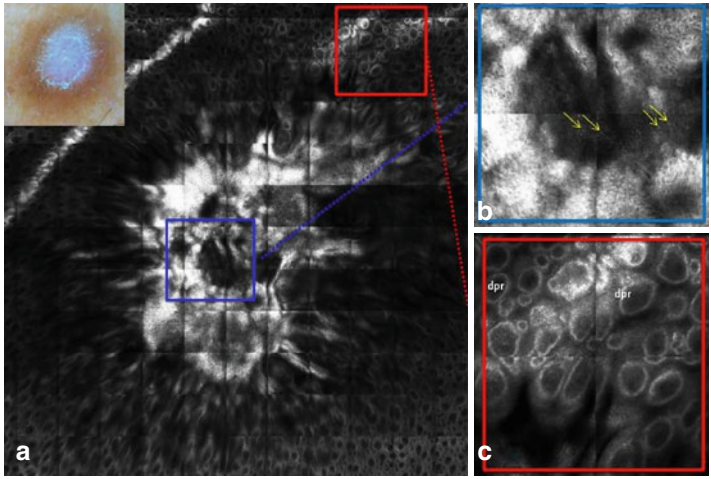

FIGURE 25.5 Dermatofibroma. Dermoscopy shows a depigmented scar of xerotic appearance with surrounding peripheral pigmented network and brown pigmentation. (**a**) RCM mosaic (6×6 mm) of the DEJ reveals increased density of bright dermal papillary rings in the periphery of the lesion. The central portion shows homogeneous and dense brightness. Red square outlines the confocal image that is magnified in image. (**b**) RCM submosaic (1×1 mm) of the central area displays presence of parakeratotic corneocytes (*yellow arrows*), possibly due to xerotic skin. (**c**) RCM submosaic (1×1 mm) of the DEJ reveals the basal layer displaying a cobblestoned pattern, together with increased density of the dermal papillary rings (*dpr*)

seen as bright specks by RCM. To draw a line between severe dysplastic nevus and early melanoma is difficult as it occurs in dermatopathology when evaluating these challenging lesions showing very low interobserver agreement [33].

Melanoma

Melanoma is a term that encompasses a number of cancers bearing in common a malignant proliferation of melanocytes. In general, prognosis correlates with the depth of invasion: melanoma with deeper roots have fewer chances of long-term survival due to metastasis. Superficial melanomas constitute ~70 % of melanomas. This type begins as an abnormal proliferation of

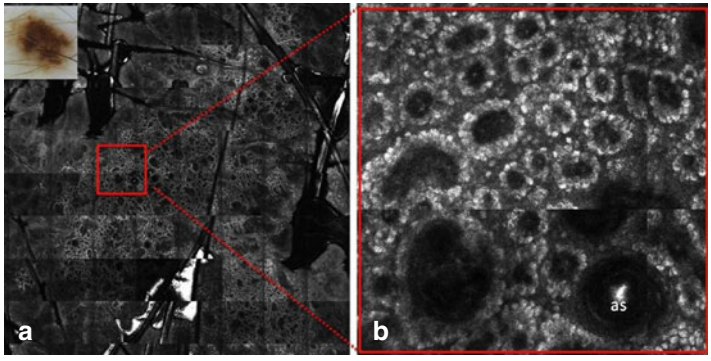

FIGURE 25.6 Common melanocytic nevus. Dermoscopy reveals dermal melanocytic nevus with peripheral reticulation. (**a**) RCM mosaic (4×4 mm) at the dermoepidermal junction level displays ringed pattern. Red square outlines the confocal image that is magnified in image. (**b**) RCM image (0.6×0.6 mm) reveals ringed pattern showing bright rings and annexial structures (*as*)

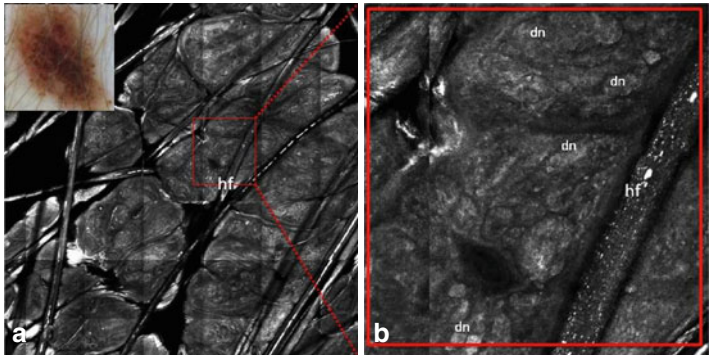

FIGURE 25.7 Intradermal nevus. Dermoscopy reveals a globular pattern. (**a**) RCM mosaic (3×3 mm) is characterized by the presence of an overall clod pattern. Of note, hair follicles (hf) are also seen. Red square outlines the confocal image that is magnified in image. (**b**) Detailed view of a RCM image (0.5×0.5 mm) within the mosaic A reveals that clod pattern is constituted by dense nests (*dn*)

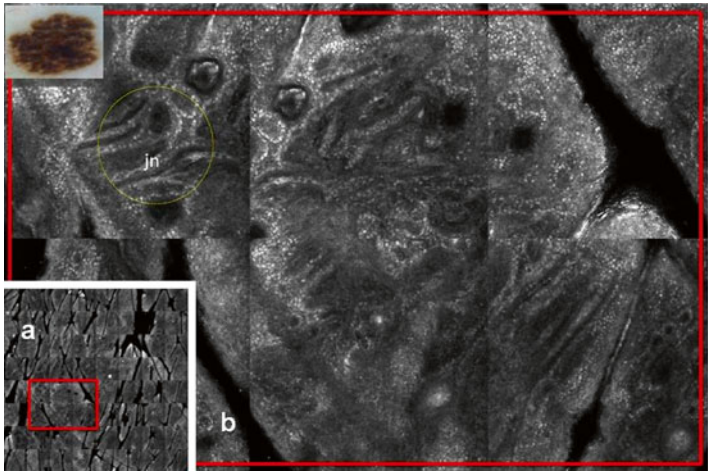

FIGURE 25.8 Compound nevus with mild displasia. Dermoscopy reveals a central globular pattern and reticular pattern at the periphery. (**a**) RCM mosaic (4.5×4.5 mm) showing a irregular ringed pattern due to irregular junctional nests. Red square outlines the confocal image that is magnified in image. (**b**) RCM image (0.5 × 0.5 mm) from the mosaic A reveals the presence of meshwork architecture (*yellow dashed line*) due to the presence of enlarged junctional nests (*jn*)

melanocytes in the epidermis. These cells invade the dermis and penetrate deeper, eventually disseminating through the bloodstream. ~15 % of melanomas are of the more aggressive nodular variety. ~10 % of diagnosis corresponds to lentigo maligna, whereas ~5 % are acral lentiginous melanoma [34, 35]. A non-pigmented variant, amelanotic (or amelanocytic) melanoma, also exist.

RCM can be used to distinguish between benign nevi and melanoma, and an automated, observer-independent score-dependent algorithm has been developed [36] that later was blindly tested [37]. It consists of a two-tiered system with two major (2 points) and four minor (1 point) criteria. Lesions with a total score ≥3 were very sensitive (97 %), whereas specificity remains to be improved (when score ≥3, specificity = 72 %) [36]. Major criteria are: (i) visualization of non-edged papillae (Fig. 25.9a, c); (ii) cytological atypia (Fig. 25.9a, c). Minor

criteria are: (i) bright, round, nucleated cells in epidermis; (ii) pagetoid structures (Fig. 25.9a, b); (iii) cerebriform aggregates; (iv) bright nucleated cells in the dermal papillae. Pagetoid morphology is a controversial criteria due to the possibility of mistaking cancer cells with intraepidermal Langerhans cells [38]. Recent application of this algorithm to a relatively large cohort of cases has yielded good results (sensitivity = almost 90 %; specificity ≥70 %), although rare variants of melanocytic tumours may introduce ambiguity and limit its success [23].

Superficial Spreading Melanoma

Superficial spreading melanoma visualization by RCM reveals DEJ with ringed and/or meshwork pattern showing pleomorphic (atypical) cells, some in pagetoid dissemination (Fig. 25.9b). Melanin dust can be observed throughout the different layers [30]. In epidermis, keratinocytes are disorganized forming bizarre-looking cobblestone layers (Fig. 25.9a). In early lesions, dermal papillae are disorganized and asymmetrical and are referred to as non-edged papillae (Fig. 25.9c)

Nodular melanoma: Since this is a penetrating type of melanoma that goes deep into the dermis, RCM is not particularly well-suited to diagnose it. Nodular and superficial spreading melanomas have similar RCM features at the DEJ. Dark papillary cavities are surrounded by brighter-than-usual cells, and sheets of bizarre-shaped melanocytes appear grouped between the basal layer of the epidermis and the superficial dermis [39]. RCM visualizes clusters of deep infiltrates of cerebriform cells in the reticular dermis. Melanophages are visualized as bright, pear-shaped structures, and enlarged blood vessels are common [39].

Lentigo maligna melanoma: RCM does not distinguish well between lentigo maligna and superficial spreading melanoma [40]. What RCM can do is distinguish it from other pigmented lesions, e.g. seborrheic keratosis, pigmented actinic keratosis or solar lentigo. The distinguishing features are: pagetoid spread of atypical melanocytes surrounding hair follicles. In the papillary dermis, bright collagen bundles and pear-shaped bright melanophages are common. In invasive tumors, RCM reveals irregular groups of atypical in the papillary dermis [41].

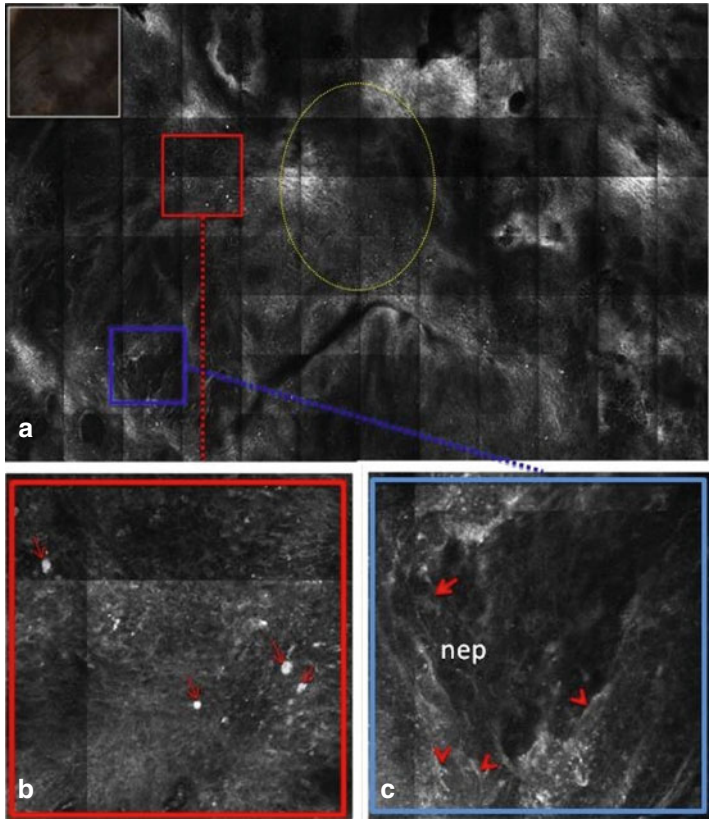

FIGURE 25.9 Melanoma. Dermoscopy displays a destructured lesion revealing the presence of crisalides and bluish white weil. (**a**) RCM mosaic (6×4 mm) reveals a disarranged pattern (*yellow dashed line*). (**b**) RCM image (0.5×0.5 mm) of the area with in the red square located in the mosaic a. It reveals at suprabasal level large pagetoid cells (*red arrows*) within atypical cobblestone pattern. (**c**) RCM image (0.5×0.5 mm) of the dermoepidermal junction from mosaic a denotes cytologic atypia typified by the presence of atypical melanocytes (*red arrowheads*) outlining nonedged papillae (*nep*). Atypical melanocytes infiltrating the upper dermis (*red arrow*) are also seen

Amelanotic melanoma: RCM reveals invasion of dendritic-shaped melanocytes in the stratum spinosum and the DEJ, as well as single bright, round or pleomorphic cells. Also, the architecture of the epidermis is disarrayed with poorly demarcated edges [41–43].

Determination of Tumour Boundaries

Due to its contrast-based nature, RCM is well-suited to improves the definition of the margins of a lesion before surgery, e.g. margin assessment of tumours with radial growth phases, including lentigo maligna [44] or hard-to-diagnose tumours, e.g. amelanotic melanoma [42].

RCM can also be used to visualize the margins in non-conventional surgery, e.g. Mohs micrographic surgery [45–48]. It takes advantage of the ability of RCM to identify cancer cells without major processing, i.e. staining, or freezing. Hence, systematic removal of the cancer is carried out until real-time examination of the excised slices is clear of cancer cells [45, 46]. In addition, such RCM-based examination is still compatible with further processing for conventional histology.

Treatment Follow-up

RCM can be used to assess the response of a skin lesion to repetitive treatment. Several studies have assessed RCM to evaluate the response of actinic keratoses and BCC to treatment with imiquimod, cryotherapy or photodynamic therapy [49–53]. The palette of application is expanding rapidly to include assessment of phototermolysis in acne [54] and photoaging [55, 56], and the effect of radiotherapy [57].

Conclusion and Future Perspectives

Reflectance-mode confocal microscopy is an important tool that adds to the ever-growing palette of non-invasive tools available in the field of clinical dermatology. RCM is still

below conventional histology in terms of depth and resolution: however, it possesses important advantages, e.g. repetitive examination of the lesion in vivo and lack of invasiveness. RCM complements histology providing a firsthand, early account of the disease; frequently RCM-based diagnosis is sufficient, and histology can be reserved for disambiguation.

RCM, along with other novel non-invasive tools, is leading the charge in the evolution of diagnosis, surgery and treatment evaluation in dermatology. In 2008, an international RCM group (www.skinconfocalmicroscopy.org) was formed. It comprises basic scientists, dermatologists and laser, microscopy and computer engineers to boost development and solve the technical problems inherent to this technique. The mission of this group is to promote awareness and advocate the use of RCM in dermatology, as well as to reach and push the limits of the current equipment.

Hopefully, the content of this chapter will require frequent updates, for this will mean that the broad palette of applications and technological developments associated to RCM keep expanding at a rapid pace.

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Chapter 26
Post-operative Wound Care and Dressings

Laiqua Khalid, Olivera Stojadinovic, and Marjana Tomic-Canic

Abstract The number of surgical procedures executed in United States during the course of 1 year is on the rise due to the increasing aging population. Consequently, a morbidity associated with infection of the surgical site is estimated to lead to medical costs between $1–10 billion annually. Therefore a good post- surgical management of wounds plays a significant role in reducing morbidity and mortality associated with improper wound management.

The role of wound dressings is to protect wound site from the further trauma while providing humidity and absorbing excess exudate, thus providing optimal environment for a

L. Khalid, MD
Laboratory on Sex and Gender Differences in Health and Disease, Department of Surgery, University of Miami Miller School of Medicine, Clinical Research Building 1,120 N.W. 14th St .4th Floor, Miami, FL 33136, USA

Department of Medicine, Jackson Memorial Hospital, 1611 NW 12th Avenue, Miami, FL 33136, USA
e-mail: laiquakhalid@gmail.com

O. Stojadinovic, MD • M. Tomic-Canic, PhD (✉)
Department of Dermatology and Cutaneous Surgery, University of Miami—Miller School of Medicine, 1600 NW 10th Ave. RMSB, Room 2023A, Miami, FL 33136, USA
e-mail: ostojadinovic@med.miami.edu; MTCanic@med.miami.edu

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successful healing. This chapter will discuss various dressings currently available on the market.

Keywords Wound • Dressing • Healing • Infection • Exudate

Introduction

Good post-operative wound management leads to a significant reduction in morbidity and mortality. The role of a wound dressing is to provide a physiological environment that is conducive for a proper wound healing. A dressing must keep the wound moist while absorbing excess exudates without leakage. It helps eliminate dead space and therefore reduces a chance of infection. Thermal insulation provided by dressing keeps the wound bed temperature closer to that of the body allowing optimal cellular function. A dressing should enable gas exchange, remove non-viable tissue and encourage scar tissue all while being non-toxic to surrounding skin and base.

A plethora of wound dressings to choose from are available in the market. A decision regarding which dressing should be used is based on type of wound and the depth of the wound. Wounds are generally classified according to depth to: Superficial (loss of epidermis only), Partial thickness (involves the epidermis and dermis) and Full thickness (involves the dermis, subcutaneous fat and sometimes bone). The American College of Surgeons classifies surgical wounds into four categories based on the level of contamination [1]. These are as follows:

- **Class I**—Clean wounds do not involve the respiratory, gastrointestinal (GI) or genitourinary tracts and show no signs of inflammation (vascular or eye surgeries, laparoscopic surgeries and surgeries involving the skin).
- **Class II**—Clean-contaminated wounds are clean wounds in the gastrointestinal, respiratory or genitourinary tracts with

a higher infection risk. The surgery has to be uncomplicated (gynecological procedures, ear surgeries and thoracic procedures).

- **Class III**—Contaminated wounds are penetrating wounds created by knife blades or bullets. Spillage of gastrointestinal tract contents, infected or highly inflamed tissue around a surgical wound is considered contaminated.
- **Class IV**—Dirty-infected surgical wounds include: traumatic wounds from a dirty source, infected surgical wounds or any wound that has been exposed to pus or fecal matter. Wounds with foreign objects lodged in them such as bullets are also considered dirty wounds.

Different wound characteristics determine choice of wound dressings. The role of wound dressing in a necrotic wound is to facilitate removal of devitalized tissue and maintain adequate moisture. This does not apply to some peripheral ischemic wounds, which are generally kept dry (dry gangrene of finger). In sloughing wounds, the slough is composed of protein, fibrin, leukocytes and serous exudate. The goal is to reduce any bacterial bioburden and prepare the wound bed with topical agents that can debride the wound and provide antimicrobial coverage. In granulating wounds, large amounts of disorganized collagen with micro arterioles are present and dressings are used to facilitate healing by providing warmth and moisture while minimally disturbing the wound bed. Epithelializing wounds are at the end spectrum of wound healing. Keratinocytes migrate from wound edges toward the center of the wound and stop due to the "contact inhibition" phenomena. Dressings in these wounds should provide enough moisture to keep the wound edges moist to encourage keratinocyte migration [2].

When making decisions about which dressing would be optimal for a wound, the type and depth of wound should be considered. However, it should be noted, for optimal wound healing to occur, moisture balance is paramount i.e. too much moisture would cause maceration of the skin and too little would desiccate the wound and cease wound healing.

Types of Dressings

Semi-Permeable Films

This is a thin, clear film of adhesive-backed polyurethane. As this film is semi permeable it can transmit moisture vapor, however this film does not absorb exudates. It can be left on wound for 7 days and it protects dry, superficial wounds from bacteria and debris while shielding against friction. Semi permeable films have also been applied to split thickness skin graft donor sites [3]. In heavier exudating wounds they can be used in conjunction with foam dressings or dressing pads as secondary dressings. Careful removal is required as damage to epidermal skin layer may occur. These films reduce pain and increase healing rates of partial thickness wounds when compared to dry dressings [4].

Minimally Adherent Dressings

These dressings are comprised of woven mesh soaked in soft paraffin, silicone or chlorhexidine. This mesh allows epithelial migration and subsequent closure of superficial wounds. Newer forms, impregnated with both ionic silver and silicone have an added benefit of antimicrobial function [5]. In wounds with low exudate such as superficial wounds or abrasions where there is a risk of adherence silver impregnated dressing are good choice. These are applied directly onto the wound with a secondary dressing, allowing for moisture retention while secondary dressing will serve as an exudate absorber. These dressing are preferred for in patients with easily broken or sensitive skin because their reduced adherence, thus ensuring minimal trauma on removal.

Alginate Dressings

This type of dressing is derived from seaweed and algae. This biodegradable wound dressing has calcium alginate, which in

the wound exchanges calcium for sodium [6]. The dressing forms a gel and keeps wound moisture. It is useful for moderate to heavy exuding wounds, deep cavity wounds and sinuses. It can be inserted and used for wound packing due to it's availability in the ribbon form, sheet or combination. Its use should be avoided on wound with low moisture as scabbing and dryness can result. This dressings need to be changed on daily basis.

Gauze Dressings

Gauze can be used as a both primary and secondary dressing. It is a thin, woven material. Sterile gauze is available on the market and although wet gauze is not a good bacterial barrier it can be impregnated with antimicrobials or bactericidal agents to cleanse an infected wound bed. In a moist form it maintains moisture in the wound bed, increases homeostasis and causes a gentle debridement on removal when moist, more aggressive when dry. In partial thickness wounds significant pain and trauma can result by the use of gauze. The use of wet to dry dressings is discouraged in modern literature. Wet to dry dressings delay wound healing by removing migrating epithelium, causing vasoconstriction and reduced leukocyte activity. Furthermore they cause pain by exposing sensitive nerve fibers in the wound bed [7].

Hydrocolloid Dressings

These interactive dressings are adhesive and occlusive. They combine absorbent colloidal materials with adhesive elastomers to manage minimal to moderate amounts of wound exudates. They react with wound exudates and become gelatinous in nature thus ensuring moisture retention in the wound bed. They are optimal for use in partial thickness and full thickness wounds. Hydrocolloid dressings should not be used in wounds with exposed tendons, minimal exudate and necrotic debris. Hydrocolloids are also available as powders and pastes that form gels after absorbing moisture. Depending

on the level of exudate this dressing can be left in place for up to 7 days. Care should be taken on dressing removal, lifting a corner of the dressing and stretching it parallel to the skin breaks the adhesive bonds prior to removal thus reducing a skin injury. If applied to an infected wound, a foul odor will be emitted from the wound.

Hydrogel Dressings

These dressings are used in partial or full thickness wounds, burns, chronic wounds and shallow wounds [8]. They work well in dry or minimally draining wounds. This type of dressing is available as an amorphous gels or sheet. It contains hydrophilic polymers in a high water content solution. They can donate or accept water from the wound bed depending on the relative state of hydration. The high water content makes hydrogels ideal dressings for autolytic debridement. Care should be taken with their use as peri-wound maceration due to over hydration has been reported [9].

Foam Dressings

Foam dressings are useful for handling large fluid volumes. They are made of silicone or polyurethane, which has a great capacity to absorb fluid. Adhesive and non-adhesive formulations are available which enable their use over a wide range of wounds. Foam dressings can be both used as primary and secondary dressings with other creams and hydrogels. Broad-spectrum antibacterial protection against hardy pathogens such as *Pseudomonas*, Methicillin-resistant Staphylococcus (MRSA) and Vancomycin-resistant Enterococcus (VRE) is provided by foam impregnated with gentian violet, methylene blue and silver [10, 11]. Foam dressings have higher patient satisfaction due to minimal discomfort during the dressing changes [12]. When used under compression, these dressings can produce ridges in the skin leading to breakdown. Therefore their use under compression should be avoided.

Antimicrobial Dressings

Microorganisms present in the wound cause a delay in wound healing. Critical colonization may present as delayed healing, malodor and new onset of pain or increasing slough despite adequate debridement [13]. It is important to account for the type and number of bacteria in the wound for targeted treatment. Curette culture is the most accurate method for sampling infected wounds but deep tissue biopsy, despite being an invasive procedure is still the "gold standard". A combination of topical and systemic antibiotics can be used guided by wound culture and sensitivities as well as the depth of the wound. Antimicrobials work equally well on both wet and dry wounds. The most commonly used antimicrobial dressings are silver, iodine and polyhexamethylene biguanide.

Silver Dressings

Silver has broad-spectrum antimicrobial coverage. It even covers MRSA and VRE [14]. The ionic form of silver is active and causes leakage of the bacterial cytoplasm by damaging bacterial cell membrane. Silver products may contain sulfa and lead. Aforementioned should not be used in patients with sulfa allergies. Lower concentration of silver dressings can be used prophylactically in immunocompromised patients.

Iodine Dressings

Iodine not only has good broad-spectrum antimicrobial activity but also has been reported to have some anti-biofilm activity [15]. Caution is advised when using iodine in patients with thyroid disease, children, lactating mothers and pregnant patients. Higher concentrations of iodine ($\geq$1 %) are toxic to skin, therefore controlled release formations such as cadexomer 0.9 % iodine should be used.

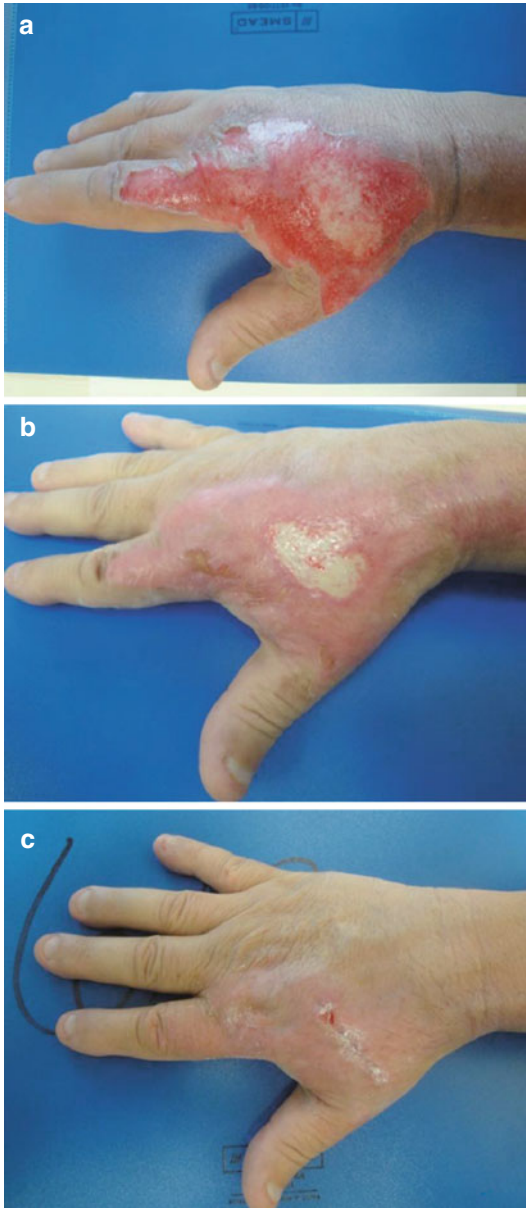
Polyhexamethylene Biguanide

Polyhexamethylene biguanide (PHMB) has a positive charge that allows binding to the negatively charged bacterial cell walls thus causing bacterial damage. Binding bacterial DNA and altering its transcription affect the bacterial cell metabolism. It is active against MRSA. This type of dressing is available as cotton-blended gauze making it suitable for packing deep wounds [14]. The biosynthesized cellulose form of PHMB allows drug delivery without dependence on wound fluid since it already contains sterile water. These dressings have demonstrated a significant reduction in length of hospital stay and post surgical mortality by significantly reducing surgical site infections [14].

Collagenase

Currently collagenase is the only FDA approved enzymatic debriding agent present at the market. Collagenase selectively targets and cleaves denatured collagen without affecting healthy tissue. Collagenase is a petrolatum-based ointment, which is sterilely packaged. It is applied to a wound daily after cleansing the wound (Fig. 26.1). It can be combined with antimicrobial powders mixed in a 50/50 ratio (polysporin, gentamycin, mupirocin or sulfamylon) [16]. Occasionally transient erythema can occur at the application site.

FIGURE 26.1 A deep partial thickness wound with a full thickness component. (**a**) The deep partial thickness healed with conservative treatment with collagenase. (**b**) The full thickness portion had to be surgically excised and the wound closed with mono filament sutures. (**c**) The hand completely healed with collagenase use (Images are courtesy of Dr Haaris S. Mir, MD)


a
b
c

Conclusion

A multitude of options are available as wound dressings. Variables such as wound depth, size, cleanliness, moisture and overall patient condition should be taken into account when choosing the most appropriate wound dressing. Optimal healing is achieved in wounds that are adequately debrided and judiciously dressed with the aim of keeping the wound bed moist while maintaining minimal bacterial burden.

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Chapter 27
Laser Complications: Etiology and Management

Martin Kassir

Abstract Currently there are many esthetic lasers and IPL devices available for use. Many wavelengths and filters exist for the treatment of a variety of conditions from hair reduction to vascular lesions, tattoos, and collagen thickening. Understanding these devices together with their correct use will enhance outcomes and limit complications. A basic knowledge of laser physics and laser-tissue interactions is critical in order to maximize results and eliminate adverse sequalae.

This chapter will review various technologies, contraindications for each technology, laser physics as it relates to practical use of each technology, and common pitfalls. The role of wavelength, pulse width, fluence, and cooling will be reviewed in relation to possible adverse sequalae. Complications for different technologies will be covered along with clinical pearls on how these complications may be avoided. Clinical examples of complications will be shown. Finally, acute and chronic management of burns and other side effects will be covered.

M. Kassir, MD, FAAD
Department of Dermatology and Lasers, Worldwide Laser Institute, 8335 Walnut Hill Lane, Suite 140, Dallas, TX 75231, USA
e-mail: theskindoctor@aol.com

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Introduction

Currently there are many esthetic lasers and IPL devices available for use. Many wavelengths and filters exist for the treatment of a variety of conditions from hair reduction to vascular lesions, tattoos, and collagen thickening. Understanding these devices together with their correct use will enhance outcomes and limit complications. A basic knowledge of laser physics and laser-tissue interactions is critical in order to maximize results and eliminate adverse sequalae.

This chapter will review various technologies, contraindications for each technology, laser physics as it relates to practical use of each technology, and common pitfalls. The role of wavelength, pulse width, fluence, and cooling will be reviewed in relation to possible adverse sequalae. Complications for different technologies will be covered along with clinical pearls on how these complications may be avoided. Clinical examples of complications will be shown. Finally, acute and chronic management of burns and other side effects will be covered.

Best Single Treatment for Laser Complications: Prevention

Why Do We Get Laser Complications?

- Inadequate training
- Inadequate supervision
- No protocols
- Incomplete histories
- Inferior equipment
- Improper use of equipment
- Don't understand laser physics

Lasers: What Are the Dangers?

- **Contraindications** not identified or ignored
- **Tanning/Peels/Retin-A** before treatments
- **Equipment** faulty
- **Ocular** lack of proper eyewear
- **Wavelength** incorrect
- **Energy** too high
- **Pulse width** too short
- **Cooling** inadequate or lacking
- **Stacking** pulses
- **Tattoos** Long pulse not Q-switch used
- **Sequence** of treatments inappropriate
- **Post-op** care inadequate

Contraindications: Absolute

- Epilepsy
- Concomitant isotretinoin use
- Concurrent bacterial or viral infections in treatment areas
- Pregnancy
- Recent other procedures
- Recent tanning, peels, scrubs, or retinoids
- Pre-existing problems (eg: infraorbital CO_2 in patient with ectropion)
- Patient with unrealistic expectations
- Faulty equipment
- Lack of proper safety

Contraindications: Relative

- Perpetual UV light exposure (summer, trips)
- Prior treatments with skin dyspigmentation, fibrosis, scarring or other complication
- Tendency to form hypertrophic scars or keloids
- Collagen vascular disease or immune disorder
- Photosensitizing condition
- Specific photoallergy (patch testing)

- Photosensitizing medication
- Koebnerization

Contraindications: Faulty Equipment

- Low powered
- Faulty
- Not serviced (used)
- Error messages ignored
- Dirty lenses not cleaned
- Dirty handpieces
- Bad fibers

Ocular Complications [1]

- Wavelength & target specific
- Corneal damage
  - Target: water
  - CO_2 or erbium lasers
- Retinal damage
  - Retinal pigment
  - Retinal vasculature
  - Target: Hgb & melanin
  - 585 nm, 694 nm, 755 nm, 1,064 nm
- Wavelength-specific eyewear must be worn by anyone in the room
  - Patients, operators, observers

Wavelength Incorrect

- LHR: LP 755 nm for dark skin
- LHR: IPL for dark skin
- Tattoos: IPL used

- Vascular: LP 1,064 nm used on face
- Vascular: LP 532 (KTP) used on LE

Energy Too High

- Any LP laser
- Especially dark skin
- Especially thin skinned areas
- Especially without cooling
- LHR with inadequate PW (not long enough)
- IPLs with "new" head

Pulse Width Too Short

- LHR: LP 755 nm for dark skin
- LHR: IPL for dark skin
- Tattoos: IPL used
- Vascular: LP 1,064 nm used on face
- Vascular: LP 532 (KTP) used on LE

Cooling Inadequate or Lacking

- Cooling:
  - Protects epidermis
  - Allows for higher energies
  - Allows for shorter pulse widths
- No cooling
- Inadequate cooling (pre, parallel, post)
- Cooling itself may cause side effects (LN2)

Stacking Pulses [2]

- LHR: fine hairs
- LHR: oral commisures
- Vascular: small veins

Tattoos Long Pulse Used

- LP lasers used for tattoos
- IPL used for tattoos

Sequence of Treatments Inadequate

- Too little time between treatments
- Multiple lasers on the same day

Post-op Care Inadequate

- Treated area not cooled after laser
- Area allowed to dry/crust
- Written instructions not given to patients
- Irritating topicals applied
- Sunscreen not used
- Tanning post procedures

Why Complications? Unwanted Epidermal Damage

Post-op Sequalae: Usual

- Tingling
- Pain
- Erythema
- Edema
- Minor crusting
- Purpura

Complications

- Severe or persistent pain
- Severe or persistent tingling/dysesthesias

- Persistent erythema
- Severe edema
- Hyperpigmentation
- Hypopigmentation
- Raised scarring
- Depressed scarring
- Erythematous scarring
- Fat atrophy +/or “potholes”

Complications by Technology: Laser Hair Reduction [3]

- Pain
- Crusts/“scabbing”
- Burns/blisters
- Hyperpigmentation
- Hypopigmentation
- Post LHR hypertrichosis
- Scarring (atrophic or hypertrophic) [2]
- Thrombophlebitis (rare, Nd:YAG)
- Figure 27.1

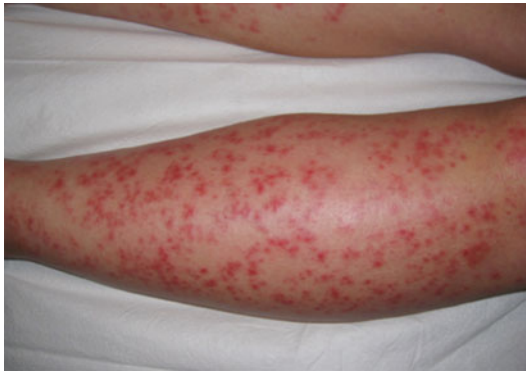

Figure 27.1 Don’t think skin type II does not burn

Post LHR Hypertrichosis [4–6]

- Patients develop a definite increase in hair density, color, coarseness, or a combination of these at treated sites
- Absence of any other known cause of hypertrichosis
- Rare but paradoxical effect
- Increased hair growth at sites previously treated for hair removal
- Seen with LP 755 and IPL
- Usually patients with black hair, dark skin
- Suboptimal fluences may have paradoxical effects on the hair follicle
- Patient perception and "pseudo hypertrichosis"

Complications by Technology: Vascular Lasers

- Severe Crusting
- Post – Inflammatory Hyperpigmentation
- Post – Inflammatory Hypopigmentation
- Atrophic Scarring [2]
- "White" Scarring
- Severe Purpura

Complications by Technology: Pigmented Lesion Lasers

- Hyperpigmentation
- Hypopigmentation
- Treatment of suspicious pigmented lesions
- Complications according to mode of treatment (Alexandrite, KTP, Q-Switch)

Complications by Technology: Tattoo Lasers

- Scarring
- Keloids

- Discoloration
- Infection
- Darkening of cosmetic tattoos [7]
  - Red or skin colored
  - Lip, eyebrow, eyelids
  - After treatment with q-switched 694 nm
  - After treatment with q-switched 755 & 1,064 nm
  - Laser-induced conversion of ferric oxide to ferrous oxide in the cosmetic tattoo ink
  - Results in black pigmentation
- Lichenoid reaction to red tattoos [8]

Complications by Technology: Ablative Lasers (CO_2) [9]

- Erythema (4–5 months)
- Hyperpigmentation (higher in darker skin types)
- Acne flares
- Milia
- Dermatitis
- HSV infection (regardless of prior HSV history)
- Other local or disseminated infection
- Persistent Hypopigmentation
- Scarring

Complications by Technology: IPL Devices

- "Photoburn" (Footprint Burns)
- Blisters [2]
- Persistent edema
- Focal purpura
- PIH
- Persistent hypopigmentation [2]

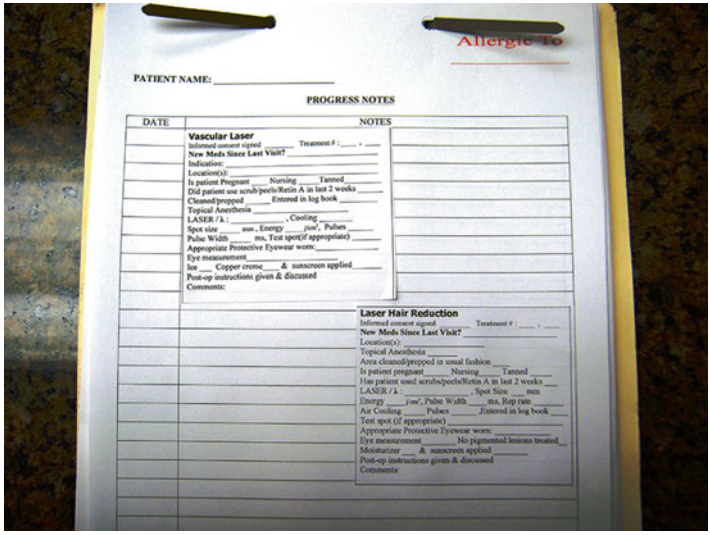

FIGURE 27.2 Laser stickers and progress notes

Prevention

Laser Stickers (Checklist Helps Prevent Complications) (Figure 27.2)

- Informed Consent Signed_____ Treatment # _____, _____
- New Meds Since Last Visit _____
- Location(S) _____ Topical Anesthesia _____
- Is Patient Pregnant ____ Nursing ____ Tanned _____
- Has Patient Used Scrubs/Peels/Retin-A Or Waxed In Last 2 Weeks ___
- Laser/ Λ : _____ Spot Size _____ Mm
- Energy _____ J/Cm^2, Pulse Width _____ Ms, Rep Rate _____ Hz
- Air Cooling @ _____ Ice _____ Pulses _____
- Appropriate Eyewear Worn: _____ Eye Measurement _____

- Moisturizer _____ & Sunscreen _____ Applied
- Post-Op Instructions Given & Discussed _____
- Comments:

Burn Protocol: Acute

- Clean with mild soap & water twice a day
- Ice/cold air
- Oxygen treatments immediately and daily
- Keep area moist (copper gel)
- Do not pick blisters or scabs/crusts
- Red led light (15–30 min/day)
- Oral antibiotics and antivirals if indicated
- Sun protection
- No smoking
- Figure 27.3

Chronic Management

- Oxygen therapy
- Twice weekly LED red light
- Sunscreen
- Make up (cover up)
- Hydroquinone
- No smoking
- No waxing
- Avoid topicals that may be irritants
- Other lasers

Other Lasers/Light (Figure 27.4)

- LED for acute management
- LED for chronic recovery
- PDL for red scars, erythema
- Q-Switch lasers for hyperpigmentation

FIGURE 27.3 Oxygen therapy

- IPL for hyperpigmentation
- IPL for erythema
- Fractional non-ablative for hyperpigmentation, atrophic scars
- Excimer for hypopigmentation

Severe Burns & Scarring

- Deep dermal or full-thickness burns produce scarring
- Scars are the sequelae of any deep burn wound

FIGURE 27.4 Red LED

Scar Management

- First: prevention
- Next: management of the scar
- Then: management of erythema and pruritis
- Then: removal of contractures (if necessary)

Burn Scars

- Seen with deep dermal burns
- Left to heal spontaneously
- The burn scar becomes raised, red and itchy within weeks of healing
- Scars are unsightly

Table 27.1 Scars: comparison [10]

	Hypertrophic scar	Keloid
Occurrence	**4–8 weeks** after wound closure or trauma	Up to several years after minor injury or spontaneous
Extent	**Confined** to site of injury	**Extends** to surrounding uninjured skin
Clinical	Linear, popular, or nodular pink-red firm tumor in wounds of high tension	Firm, tender, bosselated shiny pink tumors ± telangiectasia

Scars

- Both hypertrophic scars and keloids are included in the spectrum of fibroproliferative disorders
- These abnormal scars result from the loss of the control mechanisms that normally regulate the fine balance of tissue repair and regeneration (Table 27.1)

Treatment of Scars

- Pressure
- Silicon Gel Sheets
- Il Steroids
- Cryotherapy
- Surgery
- Lasers
- Interferon

Pressure on Maturing Scar Tissue [10]

- Conservative management for both prophylaxis & treatment
- Pressure maintained by compressive garments
- Mechanism of action is poorly understood

- Limiting blood supply and oxygen to the scar
- Leads to decreased collagen synthesis
- Increased apoptosis
- Continuous pressure of 15–40 mmHg × 6 months

Intralesional Corticosteroids (ILCS) [10]

- Mainstay of treatment
- Effects result primarily from suppressive effects on inflammatory process in the wound
- Reduce collagen & GAG synthesis
- Causes degradation of collagen & fibroblasts
- Triamcinolone Acetonide (TAC) 10–40 mg/ml at 4–6 week intervals
- ILCS can be a single modality or as an adjunct to excision
- Response rates vary from 50 to 100 %
- Improve pruritus
- Complications of repeated ILCS:
  - Atrophy
  - Telangiectasia
  - Pigmentary alteration

Cryotherapy [10]

- Liquid nitrogen
- Affects microvasculature (vascular damage may lead to anoxia)
- Causes cell damage via intracellular crystals
- 1, 2, or 3 freeze-thaw cycles lasting 10–30 s each
- Treatment may need to be repeated every 20–30 days
- Side effects
  - Blistering
  - Pain
  - Atrophy
  - Permanent hypo- or hyperpigmentation in some patients

Surgery [10]

- Surgical excision: closure with minimal tension
- Follow skin tension lines
- High recurrence rates with keloids

Radiotherapy [10]

- Primarily as adjuncts to surgical removal of keloids
- Superficial x-rays, electron-beam therapy
- Inhibition of neovascular buds and proliferating fibroblasts
- Decreased collagen production
- Risk of carcinogenesis

Lasers

- Pulse-Dyed Laser [11, 12]
  - Microvascular thrombosis & tissue hypoxia
  - Reduction of scar erythema, height, symptoms, and rigidity
- CO_2 laser: collagen shrinkage via heating [12]
- Nd:Yag Laser: inhibits collagen metabolism and production
- High recurrence rate with laser therapy

Interferon Therapy [10]

- IFN alpha
- Reduce keloidal fibroblast production of collagen
  - Type I, III
- IFN alpha 2b
  - Antiproliferative properties
  - Antagonizes effects of TGF-beta & histamine

- Adverse effects
  - Flu-like symptoms
  - Pain on injection

Bleomycin [10]

- Antineoplastic agent
- Directly inhibits collagen synthesis via decreased stimulation by TGF-beta 1
- Improvement in scar height & pliability
- Reduction in erythema, pruritis, & pain
- Systemic toxic effects not common with IL administration

Silicon Sheeting [13]

- Silicone sheets, strips, gels, sprays, foams
- Increase temperature, hydration, and oxygen tension
- Scar may flatten or soften
- Applied as an occlusive dressing
- Should be placed 12–24 h per day for 3 months

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Chapter 28
Laser Pearls

Vishal Madan

Abstract Every laser practitioner should aim to optimize treatments to achieve maximal clinical benefit whilst ensuring comfort and safety of their patients. As laser devices are frequently very expensive, a pragmatic approach should allow the practitioner to maximize benefit from each device and treat as many indications as effectively and as safely possible, thus maximizing both clinical and economic benefits. This chapter will provide some tips and pearls which readers can use in their clinical practice, hopefully leading to achievement of the above goals.

Keywords Laser pearls • Laser tips • Safety • Patient comfort

Pearls

All practitioners develop their own 'pearls' when treating their patients. These treatment pearls are based on patients' feedback and clinical responses. Experienced laser

V. Madan, MBBS (Hons), MD, FRCP
Department of Dermatology, Salford Royal NHS Foundation Trust, Stott Lane, Salford, Manchester, Lancashire, M6 8HD, England, UK
e-mail: vishal.madan@srft.nhs.uk

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practitioners continue to learn on the job and knowledge and practice of these pearls enrich patient and practitioner experience.

This chapter focuses on the following broad categories:

I. Pain Reduction and Patient Comfort Pearls
II. Vascular Laser Pearls
III. Ablative Laser Pearls
IV. Pigment Specific Laser Pearls
V. Hair Reduction Laser Pearls

Pain Reduction and Patient Comfort Pearls

Anyone involved in delivering laser treatments would appreciate the importance of delivering comfortable treatments. A comfortable laser treatment experience can be the difference between average and excellent patient feedback! Below are listed a few pearls which may prove effective in improving patients' experience of their laser treatments.

A. **Local Anesthetics**—especially useful with ablative carbon dioxide and Erbium:YAG laser treatments. Local anesthetics, especially those which contain epinephrine (adrenaline), can cause a stinging sensation when injected. The following measures can be employed to reduce the discomfort of local anesthetic injections.

- Use local anesthetics solutions that are stored at room temperature—as cooler solutions are typically more uncomfortable.
- Buffering the solution by mixing with sodium bicarbonate can increase the pH, leading to more comfortable injections

  – Slow injections
  – Minimize the number of puncture sites
  – Nerve blocks are especially helpful in reducing the number of puncture sites and amount of anesthetic required.

- Using distraction e.g. pinching skin, vibration or talking to the patient (verbal anesthesia) can be crucial and their importance should not be underestimated.

B. **Topical Anesthetics**—such as EMLA (Eutectic mixture of local anesthetics, Lidocaine 2.5 % and Prilocaine 2.5 %) are often useful in the treatment of vascular lesions, in hair reduction procedures and when using the Q switched lasers. The author routinely uses topical anesthetics for treating benign skin lesions such as syringomas with the carbon dioxide laser.
C. **Contact cooling, cold air and dynamic cooling devices**—allow for safe treatments by sparing the epidermis. These devices minimize patient discomfort—making otherwise painful treatments tolerable. Useful when treating vascular lesions with the pulsed dye laser (PDL). Also useful when using the Nd:YAG laser system for hair removal. It is also helpful when used in adjunct with intense pulsed light devices.
D. **Hydrogel pads**—Minimize patient discomfort. Useful adjunct when using Q-switched lasers. These pads reduce tissue splatter while maintaining efficacy.
E. **Post treatment cold packs**—Frozen normal saline sachets can be placed on sites after treatment with a pulsed dye laser in order to provide comfort.

Vascular Laser Treatment Pearls

Vascular laser treatments are amongst the most common laser treatments performed in the Western world. The pulsed dye laser was one of the first to exploit the theory of selective photothermolysis. Since its introduction, several modifications and improvements have been made which have led to the latest generation of lasers which offer more effective and safer treatments.

A. **Resistant and recurrent port wine stains**—Vascular lesions—especially port wine stains—can substantially

improve after treatment with the available vascular lasers. However, a large proportion of port wine stains fail to subside completely, and some may darken again over time. Predicting which lesions will respond to treatment remains a challenge. Use of video-microscopy or dermatoscopy for this indication has not translated into clinical practice. Small calibre deeper vessels are hardest to treat. Double pass technique at defined intervals between the first and second treatment has been shown to further lighten some resistant port-wine stains; however, one must consider the risks of blistering, scarring and hyperpigmentation that are associated with such a technique [1]. If available, longer wavelength, variable pulse width lasers such as the 755 nm alexandrite, 810 nm diode, 1,064 nm neodymium:yttrium-aluminum-garnet (Nd:YAG) laser, and intense pulse light systems can be used to treat the resistant port wine stains [2]. Topical photodynamic therapy has been found to be as effective as PDL, and is worth exploring in patients who don't respond to conventional laser treatments [3]. Addition of antiangiogenic agents such as rapamycin after laser irradiation appears promising and may improve treatment outcomes [4].

B. **Non Purpuric treatments—Post-operative** purpura associated with short pulsed PDL can last for 7–10 days. It can be quite debilitating for patients. Employing longer pulse durations on the PDL can achieve purpura-free treatments at the expense of loss of some efficacy, enhanced edema and increased numbers of treatments.
C. **Avoiding perilesional purpura**—for smaller lesions where similar sized laser spots are unavailable, laser light delivery through a lesional-size hole cut out in a cardboard or similar may help reduce unwanted purpura in perilesional skin.
D. **Treating nasal ala veins/periorbital veins**—these can be quite challenging to treat. The thick nasal ala veins seldom improve with short-pulsed PDL and using the long-pulsed Nd:YAG can result in scarring at the site of treatment. The elliptical spot on the new PDL (V Beam Perfecta, Candela)

has been found to be effective in the treatment of resistant nasal telangiectasia in some cases [5].

E. **Treatment of warts**—Using high fluence, short-pulsed PDL can be effective in the treatment of otherwise resistant warts. However, treatments can be painful because no adjunctive cooling is employed. Therefore, adequate analgesia or anesthetic should be administered.

F. **Hypertrophic scars and keloids**—Sequential treatment of keloids and hypertrophic scars with intralesional corticosteroids followed by PDL improves the erythema, pruritus and tenderness associated with these lesions [6].

Ablative Laser Pearls

Traditional ablative lasers have been the gold standard for skin rejuvenation and for treatment of post-acne scarring. These have largely been replaced by the fractional ablative technologies for these indications. The traditional ablative lasers still have several uses in dermatology.

A. **Using the carbon dioxide laser in the treatment of steatocystoma multiplex**—There are not many good treatments for this condition. A quick and cosmetically-acceptable treatment includes puncturing individual cysts with the super pulse CO_2 laser to achieve a small entry focus for the small Volkmann's or chalazion curette, which is then used to extricate the contents and the cyst wall. Healing occurs by secondary intention. The resultant scars are smaller than excisional scars [7]. The same technique can be employed when treating epidermoid cysts.

B. **Earlobe Keloids**—These can improve with intralesional steroids, but improvement is usually short-lived. Similarly, the risk of recurrence following excision is very high. The CO_2 laser is used to 'cut' the exuberant scar tissue. Following this, 0.2–0.3 ml of 10 mg/ml triamcinolone acetonide is injected into the wound base. The intralesional steroid injection is repeated after 4 weeks if required. Results are usually satisfactory.

C. **Treating red tattoo ink reactions**—The risk of generalized tattoo reactions following Q-switched laser treatments of tattoo reactions precludes their use. Reactions to red tattoos can be very pruritic, and the symptoms are linked to the pigment burden. This can be ablated with the CO_2/Erbium:YAG lasers—which expose the pigment. The excess pigment is then curetted from the dermis. Healing takes place within 1–2 weeks, and all patients report an improvement in appearance and reduction in symptoms.

Pigment Specific Laser Pearls

A. **Preservation of eyebrows during tattoo removal**—Eyebrow hairs, which grow from the skin at very acute angles, are unavoidable during laser tattoo removal, especially in patients with black or brown hair. If the eyebrows are brushed with a cotton swab, the hairs are lifted to stand perpendicular to the surface of the skin or reoriented in the opposite direction to hair growth. The tattoos can then be treated with the Q-switched lasers without damage to the eyebrow hairs [8].

B. **Congenital Melanocytic Nevi (CMN)**—Treatment of CMN still remains controversial due to concerns over sub-laser threshold energies stimulating nevus cells. If laser treatment is considered appropriate, the following points should help in optimizing treatment.

- Treat macular flat CMN with pigment specific lasers only
- Treat raised or mammillated CMN with ablative lasers only as additional treatment with Q switched lasers does not improve outcome.
- Treatment of flat or macular CMN on the limbs with ablative lasers can increase the risk of scarring [9].

C. **Enhancing pigment clearance**—use of topical imiquimod in conjunction with Q-swithced Nd:YAG laser can be more effective than Q-switched Nd:YAG alone in the

treatment of tattoos [10]. Four passes of Q-switched laser treatment separated by 20 min were found to be much more effective than a single pass in the treatment of tattoos [11]. No increase in the incidence of adverse effects was noted in these patients.

D. **Naevus of Ota (NO)**—The 1,064 nm QS: NdYAG laser is considered the treatment of choice for this condition characterized by benign melanocytosis. However, it is the authors' experience that not all patients responded best to this wavelength. NO show great inter- and intra-individual variation in both color and site. Consequently, treatment with alternate shorter wavelengths such as QS: 532 nm Nd:YAG may be more effective in treating superficial NO or those at anatomical sites of thinner skin.

Hair Reduction Laser Pearls

A. **Patient and laser selection**—Whilst lasers can be very effective in bringing about significant reduction of unwanted hair, proper patient selection is important to maximize the results and minimize the incidence of adverse effects. In patients with darker skin tones, the long-pulsed Nd:YAG laser is considered the safest lasers by virtue of its deeper penetrating wavelength and minimal interference with the epidermal melanocytes. For patients with lighter skin, the Alexandrite or Diode lasers are better choices as they are more effective than the long-pulsed Nd:YAG laser.

B. **Reducing risks**—The most common complications following laser hair reduction are burning, hyperpigmentation and paradoxical hypertrichosis. The practitioner must examine the patient carefully in order to avoid treatment of tanned skin as missed tan is perhaps one of the commonest reasons for burns following laser and IPL therapy for hair removal. Covering tattoos with opaque paper will prevent inadvertent laser injury to tattoo, thereby avoiding laser burns. Whilst there are no definite methods to avoid

paradoxical hypertrichosis that can be seen in up to 10 % patients undergoing laser or IPL hair reduction, cooling the adjacent skin during treatments has been shown to be of benefit [12].

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Chapter 29
Medicolegal Issues

Tanya Nino, Andrea Smith, Maryam Afshar, and Abel Torres

Abstract The number of laser and light procedures performed continues to expand with the increasing demand for these treatments. Laser and light technology has evolved to include the elective treatment of a broad array of dermatologic conditions. With the widespread use of this equipment by dermatologists and non-dermatologists alike, the potential for medical-legal complications arises. It is important to be aware of the medical-legal issues that may result from laser and light source use and to understand strategies for preventing complications.

Keywords Informed consent • Legal • Medical malpractice • Physician extenders • Off-label

T. Nino, MD (✉) • A. Smith, MD • A. Torres, MD, JD
Department of Dermatology, Loma Linda University Medical Center, 11370 Anderson Street, Suite 2600, Loma Linda, CA 92354, USA
e-mail: tanyanino@gmail.com; andrea.bassham@gmail.com; abelt@aol.com

M. Afshar, MD
Division of Dermatology, UC San Diego, 8899 University Center Lane Suite 350, San Diego, CA 92122, USA
e-mail: maafshar@ucsd.edu

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Introduction

The number of laser and light procedures performed continues to expand with the increasing demand for these treatments. Laser and light technology has evolved to include the elective treatment of a broad array of dermatologic conditions. With the widespread use of this equipment by dermatologists and non-dermatologists alike, the potential for medical-legal complications arises. It is important to be aware of the medical-legal issues that may result from laser and light source use and to understand strategies for preventing complications.

Medical Malpractice: Negligence

For a practitioner to be deemed negligent, four elements must be satisfied [1]:

- Duty
  - A laser operator's duty to the patient is to perform the laser procedure within the standard of care.
  - The standard of care is determined by the knowledge and expertise of a similarly situated specialist in that field.
  - Therefore, a dermatologist, internist, or even a non-physician performing a laser or light procedure will all be held to the same standard when evaluating negligence in a court of law.
- Breach of duty
  - This occurs when a practitioner fails to meet the standard of care obligations.
- Causation
  - The practitioner's lapse in duty must be the direct reason for the medical complication.
- Damages
  - The patient must suffer losses as a result of the practitioner's act of negligence.

Informed Consent and Documentation

Because of the elective nature of the vast majority of laser and light procedures, an adequate informed consent discussion is paramount. Detailed information should be provided to the patient as follows [2]:

- Diagnosis
- Nature, extent, and process of treatment
- Risks of the treatment
- Potential short and long term adverse effects
- Possible alternative treatments
- Costs expected – price quotation documented

After an informed consent discussion, supplementary modes of communication may help improve patient retention of pertinent information [3]:

- Educational pamphlets on diagnosis
- Brochure for indicated laser
- Handout on expectations, risks, benefits, alternatives
- Patient questionnaire documenting comprehension of consent discussion

The following items should be addressed and documented prior to laser procedures [2, 3]:

- Discussion of informed consent
- Discussion of patient expectations, clarification of unrealistic treatment goals
- A no guarantee clause—discussion that positive clinical outcome cannot be certain
- A waiver of financial liability—discussion that insurance companies may deny payment for services that are not medically necessary
- Photographic documentation of the treatment site

The following items should be recorded in the laser procedure note [2, 3]:

- Pertinent patient history (i.e. history of Herpes Simplex infections)

- Any prior treatments and outcomes
- Skin type and tone
- Pre-operative findings
- Diagnosis
- Indication for laser treatment
- Type of laser
- Type of anesthesia
- Parameters of application
- Post-procedure findings/condition

Physician Extenders: Non-physician Practice of Laser Procedures

Cutaneous laser surgery can have many advantageous cosmetic effects, causing the general public to often think of it as a "beauty treatment" rather than a medical procedure [4]. This conception is largely from the media's portrayal of these procedures as uncomplicated and without serious risk [4]. As such, many are comfortable having procedures done without the appropriate diagnosis, discussion of possible adverse outcomes or even knowledge of the operator's training. It is well established that there has been rapid growth in the number of non-dermatologist physician extenders—physician assistants, registered nurses, nurse practitioners, estheticians, cosmetologists, and electrologists—who perform laser procedures [5–7]. This is an area of some controversy; there are a number of significant medical, legal concerns regarding physician extender use of lasers [4–7]:

- Physician extenders may lack formal training in:
  - cutaneous medicine, surgery, techniques, and technology [4]
  - evaluation, diagnosis, and/or appropriate treatment of skin disease, including cancer [5]
  - indications and contraindications for procedures [4]

  - recognition of early signs of complications, resulting in delayed treatment by a qualified physician [4, 5]
  - management of complications resulting from treatment [5]

- Physician extenders have a rising rate of procedural complications, such as burns, permanent pigmentation, and scarring reported nationally [4, 5].
- The supervising physician is often ultimately vicariously liable for physician extender negligence whenever the physician extender is legally acting within his or her scope of duty while performing laser treatments [8]. This means that the physician can be held responsible for the acts of his or her subordinate.

The scope of practice and supervision of physician extenders in laser medicine is governed by state laws [7, 8]. These laws vary widely from state to state—and take precedence over dermatologic society guidelines.

- The Federation of State Medical Boards has compiled a list of the specific regulations for delegation of laser operation by state [9].
- These regulations are often formulated with the consultation of individual State Medical Boards, the Boards of Registered Nursing, the Physician Assistant Committees, and other professionals in the medical field [9].

For example, in California, the Business and Professions code is as follows:

- Electrologists, cosmetologists, estheticians, unlicensed medical assistants, and licensed vocational nurses are expressly prohibited from using laser and intense pulse light devices.
- Physicians may delegate laser or intense pulse light device procedures to physician assistants, registered nurses, or nurse practitioners.

Physicians should research their own individual state laws regarding the supervision of physician extenders in laser medicine.

Furthermore, with specific respect to physician assistants and nurse practitioners, the American Medical Association has established guidelines as follows [6]:

- A physician must be available for consultation with a physician assistant at all times, either in person or through telecommunication systems or other means
- At least one supervising physician in an integrated practice must be immediately available at all times for supervision and consultation when needed by a nurse practitioner

While lasers have the potential to provide significant cosmetic improvements, when used improperly they may have devastating consequences [4]. Some dermatologists have argued that non-dermatologists practicing dermatologic cosmetic procedures may be putting profit ahead of patient welfare, and that the potential harm from inappropriate patient care outweighs any benefit [5, 7].

Dermatologists have years of focused training on all diseases of the skin after general medical school education. This provides in-depth understanding of skin lesions, conditions, response to different types of injury and histopathology. For these reasons, dermatology has pioneered many of the techniques used in cutaneous laser surgery. The expected rate of adverse events is based on a highly skilled and trained individual performing the procedure [4]. Anyone who performs cutaneous laser surgery must be able to demonstrate similar understanding or be directly supervised by a practitioner with equivalent training. This is the best way to ensure that laser procedures are undertaken for appropriate diagnoses and followed through with careful attention to any adverse outcomes.

If physicians choose to work with physician extenders, they are responsible for being aware of the expertise and clinical skills of the physician extenders [1].

Malpractice Claims/Complications in Laser Medicine

A recent study identified 174 legal cases from 1985 to 2012 related to injury from cutaneous laser surgery [10]. These injuries are depicted in Fig. 29.1. Note that some cases alleged multiple injuries. In addition to physical injuries, the prevalence of psychological injuries is notable. Burns included second and third degree burns, as well as full thickness necrosis. Scars included hypertrophic scars, keloids, and atrophic scars.

In addition, the most common procedures resulting in litigation were identified by the same study [10] and are depicted in Fig. 29.2. Note that rejuvenation included conventional and fractional ablative and non-ablative lasers.

In addition, other authors have examined the complications in laser surgery performed by medical laypersons and non-physicians as listed below [5, 11].

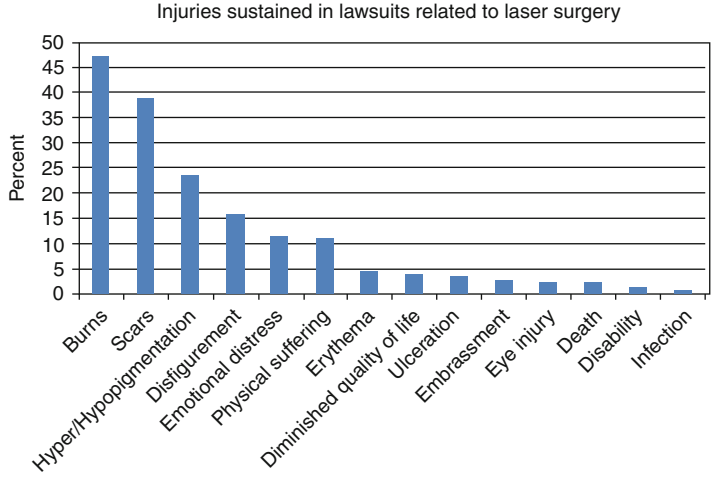

FIGURE 29.1 Injuries sustained in lawsuits related to laser surgery [10]

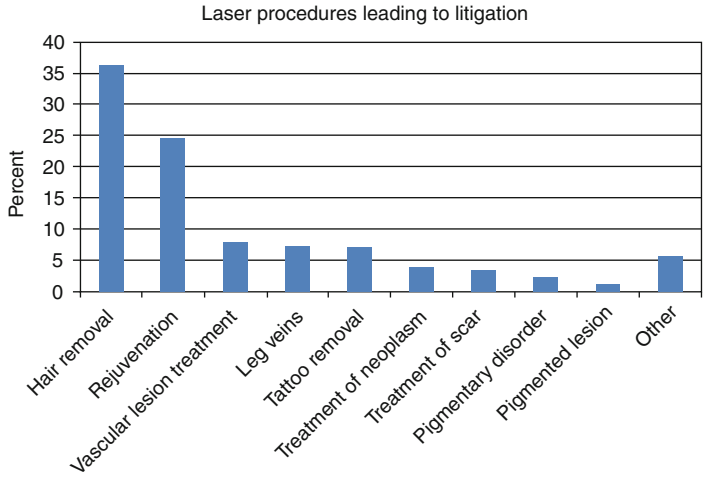

FIGURE 29.2 Laser procedures leading to litigation [10]

Most Common Sources of Error Leading to Complications

- Excessive energy application
- Wrong technology for the indication
- Inappropriate skin type/tone for treatment (Tan or Types III–VI)
- Fitzpatrick Skin Types III–VI more likely to have complications
- Inadequate cooling
- Overlapping pulses
- Inadequate information prior to procedure

These were all generally regarded to be avoidable had an individual with appropriate training taken care of the patient [11].

Off-Label/Experimental Use of Lasers

Cutaneous laser surgery is an exciting field because it is rapidly changing and expanding. However, because of this evolution, there is often a lack of scientific evidence to

support many of the procedures performed [1, 8]. In this case, the clinical "standard of care" is often ahead of any guidelines, parameters or formal research. Goldberg and colleagues refer to these as "regulatory gaps" [1, 8]. Frequently this is acceptable and allows for cutting-edge solutions for patients with certain conditions. Goldberg and colleagues highlight the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research recommendation that any "radically new" procedure have "formal research" prior to implementation [1]. However, it is also noted that very infrequently are the procedures used during cutaneous laser surgery considered "radically new" [1].

Therefore, if the goal is to always provide patients with the best possible care, then new and "off-label" uses for laser surgery can be appropriate. Prior to proceeding it is most prudent to consider whether a more traditional approach may provide a safer or more effective result.

One might consider asking the following questions prior to proceeding:

- Is there a safer alternative?
- Is there a more effective alternative?
- Are there related structures that may be harmed? Eyes, Pigmented Lesions, Potentially Malignant Lesions, etc.
- Will this cause undo harm to the patient? More Pain? Longer Healing?

Preventative Strategies

Cutaneous laser surgery offers many benefits to our patients, often improving their quality of life. Therefore, we must pursue continual improvement in performing these procedures. This will go a long way towards preventing errors and complications.

Currently there are no standardized educational requirements for persons performing cutaneous laser surgery [2]. Several dermatology centers have suggested that standardized education and testing may increase the expertise of those

performing laser procedures [2, 5]. The following were recommended [2, 5]:

- Established Laser Treatment Centers for Didactics and Hands-On Training
- Training in Basic Cutaneous Conditions, Anatomy and Physiology
- Examination and/or Demonstration of Proficiency Certification

It is imperative that prior to treatment of any condition the diagnosis be correct. Most problems treated by laser are dermatologic. Therefore, one must have a fundamental understanding of dermatology. If a lesion is incorrectly diagnosed, the patient risks serious morbidity and even mortality.

Lesions of Particular Concern

- Nevi and other pigmented lesions
- Pre-malignant lesions such as actinic keratoses
- Malignant lesions such as non-melanotic skin cancers and melanoma

Equally important to having the correct diagnosis is choosing the correct indication.

Carefully consider the following factors [2]:

- Skin type
- Skin tone
- Anatomical location of the lesion
- Pigmented lesions

Once an indicated treatment is chosen for a diagnosed condition, the safest way to usually proceed is with a test spot, confirming that the patient's skin will react as anticipated. It will also help in the prediction of any adverse effects. If any serious side effects do arise at any time during treatment, prompt consultation by a specialist physician is essential to the proper care of the patient [11].

Conclusions

- The number of elective laser and light procedures is steadily increasing, generating medical and legal issues.
- Proper documentation and informed consent is imperative.
- Physician extenders are more at risk for complications from lasers due to a possible relative lack of training and education; this rate is reduced by having a supervising on-site physician readily available for consultation at all times.
- Complications from laser use are not uncommon and typically result from excess energy application.
- While off-label use of lasers may provide the best treatment, safer alternatives should always be considered.

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Chapter 30
Photography Specific to Lasers

Maria Valéria Bussamara Pinheiro

Abstract Dermatology is a visual specialty. Dermatologists are comfortable with the act of photographing their patients, but there is plenty of room for improving the quality of clinical images.

Photography plays an important role in cosmetic procedures, such as lasers, because it allows objective comparison between the states before and after the procedure. This is particularly important in determining the efficacy of a specific treatment for facial rejuvenation and resurfacing, during which the skin texture, fine wrinkles and pigmentation irregularities can be analyzed. Because it is so descriptive, photography of such patients involves a number of variables that are interrelated, and any change could cause significant discrepancies. Therefore, the photographs should be standardized so they can truly report the effectiveness of the treatments.

In this chapter we refer to the medical photography, a specific type of photography that accurately reproduces reality, and maximizes important and relevant information.

M.V.B. Pinheiro, MD
Department of Dermatology, Federal University of São Paulo – UNIFESP Rua Afonso Brás 864 Conjunto 51,
Vila Nova Conceição, São Paulo, SP CEP 04511-001, Brazil
e-mail: valeria@valeriapinheiro.com.br

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In order to optimize the practice of photography, we introduce concepts of the photographic technique, as well as differences between cameras and standardization of the photos.

Keywords Digital photography • Medical photography • Laser • Dermatology • Cosmetic procedures

Introduction

Dermatology is a visual science [1], and the attempts to illustrate dermatologic diseases come from long ago. Though many dermatologists have become comfortable with the act of photographing their patients, there is still plenty of room for improving the quality of clinical images.

Photography plays an important role in cosmetic procedures such as laser therapy because it allows objective comparison between the states before and after the procedure [2]. This is particularly important in determining the efficacy of a specific treatment for facial rejuvenation and resurfacing, during which the skin texture, fine wrinkles and pigmentation irregularities can be analyzed. Because it is so descriptive, photography of such patients involves a number of variables that are interrelated, and any change could cause significant discrepancies. Therefore, photographs should be standardized so they can faithfully report the effectiveness of the treatments. Therefore, we are referring to a specific type of photography which is called "medical photography", and can be defined as the photography that accurately reproduces reality, and maximizes important and relevant information. As we know, dermatology is a purely visual specialty, so we can say the dermatologist is a "functional photographer", since they use the photographic capabilities by necessity of its occupation [3]. The importance of photography in dermatology can be summarized with the following aspects:

- As part of the clinical history, complementing the description of the physical examination.

- As an aid in choosing the best treatment modality.
- To help monitoring the development of lesions.
- As a medical record: "before and after" pictures of aesthetic and surgical procedures (preoperative/preprocedure planning and critical evaluation of outcomes).
- For data exchange, teaching, publications and presentations.
- As legal documentation—a good photograph leaves no doubts.

When performed properly, standard photography can accurately illustrate the subtle differences between the before and after, so the medical photography differs from "snapshots" [4]. These are photographs taken at random, informally, where the photographer does not care about eliminating details that can "pollute" the image, like makeup, accessories, clothing, background, which can divert attention from what you really want to show.

In this chapter, we'll be discussing some aspects that should be considered in order start practicing medical photography, such as:

- The choice of the appropriate equipment.
- Considerations about the adequate photographic technique, since the picture must provide color consistency and accuracy, as well as other aspects of the skin.
- Establish a photographic routine, with specific criteria of standardization of the images.

Equipment

Nowadays, advances in the digital technology field have resulted in more affordable equipment with advantageous cost effectiveness, when compared to the 35 mm cameras. Like computers, digital cameras are constantly becoming cheaper, faster and better [5]. There are many models of cameras on the market, from the most simple to professional cameras, which require extensive knowledge of the equipment for the right use [6]. It is important to remember that, in

the case of digital cameras, the electronic sensor takes the place of the film. Hereafter, we list some aspects that should be taken into consideration before purchasing a camera. To choose the equipment, you should keep in mind:

- Do you need a simple or a sophisticated camera?
- What do you want to shoot?
- Do you want to use analogical or digital technology?

Here are some information to help you decide:

Compact Cameras

Advantages

- Hundreds of models available.
- Are usually point-and-shoot type, that are ready to shoot as soon as the on/off switch is triggered.
- Have some parameter settings in the manual navigation menu, besides the automatic settings.
- Some models feature Leica or Zeiss lenses, two major manufacturers of high quality lenses.
- Tend to be cheaper than the professional and semi-professional cameras.

Disadvantages

- Do not allow to switch lenses.
- May have shutter lag, which is a delay that occurs between pressing the button and the moment the picture is taken (to avoid this, simply push the on/off button halfway to allow the camera to focus and then, push all the way through) [7].

Digital Single Lens Reflex (DSLR)

Advantages

- The image produced by the lens and viewed on the display corresponds exactly to the image formed on the sensor, thanks to a mechanism of mirrors inside the camera.

- The lenses are interchangeable, and there are several accessories that help upgrade the equipment.
- There is a choice of automatic and manual control.

Disadvantages

- Are noisier, bulkier and heavier than compact cameras.
- Are more complex and therefore more difficult to use.
- Are generally more expensive than compact cameras.

So, how to choose? Keep in mind that the camera is just a tool, and with the basic knowledge of photographic technique you can get good pictures. Also, reading the instruction manual is crucial and helps to solve many questions, so this practice should be adopted.

The Photographic Technique

A good picture depends on several parameters that are complementary. The main factors are the diaphragm (or aperture), shutter speed and ISO. These three are called "the photographic triangle". Also, some knowledge of concepts such as focal length, color temperature, white balance, macrophotography and zoom also helps produce a good photographic material [8–10].

Diaphragm or Aperture

- Corresponds to the iris of the eye, i.e., the more closed, the less light passes through.
- Controls the amount of light reaching the sensor.
- Is directly responsible for Depth of Field, which is the area of focused image, which lies between the first and last image planes. See Figs. 30.1a, b and 30.2a, b.
- Represented by the letter F, the following numerical scale: 1.2—1.4—1.8—2.0—2.8—4.0—5.6—8.0—11—16—22—32—45—90.

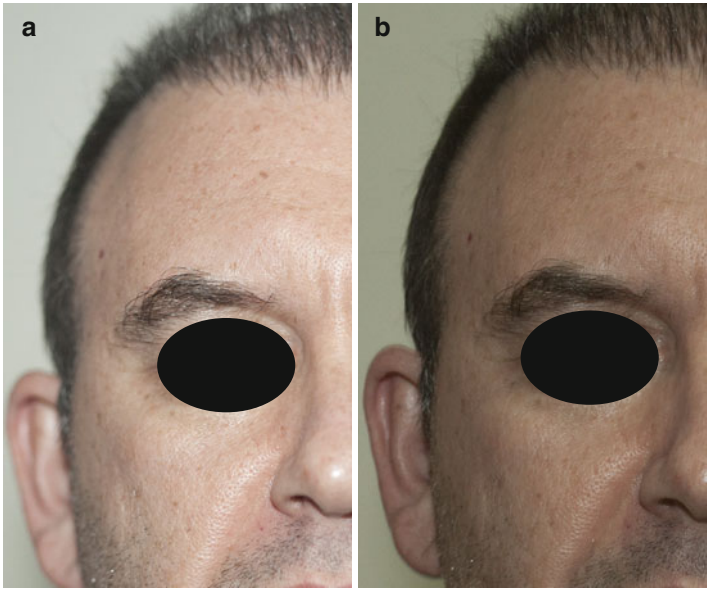


FIGURE 30.1 The photograph (**a**) was taken with an aperture of 2.8 (*f*2.8 = more opened), therefore, allowing more light to reach the sensor. It is slightly brighter than (**b**), which was taken with *f* 5.6. Another thing to notice is that the photograph (**b**) is more focused then (**a**), and this is because highest diaphragm aperture leads to less depth of field

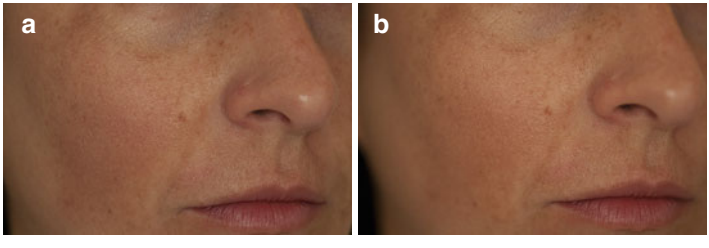


FIGURE 30.2 The depth of field on photo (**a**) is larger than (**b**), and we know that because the reflex of the flash on the tip of the nose is blurred on photo (**b**), and on photo (**a**) it's focused, so we see the reflex with more detail

- The lowest value corresponds to the largest opening of the hole, and thus allows the passage of a greater amount of light.
- As we progress towards higher values in the range, we observe a decrease in the orifice size, which leads to less light passage.
- The smaller the F number, the larger the hole size; the larger F-number, the smaller the orifice.
- For each point on the scale that we open (or decrease the number), we have twice the light reaching the sensor, and for each point we close, we reduce by half the amount of light. For example, from 2.8 to 4, the quantity of light falls by half, and from 22 to 11, it doubles the amount of light passing through the orifice.

Shutter Speed

- Corresponds to the lids, opening and closing at different speeds.
- Determines the exposure time (the time interval during which the sensor is exposed to light).
- Represented by a scale in seconds: B—30″—15″—8″—4″—2″—1″—1″/2—1″/4—1″/8 (…) 1″/30—1″/60—1″/125—1″/250 (…) 1″/4,000.
- At the lowest, B, the shutter stays open indefinitely allowing the entry of light. Thereafter, the value will decrease from 30 s (to close, which is slow) until 4,000 parts of a second, which is extremely fast, and therefore the amount of light that reaches the sensor is very small.
- The lower the speed, the slower the shutter closes and the image is brighter or overexposed.
- The higher the speed, or faster the shutter closes, and the image is darker, or underexposed.
- It relates directly to the registration of movements:
  - when it closes slowly (long exposure time) the image is blurred,
  - fast speed (short exposure time) freezes the movement.
- The use of a camera tripod avoid blurred images in the case of speeds lower than 1″/60. See Fig. 30.3.

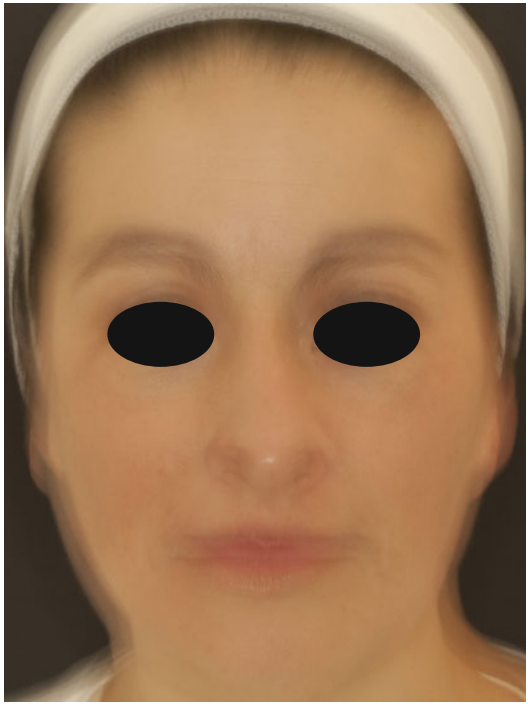


FIGURE 30.3 The image is blurred because the shutter speed is low, meaning long exposure time. To avoid this, it is better to use the camera on a tripod

- The ratio between the diaphragm and the shutter speed is inversely proportional: lower F number (aperture) = more opened = more light passin through. So, in order to avoid overexposure, the shutter closes faster (to compensate). See Fig. 30.4a–c.

International Standards Organization (ISO)

- Determines the sensitivity of sensor.
- Must be adjusted according to the ambient brightness, however, is fixed in the films.

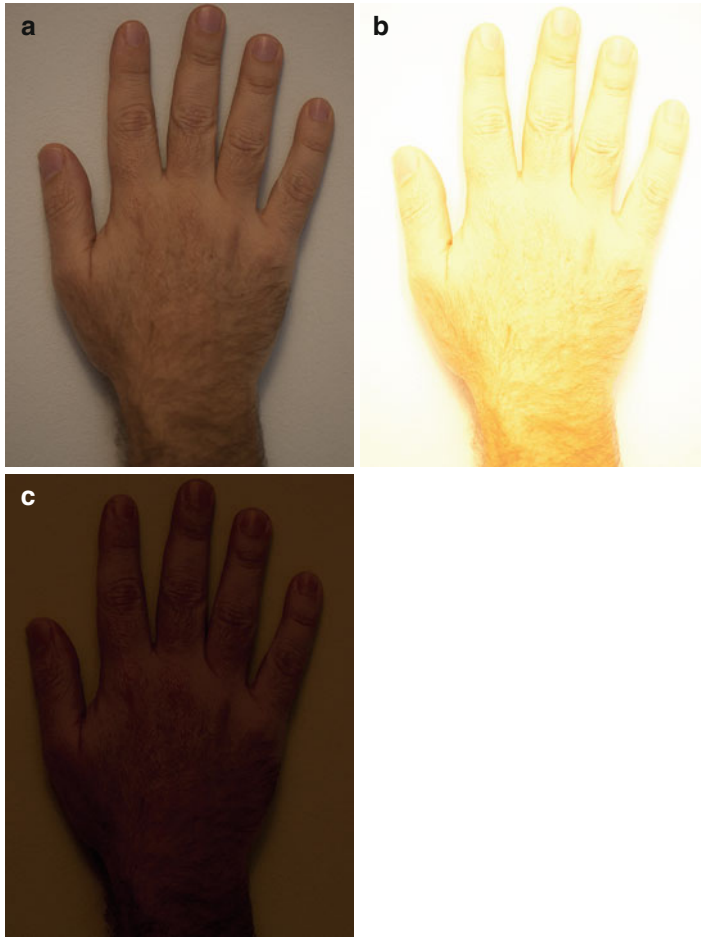


FIGURE 30.4 (**a**) Correct photometry; (**b**) overexposed (more light reached the sensor, thus the image is too bright); (**c**) underexposed (less light reaches the sensor, thus the image is too dark)

- It presents in a scale: 100—200—400—800—1,600 to 3,200 (…), until up from 20,000 in professional cameras.
- Above 400, we observe a grainy image ("noise"), which corresponds to the loss of sharpness by insufficient lighting, as in night shots.

- ISO is equivalent to the ASA (American Standards Organizations) of the films.

The ISO, the aperture and the shutter speed work together one compensating each other, thus determining the photometry, which is the measure of the amount of light that reaches the sensor. When the ISO is placed in a basic value (100), the aperture and shutter speed automatically adjust themselves, or as the value of one them increases, the other decreases. When the ambient light is low, adjusting the ISO to a higher value, we are able to maintain the relationship between aperture and shutter speed.

Focal Length (FL)

- Measured between the optical center of the lens (point at which light rays intersect) and the focal plane (the plane of the sensor or film).
- Determines the range of capture of the lens, and is represented in angles.
- The higher the FL, and the smaller the angle the larger the image that is formed.
- According to the angle, the lenses are classified into:
  - Large angle: 55° and more (includes "fish eye" which has FL < 21 mm and distorts the image edges),
  - Normal: between 43° and 55° (includes FL = 55 mm),
  - Telephoto: 43° and less (includes FL larger than 70 mm).
- A lens with FL of 50–55 mm is considered standard because corresponds to the image captured by the human eye (same angle of vision). It is good for the full body shot, but not for close ups because its wide-angle coverage distorts the image. It is a good investment for the beginners, though it usually accompanies a basic DSLR kit.
- There are two important concepts based on the focal length: macrophotography and zoom.
- **Macrophotography**: very important because it allows the photographer to shoot closer, registering a very detailed image
  - Reproduces the image in real size (1:1) or greater
  - FL ranges from 60 m (ideal = 90–110 mm)

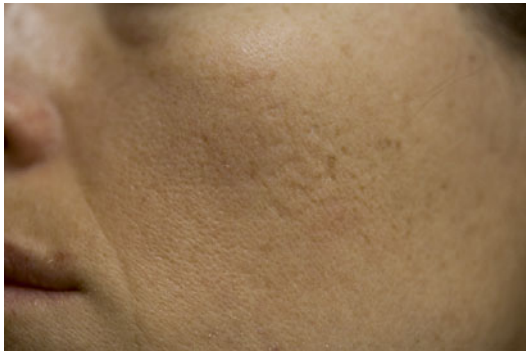


FIGURE 30.5 Macrophotography: allows taking photographs from very short distances, showing details on a real size scale

  - Macro lenses are designed for close-up photos, thus the images have flat edges, without distortion (normal perspective). These lenses are generally more expensive. See Fig. 30.5.
  - False macro or macro function (universal symbol = flower): present in compact cameras, they take pictures at a distance between 2 and 5 cm but the image is distorted, with rounded edges and blurry (aberrations), and the size on the sensor is close to the actual image size. See Fig. 30.6a, b.

- Zoom: is the way to get closer to the photographed subject without moving closer [11]. It can be:
  - Optical: physically extends the lens (the focal length changes) to magnify the subject, without changing the image quality.
  - Digital: "cuts" the image into smaller sizes and increases the resulting image to fit the frame. This process is known as interpolation and leads to loss of image quality, so it must be avoided.

When purchasing a camera, it is important to make sure that it has optical zoom.

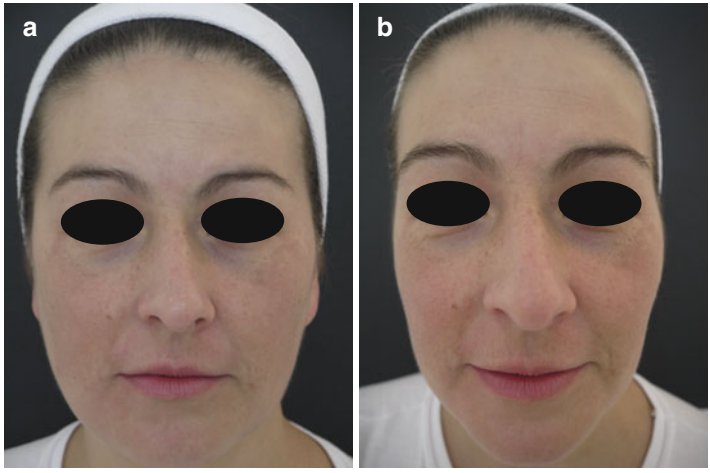


FIGURE 30.6 (**a**) Normal perspective on portraits; (**b**) the misuse of the macro function may lead to optical aberrations, like distortion of the image

Color Temperature and White Balance

These are two important concepts and should be well understood, regardless of the lighting technique employed. Different white light sources used in photography vary from an ordinary domestic light bulb (rich in red and yellow and weak in blue) teletronic flash (contains more energy in blue then in red). For most sources, it can be attributed a color temperature, measured in "kelvin" (K): the higher the kelvin value, the bluer the light. So, we have:

- Sunlight at noon: high color temperature, rendering a bluish coloration.
- Dusk and dawn: low color temperature, rendering an orange coloration.
- Flash Light: similar to the midday sun, so it corrects tungsten lighting.

We must be careful to match the color temperature of the light source to the sensor, or what is adjusted on the camera. The white balance is a function that defines to the camera what is white, because it removes colors that are not real. There are semi-automatic adjustments for each type of light, so the WB should be adjusted according to each environment. See Fig. 30.7a–e.

Lighting

In addition to the photographic technique, the ambient where photographs will be taken must be prepared. It is important to note the following aspects:

- Source of light: artificial or natural (as a window, for example). See Fig. 30.8.
- Background: must be plain and have a neutral color, so it doesn't interfere with the skin color by reflection.
- Position of the camera: distance and angle to the patient.
- Position of the patient: should be comfortable and close to the background, but not to close.

Light plays a critical role in accurate description of coloration and contours of the skin. There are six important features of lighting, according to the light source:

- Quality: can be measured by the type of shadow it makes the photographed object throw. It depends of the size of the source relative to the distance of the object. When the light falls directly on a surface coming from a single source, it is called "hard", and results are well-marked shadows (high contrast between light and dark shadows area), which enhances the marks of expression and emphasize contour changes. However, when the light falls diffusively, coming from many directions, it forms softer shadows.
- Direction: determines where the shadow will fall, which affects the appearance of the texture. See Fig. 30.9a, b.
- Contrast: ratio between the brightness of the most lit areas and the darkest shadows.

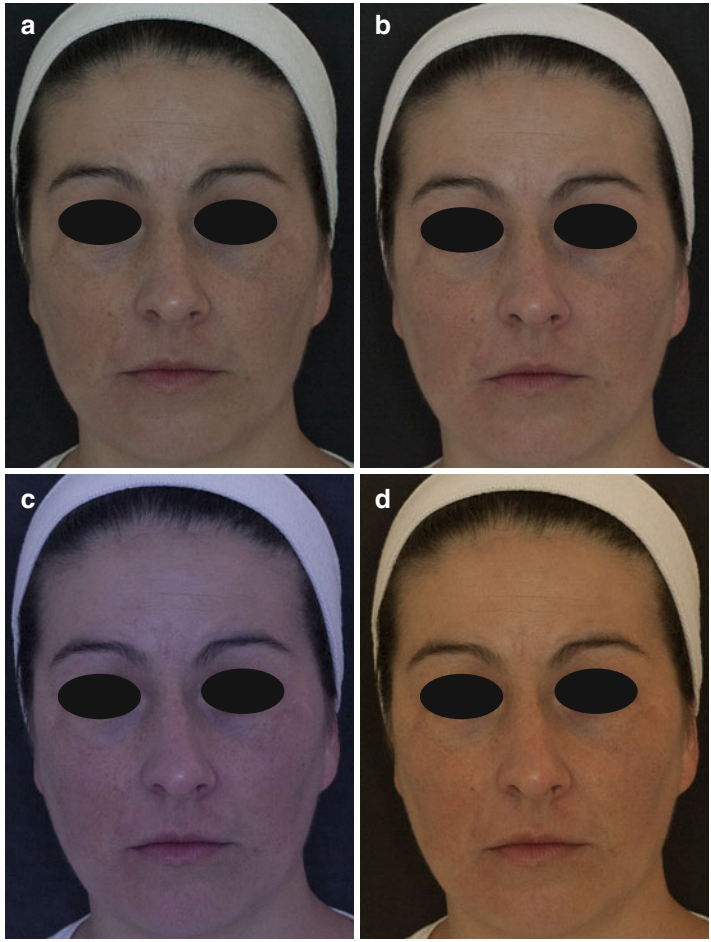


FIGURE 30.7 These photos show examples of how the color of the picture may be altered if one doesn't adjust the white balance (WB). Photo (**a**) *flash frontal:* the patient was photographed using a ring flash, and shows the correct color, as the WB was adjusted for flash; Photo (**b**) *flash lateral:* automatic white balance, which is slightly different from the real color, but is close enough, so, less trained eyes may not notice the difference; (**c**) WB on fluorescent light; (**d**) WB on daylight (or sun); (**e**) WB on tungstein light

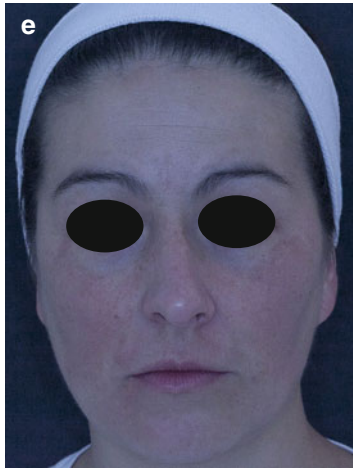


FIGURE 30.7 (continued)

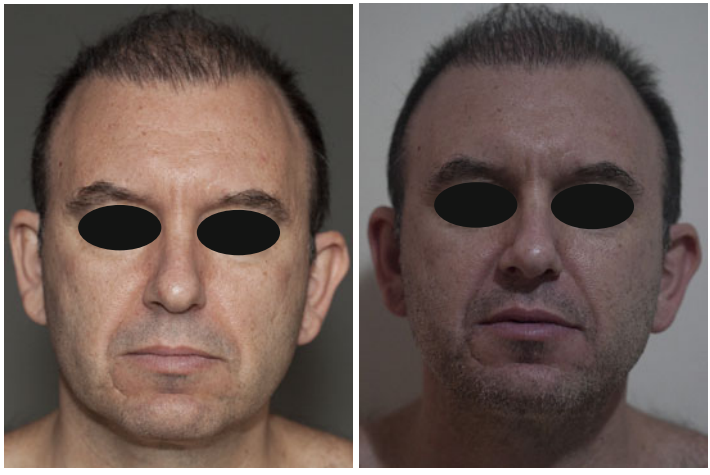


FIGURE 30.8 The patient was photographed in ambient light (small light bulbs positioned in the *middle* of the ceiling). Notice the bizarre shadows that are formed under the eyes, nose, chin and neck, and how hard the expression marks appear around the mouth

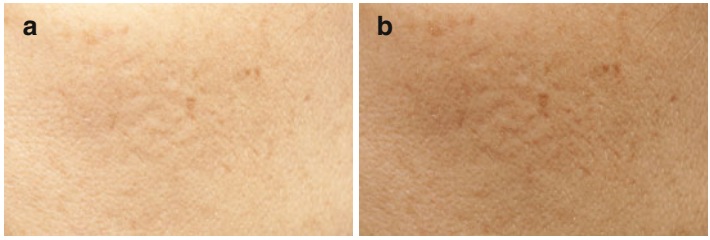


FIGURE 30.9 (**a**) Macrophotography using frontal flash bulb, which gives a more bidimensional aspect to the image, because the frontal light affects the texture; (**b**) macrophotography using lateral flash bulb, that allows to observe the right texture

- Unevenness: produced when a hard light source is used too close to the subject, thus the parts of the subjects nearest the light source are brighter then the farther ones.
- Color: as discussed before, it is important to match the color of the light source with the CCD or film, and the necessary corrections must be done.
- Intensity: or brightness. The camera's exposure settings, the sensitivity of the CCD or film control the brightness of the image. The light level indirectly affects depth of Field and movement blur.

For a medical photography, the skin should not be too dark or too bright, what would make it difficult to observe the changes. In our daily practice, we usually have the following types of light:

- Natural (window): promotes uneven lighting. It is important to remember that the light of noon is bluish while at the beginning and at the end of the day it is reddish.
- Artificial, or light of the environment (ceiling, floor or table lamps): produce well-marked shadows under the chin, nose and around the eyes. Less light causes changes in exposure and reduces the appearance of wrinkles. Tungsten lamps cause color discrepancies in photographs.

It is very difficult to reproduce the photographs consistently, thanks to the many variables that must be taken into

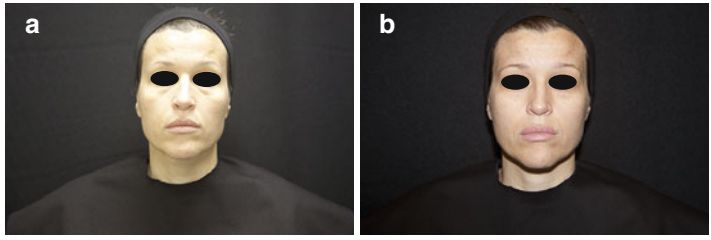


FIGURE 30.10 (**a**) Picture taken without flash, showing misplaced shadows and flaws on the background; (**b**) the flash corrects the ambient light. In this case, there is a shadow under the chin that doesn't interfere with the face. To avoid the shadow, the camera (with the flash bulb) should be positioned a little bit lower (the eyes of the photographer should match the height of the patient's eyes)

account when shooting with ambient light. That is the reason why we should consider the use of flash to correct the ambient light. See Fig. 30.10a, b. It avoids the heat and glare of tungsten lamps, giving more light in brief instants. The flash can be:

- built into compact and SLR camera bodies,
- add-on units like the ones attached to the camera (battery powered),
- studio flash units (electricity or battery powered). These are more powerful than the built into cameras and accept accessories that enhance or attenuate the light they emit.

Regarding the functioning, they may be:

- Manual: you adjust the settings according to your necessities
- Automatic: the sensor measures the reflected light and controls its duration and intensity; or the sensor measures the reflected flashgun's light that passes through the lens (TTL).

Tips for using the flash:

- Leave the ISO at 100. If higher, the sensitivity will increase and may produce very clear pictures, which hinders the observation of details.

- Avoid getting too close with built-into flashes as some features of the skin can be "erased" by excessive brightness.
- Using the add-on flashgun: getting too close to the subject may allow the formation of a shadow when the light of the flash hits the lens.
- In an environment with white walls and ceiling, the flashgun light will be bounced, increasing the intensity of the light, and the image becomes too bright. This can be avoided by closing the aperture (or increasing of F number).
- In dark environments, the pupils are dilated and reflect the flashgun light (red eyes). To avoid this, ask the patient to look for another light immediately before shooting.
- To reduce the glare caused by light reflected from the skin, remove oiliness from the area to be photographed.
- To soften the light emitted by the flash, you can attach a white piece of paper or diffusers, like soft boxes and umbrella reflectors (studio flash units), which gives soft, diffused lighting.
- A single flash unit positioned in front of the patient tends to brighten the image too much, which blemishes the wrinkles. The correct is two flash units diagonally positioned to the patient. Also, the ring flash is a good option, but leaves the image with two-dimensional aspect (too flat, without perspective).

Digital Image

The digital image photography replaced the conventional film in terms of its clinical use, and is part of the medical record.

The light that enters through the lens is captured by the electronic sensor to form the digital image. Rather than focusing on a piece of film as an analog camera, the light focuses on a semiconductor device that records the image electronically. The sensor is a silicon chip with millions of photosensitive elements, called *pixels* (from picture elements) [12]. There are two types of sensors:

- CCD (charged-coupled device)
- CMOS (complementary metal-oxide semiconductor)

The pixels are:

- responsible for converting the light captured by the lens into electrical signals (electrons) that will be processed to form an image,
- the smallest element of a digital image, thus, the image will formed by millions. —their number is directly related to the image resolution: the more pixels, the larger the size, and the more detail and better quality registered (or higher resolution). The importance of this is that a high-resolution image can be magnified or printed maintaining the sharpness.

The sensor is arranged as a chessboard, and the number of megapixels is calculated multiplying the horizontal by the vertical pixels. For dermatological use, cameras with sensors from 3 to 6 MP should be enough.

Examples of resolution:

- 640×480 resolution relatively low, good for e-mail or websites;
- $1{,}216 \times 912 = 1$ MP, good for printing, for phone and computer publications;
- $1{,}600 \times 1{,}200$ high resolution, good quality printing up to 4×5 in.;
- $2{,}240 \times 1{,}680 = 4$ MP, very good quality prints up to 16×20 in..

File Formats

Every image formed on the sensor generates a file. The higher the number of megapixels, the larger the size of the files and the more space is taken on the memory card. The digital camera uses three different types of files:

- JPEG (Joint Photographic Expert Group), the international standard, is an algorithm that compresses the image, making it much smaller without significant loss of resolution, and therefore occupying less space.
- TIFF (Tagged Image File Format) is considered industry standard file and is larger than JPEG.

- RAW format is widely used in the context of DSLR, and refers to files minimally processed that do not compress the image. It maintains the best quality of the image since there is no loss of pixels, and that is why it is called digital negatives: they contain all the information necessary to form the image. There isn't a standard RAW, and each manufacturer uses its own version.

The number of megapixels in a camera determines the final print size, which is measured in dpi (dots per inch), which refer to the density or the proximity of the dots the printer can print within a square inch. By default, images are saved at a resolution of 72 dpi, but using image editing software, it can be converted to 300 dpi, which is the normal for a digital print not to be distinguished from a film print. This supposes a normal vision and an average distance from the printed image.

Storage

The security of images is dependent on the location as well as accessibility of the storage device [13]. Proper storage of the photographs is important to prevent the loss of images.

In digital cameras—using the memory cards:

- They are the "films" that the digital cameras use to record the image.
- Can be erased and reused.
- Range in storage size from 8 MB to 64 GB.
- Greater capacity = more photos (keep in mind that the photograph taken using a 12 MP camera will require more memory space then one taken using a 6 MP).
- Higher speed = less time reading and writing.
- More megapixels + faster = more expensive.
- Important to notice the quality when purchasing, since memory cards can crash.
- There are various formats to consider: compact flash (CF), secure digital (SD), memory stick and xD cards [14].

On the computer—download the image using a media card reader or directly from the camera.

- Image editor (for reviewing, choosing the best ones, and add data).
- Organize in folders (preferably using the initials of the name to protect the privacy of the patient).
- Always back up for safety—external hard drive, DVD, CD, flashdrive.

Standardization of Images

Standardized and quality images will enhance the credibility of the treatment [15]. The only variable among photographs taken to show changes over time should be in the patient, and everything else should stay the same [16]. For comparison purposes, the medical photography requires standardization of images referring to the photographic technique, the lighting and the patient. It is important to establish a routine observing the following:

- Informed consent for the patient to sign.
- Patient identification in all pictures.
- Lighting/exposure—must be the same in the before and after pictures. Here are some tips:
  - leave the camera on autofocus;
  - for close up shots, use macro lenses or macro function (on compact cameras. In this case, to avoid distortion, zoom in and get closer to the subject);
  - use the flash whenever possible to correct the lighting of the room, but don't get too close to the photographed area, otherwise the image will be too bright and the details will disappear;
  - for close up photos, oblique positions are preferable.
- Background: neutral color (black, blue, grey, white). Any factor that distracts attention from what you are photographing should be eliminated.
- Patient: garment, accessories and make up should be removed. The hair should be held back or hidden in a cap.

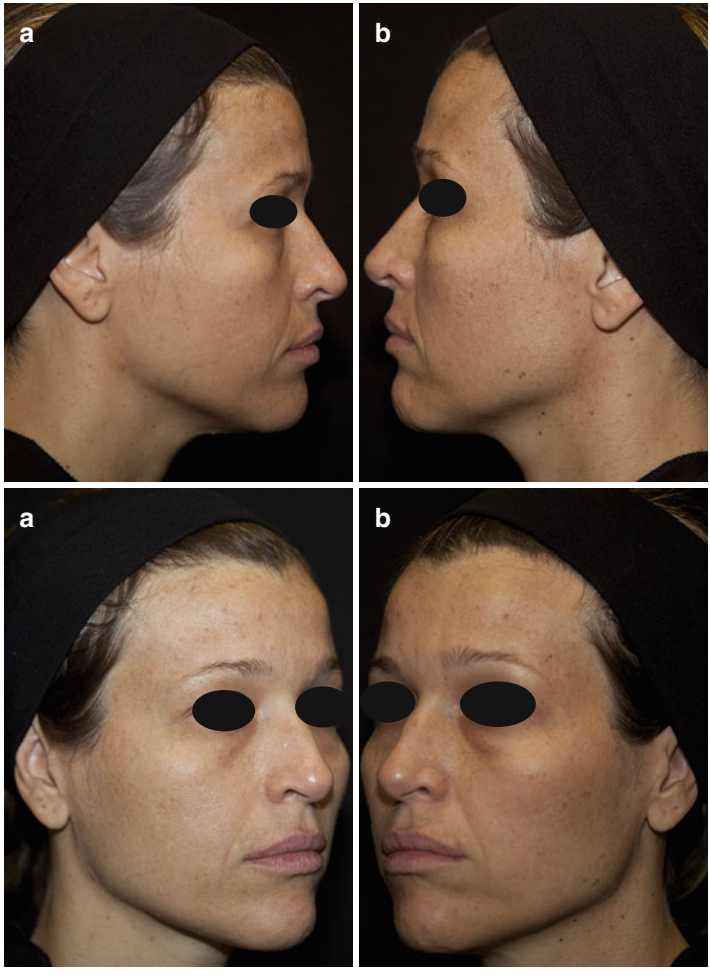
- Camera angle.
- Always take two photos of each area/position focused in case one of them blurs, because a blurred image isn't always noticeable on the LCD.
- Positioning of the patient and the physician: keeping in mind the comfort of the patient, always use:
  - the same perspective,
  - the same proportion ratio,
  - the same camera settings and lighting parameters.

Final considerations about the patient's position:

- Facial expressions must be neutral since movements of the muscles may enhance or reduce expression marks.
- The look should be directed to front.
- The head should be in a natural position and the neck shouldn't be neither flexed nor extended to avoid false impression of volume.
- Large areas or whole body: a series of at least three photos—vertical framework of the entire body, the average distance and close up.
- Small areas: a photo midway, including a recognizable area of the body and a closeup.
- Isolated areas: close up, including a recognizable point of the body, using measuring tape to indicate the size of the area/lesion. Take a picture of more than one angle, and with and without flash, selecting the one that best represents what you want to show. See Figs. 30.11a, b and 30.12a, b.

Legal Aspects

Legally, the original digital image is the data first recorded in memory, thus any printed or displayed image created from this data is a copy [17]. Thereby, it is important to photograph in RAW. However, the storage and manipulation of digital photographs has led to the growing interest and increasing concerns to the reliability of the images, as well as the preservation of the confidentiality in the era of teledermatology, an



FIGSURE 30.11A, B AND 30.12A, B (**a**, **b**) Suggested positions for lateral portraits and photographs

aspect of telemedicine that involves dermatology. Physicians using digital technology must be aware of the myriad legal ramifications [18]. Therefore, it is very important to sign an informed consent, and to avoid the misuse of software that could change the real aspect of the images.

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Chapter 31
Future Directions in Lasers and Lights

Heather K. Hamilton, Nazanin Saedi, and Jeffrey S. Dover

Abstract Exciting research is underway that will continue to advance the field of lasers in cutaneous medicine. This chapter outlines much of this important work. We will focus on new lasers for various cutaneous targets (such as vessels, pigment, hair), lasers as a delivery system for topical medications, a device that can help optimize treatment parameters, and lastly, a non-laser device that may represent a new generation of devices in photomedicine.

Keywords Future directions • Picoseconds • Delivery of medication • Optimizing outcomes • TRASER

H.K. Hamilton, MD (✉)
Waldorf Dermatology and Laser Associates,
57 North Middletown Road, Nanuet, NY 10954, USA
e-mail: heatheraklein@yahoo.com

N. Saedi, MD
Department of Dermatology and Cutaneous Biology,
Thomas Jefferson University, 833 Chestnut Street, Suite 740,
Philadelphia, PA 19107, USA
e-mail: nazanin.saedi@jefferson.edu

J.S. Dover, MD, FRCPC, FRCP
SkinCare Physicians, 1244 Boylston Street, Suite 103,
Chestnut Hill, MA 02467, USA
e-mail: jdover@skincarephysicians.net

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Introduction

Exciting research is underway that will continue to advance the field of lasers in cutaneous medicine. This chapter outlines much of this important work. We will focus on new lasers for various cutaneous targets (such as vessels, pigment, hair), lasers as a delivery system for topical medications, a device that can help optimize treatment parameters, and lastly, a non-laser device that may represent a new generation of devices in photomedicine.

Targets

Vessels: Improving Outcomes in the Treatment of Port Wine Stains (PWS)

- Port wine stains are commonly treated with pulsed dye laser (PDL) but achieving complete clearance is uncommon. When other lasers were studied for the treatment of recalcitrant PWS, the millisecond 755 nm alexandrite laser was shown to be the most effective but had a higher risk of hyperpigmentation and scarring [1]. A subsequent small observational study aimed at optimizing the parameters for treating PWS using this device demonstrated efficacy and a low risk of adverse effects using a low fluence, large spot size and pulse stacking [2].
- Laser Speckle Imaging (LSI) is a noninvasive method for monitoring blood flow, and Yang et al. demonstrated its potential use in assessing photocoagulation during laser treatment of PWS [3]. Subsequently, the investigators found that LSI of PWS during laser treatment provides real-time monitoring of skin perfusion dynamics and may assist clinicians in improving efficacy of PWS laser treatment [4].

Pigment

Improving Laser Tattoo Removal

- The gold standard for tattoo removal for the last two decades has been nanosecond domain (Q-switched) lasers, which typically require multiple treatments. Treatment with the first commercially available picosecond, 755-nm alexandrite laser has been shown to achieve up to 75–100 % clearance of blue and/or green pigment tattoos after one to two treatments [5]. In a study of multicolor and black tattoos, the average number of treatments needed to achieve >75 % clearance was 4.25, half the number of treatments needed historically [6].
- Research to optimize tattoo removal treatment with the traditionally used Q-switched (QS) lasers continues. Treatment with multiple passes per session has been shown, in one study, [7] to improve the speed of tattoo clearance, but it requires the resolution of the laser-induced whitening before each pass in order to be effective. Since the spontaneous resolution of the whitening reaction requires an average of 20 min, the repeat treatments at the same session (the R20 method) can be lengthy and impractical. Recently, application of topical perflurodecalin was shown to clinically resolve whitening reactions within 10 s and thereby allow multiple pass treatment in on average 5 min (R0 method) with the same efficacy as the R20 method [8].
  - Perhaps adding the R0 method to treatment with the picosecond 755 nm-alexandrite laser might be one way to optimize laser tattoo removal. Whether repeat treatments on the same day is any better than a single QS laser treatment remains unclear. Stankiewicz and colleagues demonstrated that the R20 method was not significantly better than the standard single treatment

in a comprehensive trial that was presented at the Annual Meeting of the American Society for Lasers in Medicine and Surgery in 2012. In the study, each tattoo was divided into 4 quadrants. One quadrant was treated with the standard single QS treatment, one with the R20, another with the R20 followed by treatment with an ablative erbium:yttrim-aluminum-garnet (Er:YAG) laser, and the last quadrant with the R20, ablative laser, then followed by treatment with urea ointment (20 %) for 2 weeks. The R20, ablative laser, and urea treatment was slightly better than the standard treatment. The treatments with the ablative laser had greater risk for scarring and dyspigmentation [9].

New Treatments for Melasma

- Many treatments for melasma have been tried with varying degrees of success. Kauvar recently reported successful treatment using a low fluence, large spot size QS neodymium-doped yttrium aluminum garnet (Nd:YAG) laser preceded by microdermabrasion in combination with a hydroquinone based home skin care regimen in an observational study of 27 patients. Eighty-one percent of patients had >75 % clearance of their melasma and 40 % had >95 % clearance. The average number of treatments was 2.6 and remission lasted at least 6 months [10]. It appears that this technique works. The real question is whether this improvement is temporary or whether the treatment changes the natural history of the disease.
- In addition, treatment with a new low energy, low density non-ablative 1,927 nm diode laser (Clear and Brilliant Permea, Solta Hayward, CA) has been shown to result in significant improvement in melasma [11]. Prior studies demonstrated that fractional 1,550 and 1,927 nm lasers helped melasma. Improvement, however, may be temporary as recurrences have occurred [12, 13].

Depigmentation in Vitiligo

- While monobenzyl ester of hydroquinone (MEBH) is well established as a depigmentation therapy for patients with widespread vitiligo, lasers have also been explored for this purpose. Case reports have suggested safety and efficacy of the QS ruby laser [14, 15]. Recently, a case series was presented demonstrating greater than 75 % depigmentation in 23 of 46 patients when treated with a 694-nm QS ruby laser [16]. The 755-nm QS alexandrite laser has also been reported to achieve depigmentation in patients with vitiligo [17, Saedi oral communication February 2013].

Scars

Improving the Treatment of Acne Scars

- Nonablative fractionated lasers are a mainstay of acne scarring treatment. The parameters, however, are still being optimized. Since some acne scars are thought to be deep, some investigators find high energy (70 mJ) with very high density (70 %) to be more efficacious than low energy and low density [18] while others have found no difference in results when higher energy/deeper treatments (70 mJ/1,300 μm deep vs. 40 mJ/600 μm deep) are used [19].
- Ablative fractional resurfacing has also been shown to be effective for treatment of acne scars and may achieve more dramatic results with fewer sessions, but is associated with more downtime and risk [20, 21]. Minimizing such risk is the subject of study. For example, application of clobetasol ointment for 2 days after ablative fractional CO_2 laser resurfacing for acne scars in Asian patients resulted in decreased incidence and severity of PIH [22].

- Other lasers have also been found to be useful in the treatment of acne scarring including the 755 nm Alexandrite picosecond laser [23]. After three treatments with the 755 nm Alexandrite picosecond laser, 10 of 15 patients demonstrated greater than 50 % improvement in texture and appearance of their acne scars. Treatment was done without pre-procedure anesthesia, and downtime was limited to transient erythema [23].

Improvement in Treating Surgical Scars

- The 595 nm PDL and non-ablative fractional lasers are useful in the treatment of cosmetically unsatisfactory surgical scars [24, 25]. Non-ablative fractional resurfacing with micro-compression optics may provide additional improvement by enabling deeper penetration and creating deeper columns of injury [26].

Improving Functional Impairment in Scar Contractures

- In addition to providing cosmetic improvement in scars, lasers have recently been shown to offer functional improvement in scars. Kineston et al. [27] reported full return of range of motion when a contracture that was related to morphea (a scar-like process) and recalcitrant to multiple treatments was treated once with a fractional ablative CO_2 laser. The same group reported functional improvement in a scar contracture with a series of fractional ablative resurfacing [28].

Fat

- Noninvasive body contouring has become a well sought after cosmetic procedure. Cryolipolysis and high-intensity focused ultrasound are frequently being used to reduce unwanted pockets of fat. Lasers also show promise in

treating lipodystrophy as well. Anderson et al. [29] found selective absorption of fat at a variety of wavelengths including 1,206–1,214 nm. Subsequently, they found histological evidence of laser-induced damage of fat in a human pilot study using a 1,210 nm laser [30]. There is ongoing research to further study the potential of this laser in noninvasive fat reduction. It appears the exposure duration can be adjusted to include or avoid damage to the lower dermis [31].

Hair

- Laser hair removal is a popular cosmetic procedure but is traditionally accompanied by discomfort even with the use of pretreatment topical anesthesia. Technology aimed at increasing tolerability while maintaining efficacy has been a focus of recent laser hair removal research. A long-pulsed 800-nm diode laser with a large spot size and vacuum-assisted suction (Light Sheer Duet HS, Lumenis, Santa Clara, CA) has been shown to be safe and effective and associated with mild to moderate pain without the use of pretreatment anesthesia [32]. An 810-nm laser with low fluence and high average power with an 'in motion' multiple pass technique (Soprano XL SHR, Alma Lasers, Buffalo Grove, IL) has been shown to be even more tolerable and efficacious [33].

Tumors

- Studies using CO_2, diode, pulsed dye, Nd:YAG, and alexandrite lasers alone or in combination in single and multiple treatment sessions show potential in the treatment of basal cell carcinomas and squamous cell carcinomas in situ [34, 35]. While not a widely accepted treatment option at this time, research continues to further elucidate the role of lasers in the treatment of nonmelanoma skin cancers [36].

Onychomycosis

- Much research has been done to investigate the role of lasers and light therapy in the treatment of onychomycosis [37]. Bornstein et al. showed photoinactivation of fungus in vitro and in a human pilot study with a combined 870 and 930 nm laser system [38]. The same group subsequently performed a randomized controlled study involving 37 affected nails treated with the combined 870 and 930 nm lasers for four sessions. They found that 60 days after the last treatment, 39 % of the treated nails had a negative culture and at least 3 mm of clear nail growth although this was not statistically different from the control group [39].
- In recent years, the 1,064 nm Nd:YAG has shown promising results [40, 41]. It appears that rather than working by selective photothermolysis, laser treatment of onychomycosis works by using heat to nonspecifically kill fungi. The Nd:YAG lasers are well suited for this purpose because their wavelengths are not well absorbed and hence much of the energy delivered is converted to heat.
- In a randomized, placebo-controlled study, four treatments with the 1,320 nm Nd:YAG laser were associated with mycologic cure in 50 % of toenails treated [42]. Further investigation is needed to determine the most effective device, parameters, and treatment schedule and to compare laser and light based treatment to traditional onychomycosis therapies.

Hyperhidrosis

- Lasers have recently been explored for their potential use in the treatment of axillary hyperhidrosis. While a study with an 800-nm diode laser failed to find significant reduction in sweat rate [43], the Nd:YAG laser shows more promise [44, 45]. In a pilot study of six patients, Letada et al. found improved measures of sweating using a

long-pulsed Nd:YAG 1,064 nm laser at hair reduction settings [44]. Furthermore, results may be durable. In a study with a 1,440 nm Nd:YAG, those who responded with one treatment maintained their improvement at the 1 year follow-up [45].

- Other energy devices have been studied for their potential role in treating axillary hyperhidrosis. A microwave device (miraDry System; Miramar Labs, Sunnyvale, CA) has recently been FDA approved as an effective treatment for axillary hyperhidrosis. It appears to work by selectively heating the layer of skin where the eccrine and apocrine glands reside with results that persist for at least 1 year [46, 47].

Delivery of Medication

- Ablative fractional resurfacing is being investigated for its possible role in the delivery of topically applied drugs to the skin. The vertical channels of ablated tissue created by ablative fractional lasers may enable topical medications to achieve greater penetration and therefore better efficacy. In animal studies, pretreatment with a fractional CO_2 laser facilitated the delivery of topical methyl 5-aminolevulinate (MAL) into the skin [48] and enhanced its uptake and photoactivation [49]. Similarly, pretreatment with a fractional Er:YAG was found to improve the percutaneous delivery of imiquimod [50]. A recent study demonstrated that fractional CO_2 laser treatment facilitates uptake of molecules with molecular weights ranging from 400 to 3,350 Da into and through human skin and that laser density can be adjusted to optimize delivery [51].
- In clinical studies, ablative fractional resurfacing prior to photodynamic therapy (PDT) with MAL for actinic keratoses was found to be more effective than either PDT [52] or ablative resurfacing alone [53]. Research is underway to further investigate the role of ablative resurfacing in enhancing the percutaneous uptake of other topical drugs

such as ingenol mebutate [54] and in allowing for absorption of molecules that could otherwise not penetrate the stratum corneum such as poly-L-lactic acid in the treatment of atrophic scars [55].
- Nonablative fractional resurfacing may also enhance uptake of topical applications as shown in a study of a low fluence, low density 1,927 nm laser with an antioxidant serum [56].

Instruments to Optimize Laser Treatments

- The Skintel Melanin reader (Palomar Medical, Burlington, MA) is a device that uses an objective measure of skin melanin content to guide IPL treatment parameters to maximize effectiveness and avoid complications [57, 58]. The Skintel device works by measuring the skin diffuse reflectance at three wavelengths (640, 700, and 910 nm). These values are computed into a Melanin Index Value. The Melanin Index Value then suggests a range of fluences for a pulse duration that the provider selects. Further testing has led to refinement in the recommended settings [59].

Total Reflection Amplification of Spontaneous Emission of Radiation (TRASER)

- Total reflection amplification of spontaneous emission of radiation (TRASER) is a device that uses energy from a flashlamp to induce spontaneous emission of photons from a fluorescent dye or crystal. Compared to a laser, a TRASER is simpler in design, is more ecofriendly and safer than corresponding dye lasers, and can mimic lasers with a wide range of wavelengths and pulse durations [60]. Current work is being done to further elucidate its clinical applications. Treatment with a 544 nm wavelength resulted in histological intravascular thrombosis of nearly all the

vessels in the fields of view. Treatments with a 654 nm wavelength resulted in acute follicular changes similar to those seen with laser hair removal and were limited to the target structures [61].

Conclusions

The field of lasers and lights continues to evolve. Innovative research and well-designed studies will help to advance our capabilities to improve treating dermatologic disorders and cosmetic concerns.

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