



LASER-tissue interactions

Lisa Carroll, MD^b, Tatyana R. Humphreys, MD^{a,*}

^a*Department of Dermatology and Cutaneous Biology, Jefferson Medical College of Thomas Jefferson University, Philadelphia, PA 19107, USA*

^b*Dermatology LTD., Media, PA 19063, USA*

Abstract As new laser devices continue to emerge, it becomes increasingly important for the clinical dermatologist to understand the basic principles behind their operation. A fundamental understanding of how lasers interact with tissue will enable the physician to choose the most appropriate laser for a given clinical situation. Although the physical laws guiding laser design are vastly complex, the fundamental principles of laser-tissue interaction can be summarized as they are applicable to the clinician.

© 2006 Elsevier Inc. All rights reserved.

LASER-tissue interactions

The role of lasers in dermatology has increased dramatically over the past two decades. A fundamental understanding of laser-tissue interactions is vital for the proper and appropriate use in clinical practice. Several excellent review articles have been published addressing principles of laser physics.¹⁻⁷ This review will focus on concepts with particular relevance to the clinician.

Properties of laser light

The word *laser* is an acronym for *light amplification by stimulated emission of radiation*. In the process of spontaneous emission, a photon will be emitted spontaneously from an excited atom after a given length of time. A laser uses a power source, a lasing medium, and a chamber to stimulate the emission of photons. In stimulated emission, an external power source creates excitation of the atoms in

the lasing medium. As unstable atoms release their photons, these photons collide with other excited atoms in the lasing medium and trigger a cascade of reaction resulting in numerous photons released at the same moment of identical wavelength, energy, and phase. As long as the population inversion to an excited state continues, the laser light continues to be amplified.

Laser light has several unique characteristics that differentiate it from other light sources. These key properties (monochromaticity, coherence, collimation, and high power) are the basis for the therapeutic applications of laser energy.

Non-laser light sources, such as intense pulsed light devices, emit light of many wavelengths modulated by a cutoff filter. Laser light, on the other hand, is monochromatic, meaning that all of the light emitted by a laser is of a single, discrete wavelength determined by the lasing medium (see [Table 1](#)). The monochromatic nature of laser light is a critical property for the application of laser technology in clinical practice because cutaneous chromophores selectively absorb different wavelengths. The specific wavelength of laser light also affects the distance it can penetrate into tissue. In general, the depth of penetration of laser light increases with increasing wavelength within the

* Corresponding author. Tel.: +1 215 955 4118.

E-mail address: tatyana.humphreys@jefferson.edu (T.R. Humphreys).

Table 1 Commonly used dermatologic lasers

Wavelength (nm)	Laser	Chromophore
308 (UV-B)	Excimer	DNA/RNA
532 (green)	KTP	Hemoglobin
585-600 (yellow)	Q-switched Nd:YAG	Tattoo ink (red)
	Pulsed dye	Hemoglobin
694 (red)	Q-switched ruby	Hematoporphyrins
	Long-pulsed ruby	Tattoo ink (black, blue)
755 (infrared)	Q-switched alexandrite	Melanin
	Q-switched alexandrite	Tattoo ink (blue, black, green)
	Long-pulsed alexandrite	Melanin
810 (infrared)	Diode	Melanin
1064 (infrared)	Q-switched Nd:YAG	Tattoo ink
	Long pulsed Nd:YAG	Melanin
1320 (infrared)	Long pulsed Nd:YAG	Water
1450 (infrared)	Diode	Water
1540 (infrared)	Er:glass	Water
2940 (infrared)	Er:YAG	Water
10,600 (infrared)	carbon dioxide	Water

spectrum of visible light. The depth of the target chromophore as well as the specific wavelength absorbed by that chromophore must be taken into account when one chooses a laser for clinical use.

Another unique characteristic of laser light is that the light is coherent, meaning that the waves of light are in phase with each other in both time and space. The coherent nature of laser light is due to the process of stimulated emission. As light is emitted from a laser, it is emitted in the same direction and in the same phase.

Collimation refers to the parallel nature of the waves emitted by a laser.¹ A laser creates a collimated beam by reflecting the light in a chamber between two mirrors that allows the exit of parallel waves only. Because the waves of light run parallel to each other, the tendency toward divergence is low. Owing to this organized pattern of light, a laser beam can be propagated across long distances via optical fibers without loss of light by spreading. In the clinical setting, the beam of light is directed at the clinical target using optical fibers or an articulated arm with a handpiece. The parallel light beam is then focused down to a diffraction-limited spot, or smallest possible spot, through a lens.⁴

The amplification process within the laser cavity produces a high power density. Power density is a function of energy, power, fluence, and irradiance (see Table 2). Energy and power both quantify the amount of light emitted from a laser. Energy, which is measured in joules, represents work. Power is the rate at which energy is expended (joules per second). Fluence refers to the energy density of a laser beam measured in joules per square centimeter. Irradiance, the power density of a laser beam, is the power of the laser beam divided by the area of the laser beam (spot size) and is

expressed as watts per square centimeter. Fluence and irradiance are directly proportional to each other (fluence = irradiance \times exposure time). By manipulating the fluence, irradiance, and exposure time, one can tailor the use of laser for specific clinical uses.

Laser-tissue interactions

Light can interact with tissue in four key ways: transmission, reflection, scattering, and absorption. Transmission refers to the passage of light through a tissue without having any effect on that tissue or on the properties of the light. Reflection refers to the repelling of light off the surface of the tissue without an entry into the tissue. Approximately 4% to 7% of light is reflected off skin.² The amount of light reflected increases with increasing angle of incidence with the least reflection occurring when the laser beam directed perpendicular to the tissue. If enough reflection occurs to create a high-intensity beam, damage to unintended targets could occur. For example, an errant 10,600-nm beam can cause damage to the cornea because of its water content whereas a reflected 595-nm pulsed dye laser beam can damage the retina because of its pigment content. Protective eye wear guards against reflected and direct exposure to laser light.

Scattering of light occurs after light has entered the tissue. Scattering is due to the heterogenous structure of tissue, with variations in particle size and the index of refraction between different parts of the tissue determining the amount of scatter. Scattering spreads out the beam of light within the tissue, resulting in radiation of larger area than anticipated. Scattering also limits the depth of penetration because it can occur backward as well as forward. In skin, most scattered light is due to interaction with dermal collagen. In general, the amount of scattering of laser light is inversely proportional to the wavelength of the laser. Longer wavelengths thus penetrate tissue more deeply. An exception to this rule is laser light beyond the mid-infrared region of the electromagnetic spectrum.⁵ Laser light with wavelengths above 1300 nm only penetrate superficially owing to the high absorption coefficient of tissue water.

Laser light absorption by specific tissue targets is the fundamental goal of clinical lasers. According to the Grothus-Draper law, light must be absorbed by tissue to produce an effect in that tissue. The absorption of the photons of laser light is responsible for its effects on the tissue. The components of the tissue that absorb the photons

Table 2 Measurements of laser output

Spot size	= laser beam cross-sectional area
Fluence	= watts \times seconds/cm ² = joules/cm ²
Irradiance	= laser output \times pulse duration / spot size
	= Watts/cm ²
	= laser output / spot size

preferentially depend on wavelength. These light-absorbing tissue components are known as chromophores. Frequently targeted chromophores in the skin include melanin, hemoglobin, and water, as well as exogenous tattoo inks. Absorption of energy by a chromophore results in conversion of that energy into thermal energy.

Selective photothermolysis

The theory of selective photothermolysis³ refers to laser energy absorption by a target chromophore without significant thermal damage to surrounding tissue. To achieve selective photothermolysis, the laser must produce a beam of light with a wavelength preferentially absorbed by the chromophore in the lesion. Equally important, the pulse duration of the laser beam must be shorter than the thermal relaxation time of the chromophore to prevent the spread of thermal energy beyond the targeted chromophore. The thermal relaxation time is defined as the time needed for the chromophore to cool to half of its peak temperature after laser irradiation, which is proportional to the square of the size of the chromophore.

In general, smaller objects cool faster than larger ones. For example, 0.5- to 1.0- μm melanosomes have a thermal relaxation time of approximately 1 microsecond whereas 10- to 100- μm capillaries have a thermal relaxation time of approximately 1 millisecond.⁵ If the pulse width is greater than the thermal relaxation time, nonspecific thermal damage occurs because of heat diffusion. Finally, the energy delivered to the site (fluence) must be high enough to destroy the chromophore within the pulse duration. Based on the theory of selective photothermolysis, the wavelength, pulse duration, and fluence of a laser can be tailored to result in selective damage to the lesions without nonspecific thermal damage to the surrounding tissues.

Lasers emitting visible light were designed on the basis of selective photothermolysis. These lasers include the pulsed dye, Q-switched ruby, Nd:YAG, and alexandrite lasers. The wavelength of each laser is preferentially absorbed by certain chromophores (see Table 1). Primary cutaneous chromophores targeted by visible light include melanin and oxyhemoglobin. Oxyhemoglobin has three main absorption peaks (418, 542, and 577 nm),^{6,7} whereas melanin has a broad overlapping absorption band ranging across ultraviolet, visible, and near infrared spectrum with decreasing absorption as the wavelength increases.⁸ Water absorbs mainly infrared laser energy. Depth of penetration affects the ability to treat certain chromophores at certain depths with certain wavelengths. For example, the dominant absorption peak for hemoglobin is at 420 nm, but this wavelength only penetrates to the dermal-epidermal junction (100 μm), which would limit use of a laser of this wavelength for cutaneous vascular lesions. The smaller absorption peak of oxyhemoglobin at 577 nm is more useful clinically because of the deeper penetration achieved at this wavelength.

Laser parameters and tissue interactions

Beam characteristics

An important feature of the light produced by a laser is how the intensity is distributed across the beam diameter. Most cutaneous lasers produce a beam with a Gaussian profile in which the intensity peaks at the center of the beam and attenuates at the periphery. Clinically, this results in the necessity of treating tissue with some overlap of the laser beam to deliver energy to tissue in a more uniform manner. Other modes of operation for lasers result in a doughnut-shaped or target-shaped distribution of energy delivery, with the intensity of the laser light at the edge of the beam being greater than in the center or fluctuating across the diameter of the beam.⁴ These modes tend to approach a more constant intensity profile, thus overlapping needs to be kept to a minimum to prevent over heating of the tissue at the periphery of the laser beam. These modes are somewhat limited in clinical use because of having a much larger minimum spot size than the fundamental mode.

Spot size

The spot size of a laser is equivalent to the laser beam cross section. The spot size directly affects the fluence and the irradiance of a laser beam, as mentioned above. Fluence and irradiance are inversely proportional to the square of the radius of the spot size. As such, halving the spot size increases the energy density or power density by a factor of 4. Spot size is also important clinically owing to laser scattering in the skin. A small spot size allows more scattering both backwards and sideways than a larger spot size. This results in a more rapid reduction of energy fluence in tissue than with a larger spot size. A large spot size of 7 to 10 mm is needed for maximal penetration of laser light to mid-dermal or deeper targets. Increasing depth of penetration levels off with spot sizes of 10 to 12 mm.

Pulse duration

Laser light can be delivered in a continuous wave or a pulsed wave. Continuous wave lasers emit a constant beam of light that may result in nonselective tissue injury. Pulsed delivery of laser light allows for more selective tissue damage. The duration of time of exposure to a laser beam determines the rate at which the laser energy is delivered. Pulse duration ranges from very short (nanoseconds) as in the case of Q-switched lasers to long (milliseconds) as in the case of hair removal lasers. The pulse duration of any given laser will be determined by the thermal relaxation time of the intended target (Table 3). The thermal relaxation time is generally proportional to the size of the target structure. For example, Q-switched lasers target very small structures with short thermal relaxation times such as melanosomes⁸⁻¹⁰ and tattoo ink¹¹ in the case of the Q-switched Nd:YAG laser. Increasing the pulse duration of

Table 3 Thermal relaxation times of common laser targets

Target	Size (μm)	Thermal relaxation time
Tattoo ink particle	1	10 ns
Melanosome	1	1 μs
Erythrocyte	7	20 μs
Epidermis	50	1 ms
Blood vessel	50	1 ms
Ectatic blood vessel	100	15 ms
Hair follicle	200	20-100 ms

a YAG laser increases its selectivity for larger structures as in the case of laser hair removal targeted toward pigmented hair follicles.

Surface cooling

When the chromophore contained in the target for ablation, such as melanin in a hair follicle, is located deeper in the skin than unintended targets such as epidermal melanin, the selectivity of the laser for its intended target can also be improved by surface cooling. There are three principal delivery methods for surface cooling: precooling, parallel cooling, and postcooling.¹² Precooling consists of cooling the temperature of the epidermis immediately before the laser pulse, usually by cryogen spray. In contrast, parallel cooling occurs at the same time as the laser pulse usually by use of a water-cooled sapphire tip. Parallel cooling is preferable for laser devices with longer pulse duration. Postcooling with ice helps reduce pain and edema but likely has little effect on the distribution of laser-induced thermal injury.

Photothermal ablation and nonablative dermal remodeling

Infrared lasers such as the carbon dioxide (10,600 nm) and erbium:YAG (2940 nm) lasers target water as a chromophore. Both ablative and nonablative infrared lasers heat tissue by using water as a target chromophore. The change in tissue temperature and the rate of heating determines the tissue response. Cellular injury with subsequent inflammation and repair occur after tissue temperature increases by only 5°C to 10°C.¹³ Deactivation of cellular enzymes occurs at temperature of 40°C to 45°C, with reversible damage that becomes irreversible with sustained exposure. Temperatures above 60°C lead to denaturation of most proteins, whereas further increases above 70°C lead to denaturation of DNA. Vaporization of tissue water with cell shrinkage, hyperchromasia, membrane rupture, protein denaturation, and collagen hyalinization occurs at temperatures of 60°C to 140°C. This results in coagulation, with blanching macroscopically. With sustained exposure to these temperatures, explosive vaporization occurs. At temperatures of 300°C to 1000°C, tissue ablation occurs with smoke generation.^{14,15}

Resurfacing lasers are high-energy pulsed lasers that generate photothermal ablation that occurs with rapid heating when tissue absorbs enough laser energy to cause the water in the tissue to vaporize. Damage also occurs in the tissue surrounding the ablated area due to thermal diffusion and scatter (zone of thermal damage). The CO₂ laser has a high absorption coefficient for tissue water¹⁶ that allows minimal residual thermal damage if the power density is significant enough to cause tissue vaporization that outpaces the speed of thermal diffusion; the energy delivered is less than the thermal relaxation time; or the fluence is only enough to result in only a thin layer of collagen being denatured.^{16,17} With each pass of the CO₂ laser, a predictable thickness of tissue is vaporized. The depth of ablation of the CO₂ laser is approximately 30 μm per pass^{16,18,19}; however, the underlying zone of thermal damage from heat diffusion is typically 300 μm or more because the thermal relaxation time of the 30- μm tissue layer heated by the laser is less than 1 microsecond.¹⁶

Collagen shrinkage and remodeling require an additional one to two passes after the initial pass results in epidermal ablation. The total depth of dermal injury consists of the thermally damaged base in addition to the thin layer of ablation.²⁰⁻²² The depth of ablation can be accurately controlled by adjusting the power, spot size, and number of passes used. Residual thermal damage gradually increases with each pass of the CO₂ laser while the ablation depth of each pass below the papillary dermis decreases due to decreasing water content. While increasing depth of dermal injury increases clinical response up to a point, overheating due to an excess number of passes or rapid overlapping of pulses can result in scarring. Overlap of the CO₂ laser spot should be 10% or less.²² The short-pulsed erbium:YAG laser has a higher absorption coefficient than that of the CO₂ laser, resulting in more efficient absorption of erbium laser energy by water-containing tissue.²³⁻²⁶ Given the higher coefficient of absorption of the erbium:YAG laser by tissue water, each pass produces a tissue ablation to a depth of 2 to 5 μm per J/cm² with an underlying zone of thermal necrosis of 10 to 15 μm . Pulse stacking does not seem to increase the depth of thermal damage in contrast to the CO₂ laser. Less depth of thermal injury results in shorter healing time with erbium:YAG laser treatment but less skin-tightening effect due to collagen shrinkage than the CO₂ laser.²⁷⁻²⁹ Modulated erbium:YAG lasers with extended pulse durations up to 500 microseconds result in larger zones of thermal necrosis compared with traditional short-pulsed laser systems. These larger zones of collateral damage result in enhanced tissue tightening effects approaching the CO₂ laser.^{29,30}

Nonablative laser resurfacing results in collagen remodeling by inducing selective heating of tissue water in the dermis without injury to the epidermis.³¹⁻³⁴ The fundamental difference compared with ablative lasers is the slower rate of delivery of laser energy and the use of surface cooling. With the use of cooling devices, the energy of the

laser beam largely bypasses the epidermis and is absorbed deeper within the papillary dermis. The clinical importance of this treatment approach is that it offers a modality with significantly less morbidity and downtime than with ablative laser therapy. Although heating of dermal collagen can be achieved by a variety of lasers with different wavelengths, the most effective nonablative lasers are infrared lasers (1000-1500 nm)³⁵ that target water in the dermis. Infrared lasers successfully used for nonablative tissue remodeling include the 1064-nm Nd:YAG,³⁶⁻³⁹ the 1320-nm Nd:YAG,⁴⁰⁻⁴⁴ the 1450-nm diode,⁴⁵⁻⁵⁰ and the 1540-nm erbium:glass⁵¹⁻⁵⁴ lasers. The 1320-nm Nd:YAG laser has been shown to induce increases in collagen thickness and parallel alignment of collagen.^{42,44} Non-infrared light modalities have also been used for nonablative rejuvenation, including the 585-nm and 595-nm PDL.⁵⁵⁻⁵⁷

Conclusions

Given the rapid evolution of laser therapy in dermatology, a clear understanding of the principles of laser light physics and tissue interactions is vital for proper management of patients. The unique properties of laser light, including monochromaticity, coherence, collimation, and high power, are the basis for the therapeutic applications of laser energy. The energy, power, fluence, and irradiance are specific parameters of laser light that can be adjusted for specific clinical uses. The theory of selective photothermolysis guides the clinical application of lasers visible spectrum. High-energy pulsed ablative lasers in the infrared range result in the vaporization of water-containing tissues. Nonablative laser therapy causes heating of dermal collagen while sparing the epidermis. Cooling devices optimize delivery of laser energy to deeper targets. Further refinements of laser-tissue interactions will result in the enhancement of existing technology as well as novel clinical applications in the future.

References

1. Tanzi EL, Lupton JR, Alster TS. Lasers in dermatology: four decades of progress. *J Am Acad Dermatol* 2003;49:1-31.
2. Anderson RR, Parrish JA. The optics of human skin. *J Invest Dermatol* 1981;77:13-9.
3. Anderson RR, Parrish JA. Selective photothermolysis: precise microsurgery by selective absorption of pulsed radiation. *Science* 1983;220:524-7.
4. Reinisch L. Laser physics and tissue interactions. *Otolaryngol Clin North Am* 1996;29:893-914.
5. Herd RM, Dover JS, Arndt KA. Basic laser principles. *Dermatol Clin* 1997;15:355-72.
6. Massey R, Marrero G, Goel-Bansal M, et al. Lasers in dermatology: a review. *Lasers Dermatol* 2001;67:477-84.
7. Ries W, Spewey M. Cutaneous applications of lasers. *Otolaryngol Clin North Am* 1996;29:915-29.
8. Anderson RR, Margolis RJ, Watanabe S, et al. Selective photothermolysis of cutaneous pigmentation by Q-switched Nd:YAG laser pulses at 1064, 532, and 355 nm. *J Invest Dermatol* 1989;93:28-32.
9. Ara G, Anderson RR, Mandel KG, et al. Irradiation of pigmented melanoma cells with high intensity pulsed radiation generates acoustic waves and kills cells. *Lasers Surg Med* 1990;10:52-9.
10. Polla LL, Margolis RJ, Dover JS, et al. Melanosomes are a primary target of Q-switched ruby laser irradiation in guinea pig skin. *J Invest Dermatol* 1987;89:281-6.
11. Taylor CR, Anderson RR, Gange RW, et al. Light and electron microscopic analysis of tattoos treated by Q-switched ruby laser. *J Invest Dermatol* 1991;97:131-6.
12. Anderson RR. Lasers in dermatology: a critical update. *J Dermatol* 2000;27:700-5.
13. Thomsen S. Pathologic analysis of photothermal and photomechanical effects of laser-tissue interactions. *Photochem Photobiol* 1991;53:825-35.
14. Welch AJ, Motamedi M, Rastegar S, et al. Laser thermal ablation. *Photochem Photobiol* 1991;53:815-23.
15. Walsh J, Deutsch T. Pulsed CO₂ laser ablation: measurement of the ablation rate. *Lasers Surg Med* 1988;8:264-75.
16. Venugopalan V, Nishioka N, Mikic B. The effect of laser parameters on the zone of thermal injury produced by laser ablation of biological tissue. *Am J Ophthalmol* 1994;116:62-70.
17. Alster TS. Cutaneous resurfacing with CO₂ laser and erbium:YAG lasers: preoperative, intraoperative, and postoperative considerations. *Plast Reconstr Surg* 1999;103:619-32.
18. Alster TS, Nanni CA, Williams CM. Comparison of four carbon dioxide resurfacing lasers: a clinical and histopathologic evaluation. *Dermatol Surg* 1999;25:153-9.
19. Alster TS, Kauvar ANB, Geronemus RG. Histology of high-energy pulsed CO₂ laser resurfacing. *Semin Cutan Med Surg* 1996;15:189-93.
20. Green HA, Domankevitz Y, Nishioka NS. Pulsed carbon dioxide laser ablation of burned skin: in vitro and in vivo analysis. *Lasers Surg Med* 1990;10:476-84.
21. Green JA, Burd E, Nishioka NS, et al. Middermal wound healing. A comparison between dermatomal excision and pulsed carbon dioxide laser ablation. *Arch Dermatol* 1992;128:639-45.
22. Dover JS, Hruza GJ, Arndt KA. Lasers in skin resurfacing. *Semin Cutan Med Surg* 2000;19:207-20.
23. Walsh JT, Flotte TJ, Deutsch TF. Er:YAG laser ablation of tissue: effect of pulse duration and tissue type on thermal damage. *Lasers Surg Med* 1989;9:314-26.
24. Kaufmann R, Hibst R. Pulsed 2.94 nm erbium:YAG laser skin ablation: experimental results and first clinical application. *Clin Exp Dermatol* 1990;15:389-93.
25. Hibst R, Kaufmann R. Effects of laser parameters on pulsed erbium:YAG laser skin ablation. *Lasers Med Sci* 1991;6:391-7.
26. Alster TS. Clinical and histologic evaluation of six erbium:YAG lasers for cutaneous resurfacing. *Lasers Surg Med* 1999;24:87-92.
27. Stringer H, Parr J. Shrinkage temperature of eye collagen. *Nature* 1964;204:1307.
28. Gardner ES, Reinsch L, Stricklin GP, et al. In vitro changes in non-facial human skin following CO₂ laser resurfacing: a comparison study. *Lasers Surg Med* 1996;19:379-87.
29. Ross EV, Naseef GS, Skrobal M, et al. In vivo dermal collagen shrinkage and remodeling following CO₂ laser resurfacing. *Lasers Surg Med* 1996;8:38.
30. Alster TS, Hirsch RJ. Single-pass CO₂ vs multiple-pass Er:YAG laser skin resurfacing: comparison of postoperative wound healing and side effect rates. *Dermatol Surg* 2003;29:80-4.
31. Bitter PH. Noninvasive rejuvenation of photodamaged skin using serial, full-face intense pulsed light treatments. *Dermatol Surg* 2000;26:835-42.
32. Goldberg D, Cutler KB. Nonablative treatment of rhytides with intense pulsed light. *Lasers Surg Med* 2000;26:196-200.
33. Kelly KM, Majaron B, Nelson JS. Nonablative laser and light rejuvenation: the newest approach to photodamaged skin. *Arch Facial Plast Surg* 2001;3:230-5.

34. Tope WD, Kageyama N. New methods in cutaneous resurfacing. *Adv Dermatol* 2001;17:301-23.
35. Alster TS, Lupton JR. Are all infrared lasers equally effective in skin rejuvenation? *Semin Cutan Med Surg* 2002;21:1-6.
36. Goldberg DJ, Silapunt S. Histologic evaluation of a Q-switched Nd:YAG laser in the nonablative treatment of wrinkles. *Dermatol Surg* 2001;27:744-6.
37. Goldberg DJ, Whitworth J. Laser skin resurfacing with the Q-switched Nd:YAG laser. *Dermatol Surg* 1997;23:903-6.
38. Goldberg DJ, Metzler C. Skin resurfacing utilizing a low-fluence Nd:YAG laser. *J Cutan Laser Ther* 1999;1:23-7.
39. Kelly KM, Nelson JS, Lask GP, Geronemus RG, Bernstein LJ. Cryogen spray cooling in combination with nonablative laser treatment of facial rhytides. *Arch Dermatol* 1999;135:691-4.
40. Goldberg DJ. Nonablative subsurface remodeling: clinical and histologic evaluation of a 1320nm Nd:YAG laser. *J Cutan Laser Ther* 1999;1:153-7.
41. Goldberg DJ. Full-face nonablative dermal remodeling with a 1320 nm Nd:YAG laser. *Dermatol Surg* 2000;26:915-8.
42. Trelles MA, Allones I, Luna R. Facial rejuvenation with a nonablative 1320 nm Nd:YAG laser: a preliminary clinical and histologic evaluation. *Dermatol Surg* 2001;27:111-6.
43. Levy JL, Trelles M, Lagarde JM, Borrel MT, Mordon S. Treatment of wrinkles with the nonablative 1320-nm Nd:YAG laser. *Ann Plast Surg* 2001;47:482-8.
44. Fatemi A, Weiss MA, Weiss RA. Short-term histologic effects of nonablative resurfacing: results with a dynamically cooled millisecond-domain 1320 nm Nd:YAG laser. *Dermatol Surg* 2002;28:172-6.
45. Tanzi EL, Williams CM, Alster TS. Treatment of facial rhytides with a nonablative 1450 nm diode laser: a controlled clinical and histologic study. *Dermatol Surg* 2003;29:124-8.
46. Goldberg DJ, Rogachefsky AS, Silapunt S. Nonablative laser treatment of facial rhytides: a comparison of 1450-nm diode laser treatment with dynamic cooling as opposed to treatment with dynamic cooling alone. *Lasers Surg Med* 2001;30:79-81.
47. Alster TS, Tanzi EL. Treatment of transverse neck lines with a 1450 nm diode laser. *Lasers Surg Med* 2002;31:108.
48. Ross EV, Sajben FP, Hsia J, et al. Nonablative skin remodeling: selective dermal heating with a mid-infrared laser and contact cooling combinations. *Lasers Surg Med* 2000;26:185-95.
49. Hardaway CA, Ross EV. Nonablative laser skin remodeling. *Dermatol Clin* 2002;20:97-111.
50. Lupton JR, Williams CM, Alster TS. Nonablative laser skin resurfacing using a 1540 nm erbium glass laser: a clinical and histologic analysis. *Dermatol Surg* 2002;28:833-5.
51. Levy JL, Besson R, Mordon S. Determination of optimal parameters for laser nonablative remodeling with a 1540nm Er:glass laser: a dose-response study. *Dermatol Surg* 2002;28:405-9.
52. Fournier N, Dahan S, Barneon G, et al. Nonablative remodeling: clinical, histologic, ultrasound imaging, and profilometric evaluation of a 1540 nm Er:glass laser. *Dermatol Surg* 2001;27:799-806.
53. Mordon S, Capon A, Creusy C, et al. In vivo experimental evaluation of skin remodeling by using an Er:glass laser with contact cooling. *Lasers Surg Med* 2000;27:1-9.
54. Zelickson BD, Kilmer SL, Bernstein E, et al. Pulsed dye laser therapy for sun-damaged skin. *Lasers Surg Med* 1999;25:229-36.
55. Bjerring P, Clement M, Keickendorff L, et al. Selective nonablative wrinkle reduction by laser. *J Cutan Laser Ther* 2000;2:9-15.
56. Hohenleutner S, Hohenleutner U, Landthaler M. Nonablative wrinkle reduction: treatment results with a 585-nm laser. *Arch Dermatol* 2002;138:1380-1.
57. Rostan E, Bowes LE, Iyer S, et al. A double-blind, side-by-side comparison study of low fluence long pulse dye laser treatment for wrinkling of the cheeks. *J Cosmet Laser Ther* 2001;3:129-136.2002;30:298-305.