ELSEVIER

Seminars in Cutaneous Medicine and Surgery

# Fractionation: Past, Present, Future

Nazanin Saedi, MD,* H. Ray Jalian, MD,† Anthony Petelin, MD,‡ and Christopher Zachary, MBBS, FRCP‡

**The development of fractional photothermolysis is a milestone in the history of laser technology and cutaneous resurfacing. Based on the concept that skin is treated in a fractional manner, where narrow cylinders of tissue are thermally heated and normal adjacent skin is left unaffected, the fractional devices have shown effectiveness in treating a variety of conditions. Since its development, we are becoming more adept at using optimal parameters to induce near carbon dioxide laser benefits with a much more comfortable postoperative period and fewer complications. The future remains bright for fractionated laser devices and with new devices and wavelengths, the applications of this technology continue to grow.**
**Semin Cutan Med Surg 31:105-109** 

**KEYWORDS** fractional, Fraxel, fractionation, laser, resurfacing, photothermolysis

## History

Fully ablative laser skin resurfacing with either the continuous-wave carbon dioxide ($CO_2$) or erbium:yttrium-aluminum-garnet (Er:YAG) lasers gained popularity in the 1990s as the standard for facial rejuvenation.[1] Water is the major chromophore, and the $CO_2$ laser emits light in the far infrared spectrum at 10,600 nm. The suprathreshold fluences result in rapid cellular heating and instant tissue vaporization known as ablation. Adjacent to the vaporized zone, subablative fluences induce tissue coagulation and protein denaturation through heat transfer.[2] The thermomechanical destruction generally extends 200-300 $\mu$m within the dermis and is followed by a predictable and beneficial "skin tightening" phase through a process of heat-induced shrinkage of collagen and the initiation of new collagen formation.

The Er:YAG laser uses a 2940-nm wavelength, and it is absorbed 10 times better by water than the $CO_2$ laser. This results in more superficial ablation, less collateral heating resulting in reduced hemostasis, absorption and ablation of the residual heated collagenous debris, and subsequent ability to drill deeply into the skin. Minimization of thermal injury enhances healing and re-epithelialization, but it induces less dermal collagen contraction and remodeling than with the $CO_2$ laser.[1]

Owing to the dramatic results, traditional ablative laser resurfacing remains the gold standard in skin rejuvenation, but the significant postoperative morbidity and complications ultimately led to a reduction in its use. Ablation of the entire epidermis is associated with copious oozing and crusting in the days after the procedure. Delayed healing can result in several weeks of uncomfortable dressing changes and debridement, often requiring weeks off work or social activities. In many instances, erythema lasts 3-6 months.[2] The destroyed barrier protection significantly increases the risk of infection throughout the recovery period and requires extensive home care. The risk of scarring, delayed-onset permanent hypopigmentation, and demarcation lines was significant even in the hands of an experienced operator.

In an effort to overcome these problems, nonablative dermal remodeling became popular in the ensuing years. Using a variety of wavelengths, including near-infrared 1320-, 1450-, or 1540-nm lasers; radio frequency or intense pulsed light; pulsed dye laser; and radio frequency and focused ultrasonography, selective injury of the dermis with relative or absolute sparing of the epidermis was established and termed "nonablative."[3] The theory implied that bulk heating of the dermis without destruction of the epidermis may cause enough protein denaturation to stimulate collagen remodeling and synthesis. Maintaining an intact epidermis using var-

*SkinCare Physicians, Chestnut Hill, MA.
†Wellman Center for Photomedicine, Massachusetts General Hospital, Boston, MA.
‡Department of Dermatology, University of California, Irvine, CA.
*Conflicts of Interest Disclosures*: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr. Zachary has received honorarium from Solta Medical, Inc. All other authors have no conflicts to report.
Address reprint requests to Nazanin Saedi, MD, SkinCare Physicians, 1244 Boylston St, Suite 103, Chestnut Hill, MA 02467. E-mail: nsaedi@skincarephysicians.net

1085-5629/12/$-see front matter 
doi:10.1016/j.sder.2012.02.003

ious cooling techniques prevented superficial wounds and lacked the side effects known to occur with the destruction of this layer. Because of these mechanisms, gradual and tentative steps toward nonablative dermal remodeling were achieved. This was much better tolerated than resurfacing with the $CO_2$ laser and the downtime was minimal; however, the results were not impressive.

In the setting of these suboptimal options for resurfacing, came the idea of fractionated laser technology. The concept of fractionated laser surgery was first used in hair transplant surgery, where tiny 1-mm holes were drilled in the bald scalp as recipient sites for hair transplants. Although the transplanted hairs looked no better than in conventional hair transplantation, in retrospect, the holes healed up just fine, with very limited scarring.[3] This approach was incorporated into the work of Dr Manstein and Dr Anderson, who first developed the functional concepts of fractionated laser surgery, at the Wellman Center for Photomedicine. It debuted in the literature in 2004 as the 1550-nm nonablative "Fraxel" laser, now called the Fraxel re:store (Solta Medical, Inc, Hayward, CA).[3]

# Mechanism

Fractional photothermolysis (FP) uses narrow beams of high-energy light applied to the skin in a pixilated pattern. Depending on the device, depths of up to 1.5 mm can be reached. These focal zones of treatment, so-called "microthermal zones" (MTZs), represent narrow columns of tissue heating. There is sufficient energy in the fractionated columns of the beam to induce thermal damage or ablation without spread to the adjacent tissue. These surrounding "skip areas" act as a nutritional and structural reservoir that provides the scaffolding necessary for rapid healing. Since its introduction, FP has evolved to encompass both nonablative and ablative devices. The key difference lies in the preservation of the stratum corneum and confined thermal injury in nonablative devices when compared with columns of complete tissue vaporization in the ablative devices. Nevertheless, the concept of focal microscopic zones of treatment surrounded by islands of sparing is the fundamental unifying theme of FP and is essential for the improved safety profile and recovery time seen with these devices.

After treatment with fractional resurfacing, columns of thermal injury are seen on routine histology. In a previous study, lactate dehydrogenase viability staining revealed microscopic areas of both dermal and epidermal necrosis within the MTZs.[4] These necrotic debris, termed "microscopic epidermal necrotic debris" (MENDs), are rapidly extruded with complete loss approximately 2 weeks after treatment. The exfoliation of the MENDs occurs simultaneously with reepithelialization. In addition to debris, the MENDs contain significant amounts of melanin. This is the likely mechanism for the efficacy of FP for the treatment of pigmentary disorders. On the ultrastructural level, FP stimulates collagen remodeling. Cellular markers for neocollagenesis, including heat shock proteins and collagen III, are seen using immunohistochemical stains after treatment.[5] Heat shock protein 47, required for collagen remodeling and maturation, may persist for up to 3 months, indicating ongoing tissue remodeling.[5]

# Indications

FP can be used to treat a variety of conditions, including photoaging, pigmentation, superficial or deep rhytids, and scars. The benefits are the reduction in downtime, the lack of discomfort in the healing period, and the relative low risk of adverse effects.

## Photoaging

In the initial studies using the 1550-nm nonablative device, Manstein et al[4] reported significant improvements in periorbital rhytids and skin texture after treatment with their prototype. The authors found a linear pattern of shrinkage related to the thermal injury.[4] The initial tissue shrinkage was followed by an apparent relaxation after 1 month, with retightening seen at 3 months.[4] This pattern of injury and healing is seen clinically with tissue contraction up to 12 months and a subsequent 10% relaxation thereafter.[4]

Since these initial studies, several others have also shown improvements in photodamaged skin with both ablative and nonablative FP, including improvement of mild-to-moderate rhytids, photoaging of the hand,[6] photoaging of nonfacial skin,[2] and poikiloderma of Civatte.[7] The MTZs of thermal injury induced with a nonablative FP device resulted in rapid healing and clinical improvement in pigmentation and texture variation associated with this condition.[8]

The newer 1927-nm fractionated device (Fraxel Dual, Solta Medical, Inc, Hayward, CA) has been shown to be effective in treating facial actinic keratoses.[9] This newer wavelength appears to be more superficial (depth of 200 $\mu$m), but the exact mechanism in treating the precancerous lesions remains unknown.

## Acne Scarring

The initial studies of fractionated lasers on acne scarring were done with nonablative devices.[2] The nonablative devices have also demonstrated efficacy in atrophic-type acne scars.[10] Ablative fractional resurfacing has not only shown significant efficacy in the treatment of acne scarring but it also appears to be superior to the nonablative modalities.[11] Of note, when treating acne scarring, very high energy (70 mJ) in combination with very high density (70%) is more efficacious than low energy and low density.

FP is becoming increasingly popular in the treatment of darker-skinned patients (Fitzpatrick skin types III-VI) with acne scarring.[12] In Korean patients (Fitzpatrick skin types IV-V) with moderate-to-severe scarring, the patients had self-assessed degrees of moderate-to-excellent improvement.[13]

Improvement of postinflammatory erythema associated with acne has also been described with the use of nonablative FP lasers.[14] It is speculated that the 1550-nm wavelength targets tissue water and may lead to thermally induced destruction of dermal blood vessels, resulting in improvement of erythema.[11]

## Other Forms of Scars

The 1550-nm Fraxel re:store (Solta Medical, Inc, Hayward, CA) has been shown to be effective in the treatment of hypopigmented facial scars.[15] Tierney et al[16] compared the efficacy of nonablative FP with that of the pulsed dye laser for the improvement of surgical scars and noted greater improvement with the fractionated device. The scars with significant hypopigmentation showed more repigmentation after treatment with the fractional device as well. These authors postulated that the greater depth of penetration and focal MTZs of injury with nonablative FP, inducing collagenolysis and subsequent neocollagenesis, accounted for its superiority in scar remodeling.[16] Hypertrophic scars also seem to improve, but, unlike the treatment of acne scarring, better results are obtained when treated with lower densities.[17]

## Pigmentation

In the initial reports on the efficacy of nonablative FP in treating melasma, 10 female patients (Fitzpatrick skin types III-V) were treated at 1- to 2-week intervals with the Fraxel re:store (Solta Medical, Inc, Hayward, CA).[18] After 4-6 sessions, physician evaluation confirmed that 60% of patients achieved 75%-100% clearance.[18] Clinical improvements in melasma were less extensive in patients with progressively darker skin types. Other conditions that have been successfully treated using FP technology include residual hemangioma,[19] minocycline-induced hyperpigmentation,[20] granuloma annulare,[21] disseminated superficial actinic porokeratosis,[22] and colloid milium.[23] Recently, there is new research on using this technology to improve function in patients with contractures due to sclerosing disorders such as scleroderma.[24]

# Complications

Nonablative and ablative fractional resurfacing procedures have proven to be safer with fewer complications than traditional ablative lasers. Although inherently safer because of the pixilated manner of the treatment, complications can be further prevented with attentive surgical technique and judicious use of prophylaxis. As these fractional devices continue to gain popularity, new complications will continue to be reported.

## Infections

Herpes simplex virus is the most common infectious complication after fractional resurfacing, with reported ranges up to 2%.[25] Viral infections related to herpes simplex virus present as superficial erosions in the first week after treatment and are often accompanied by pain. Occurrence can dramatically increase the risk of scarring.[25] Antiviral prophylaxis can minimize the reactivation to $<0.5\%$.[25] In contrast, the incidence of bacterial infection after FP appears to be extremely low, with an incidence of 0.1% of all treated cases.[25] The use of occlusive dressings and ointments may be a potential cause of pathogen overgrowth leading to growth of both *Staphylococcus aureus* and *Pseudomonas aeruginosa*.[26] Care should be taken to evaluate patients who develop postoperative infections that fail to respond to conventional antibiotics. In this setting, one must exclude methicillin-resistant *Staphylococcus aureus* and other atypical organisms. A single case of *Mycobacterium chelonae* infection has also been reported after an ablative fractional resurfacing procedure, likely related to inadequate sterilization of the device tip or the use of tap-water dressings.[27] Candidal and pityrosporum infections can also occur, with a recent retrospective study reporting a rate of 1.2%.[28]

## Acneiform Eruptions

Milia may occur in nearly 20% of treated patients.[25] The use of occlusive moisturizers and dressings can exacerbate these eruptions, and noncomedogenic equivalents should be used when appropriate.[29] Acneiform eruptions are common after fractional skin resurfacing, occurring at a rate of 2% to 10%. The rates are significantly lower than that of traditional skin resurfacing.[24] With moderate-to-severe acne flares, a short course of oral tetracycline-based antibiotics is often helpful and can even be used before subsequent treatments to prevent outbreaks.[10]

## Prolonged Erythema

Immediate post-treatment erythema after nonablative fractional resurfacing is expected and may persist for up to 3 days.[25] Redness that lasts longer than 4 days after nonablative fractional resurfacing is termed prolonged erythema.[25] It has been reported in $<1\%$ of patients.[25] Persistent erythema is redness lasting more than 1 month beyond ablative fractional resurfacing. The rate of prolonged erythema after ablative fractional resurfacing is significant, affecting nearly 12.5% of patients.[30] The erythema typically resolves within 3 months. Although persistent erythema can be concerning, it should be emphasized that erythema is expected and is a sign of continued wound healing and collagen remodeling.

## Pigmentary Alteration

In contrast to full-face $CO_2$ laser resurfacing, delayed-onset permanent hypopigmentation is an extremely rare complication of ablative fractional resurfacing. An isolated case involving transient hypopigmentation 15 days after treatment has been reported, and this was attributed to the prophylactic use of topical bleaching agents.[31] Hyperpigmentation is a well-known side effect of both nonablative and ablative fractional resurfacing, particularly in patients with darker skin types (Fitzpatrick skin types III-VI). Hyperpigmentation occurs much less frequently with FP laser skin resurfacing compared with traditional resurfacing. The incidence appears to be dependent on the system used, the parameters applied, and skin types treated, but can be upwards of 12% in certain populations.[32]

### Scarring

Hypertrophic scarring can be rarely associated with fractionated devices. Vertical and horizontal bands have been described after ablative fractional resurfacing of the neck.[33] While these are likely related to bulk heating due to excessive stamping or scanning, the use of excessively high-energy densities on underprivileged areas, such as the neck, may be associated with complications. If these areas become infected, scarring may occur.[34] The periorbital and mandibular ridge can also be scar prone and should be treated with more conservative parameters. Counterintuitively, nonablative or ablative fractionated devices at low energies and densities can be useful in the treatment of scarring, including hypertrophic scars, as described previously.

## Future Trends

### Drug Delivery

Ablative fractional resurfacing creates microscopic vertical holes in tissue, leaving an open channel into which topically applied drugs can migrate. Fractional $CO_2$ lasers have been used in animal models to deliver topical methyl-aminolevulinic acid, a photosensitizer, with amounts and depths far greater than that of intact skin. Ablative fractional resurfacing–assisted drug uptake induced large amounts of porphyrin synthesis throughout the skin depth 15-50 times higher when compared with intact skin. Lateral migration of a drug up to 1.5 mm from each laser hole was also observed, implying low-density treatment would be sufficient for even, deep dermal drug delivery.[35] Treatment of skin in a porcine model showed enhanced depth of photodynamic therapy following porphyrin application after pretreatment with fractional resurfacing.[36] An in vitro study using low-fluence fractionated Er:YAG demonstrated upward of a 125-fold increase in imiquimod delivery.[37] These early animal studies show significantly enhanced dermal drug delivery after ablative fractional resurfacing. Clinical trials are currently underway to determine the feasibility and safety of this enhanced drug delivery in humans. Although far from being optimized, ablative fractional resurfacing may serve as a channel for the delivery of large molecules that are unable to penetrate intact skin. Perhaps ultimately, it may be used for drug delivery, including biological peptides and vaccines.

### Tattoo Removal

Treatment with ablative fractional lasers results in removal of an array of microscopic columns of tissue that with appropriate parameters can represent a large portion of the entire treatment area. It is not surprising then that this can be useful for tattoo removal. An initial report showed ablative fractional resurfacing in conjunction with Q-switched lasers (QSL) enhanced tattoo removal when compared with tattoo removal alone.[38] The likely efficacy of this is multifactorial. It is postulated to be related to both vaporization of microscopic zones of the tattoo and providing a conduit for passive ink drainage after treatment with QSL.[38] Ibrahimi et al[39] reported the use of ablative fractional lasers for the successful treatment of allergic tattoos, in which use of a QSL can be challenging, given the risk of releasing antigenic proteins into lymphatic circulation. In this case series, there was significant lightening of the tattoo and, more importantly, relief in the pruritus associated with the allergic reaction. Given the physical ability to remove microscopic zones of tattoo, ablative fractional resurfacing might have a greater role in tattoo removal in the future, given its ability to physically remove ink. The lack of color sensitivity may prove useful as tattoos with more vibrant and complex color compositions become more commonplace.

### Home Devices

Although this technology is relatively new, it is becoming increasingly accessible to patients. A variation of the fractionated technology is available for estheticians to use with the development of Clear + Brilliant (Solta Medical, Inc, Hayward, CA), operating at 1440-nm wavelength with a low density (9%) and at a low energy (4-9 mJ). These treatments should have minimal-to-no downtime and improve skin texture after 4-6 treatments.

Recently, 2 home fractionated laser devices were introduced to the market: the PaloVia (Palomar Medical Technologies, Inc, Burlington, MA) and RéAura (Solta Medical, Inc, Hayward, CA). It should be noted that at time of publication, only the PaloVia has received clearance from the Food and Drug Administration for treating fine lines around the eyes. The PaloVia is a 1410-nm wavelength device with a maximum energy of 15 mJ. In the pivotal trials, 90% of the patients (n = 124) were noted to have some improvement in the appearance of periocular rhytides.[40] These patients had an active phase of treatment, in which they used the devices daily for 4 weeks, and then a maintenance phase, in which they only completed the treatment twice a week. The RéAura has yet to receive clearance from the Food and Drug Administration, and it is a product of collaboration between Solta Medical and Philips. The device is a fractionated 1435-nm laser with an output of 1.2 W. This is a second-generation device, with investigations underway in anticipating approval for home use.

Despite advances to make these devices available at home, they are not a replacement for the existing nonablative and ablative fractionated devices. The technology does provide improvement in the skin texture but cannot obtain the deep level of injury created by the other devices. The home devices appeal to a different patient population than those who are coming to see physicians for more intense laser procedures.

## Conclusions

The development of FP is a milestone in the history of laser technology and cutaneous resurfacing. The science has demonstrated clear efficacy in the treatment of skin surface and textural abnormalities, scarring, rhytids, laxity, and numerous other conditions. With new devices and wavelengths, the applications of this technology continue to grow. The future remains bright for fractionated laser devices, and we embrace what is to come.

## References


1. Gold MH: Update on fractional laser technology. J Clin Aesthet Dermatol 3:42-50, 2010
2. Geronemus RG: Fractional photothermolysis: Current and future applications. Lasers Surg Med 38:169-176, 2006
3. Saedi N, Petelin A, Zachary C: Fractionation: A new era in laser resurfacing. Clin Plast Surg 38:449-461, 2011
4. Manstein D, Herron GS, Sink RK, et al: Fractional photothermolysis: A new concept for cutaneous remodeling using microscopic patterns of thermal injury. Lasers Surg Med 34:426-438, 2004
5. Hantash BM, Bedi VP, Kapadia B, et al: In vivo histological evaluation of a novel ablative fractional resurfacing device. Lasers Surg Med 39:96-107, 2007
6. Jih MH, Goldberg LH, Kimyai-Asadi A: Fractional photothermolysis for photoaging of hands. Dermatol Surg 34:73-78, 2008
7. Behroozan DS, Goldberg LH, Glaich AS, et al: Fractional photothermolysis for treatment of poikiloderma of Civatte. Dermatol Surg 32: 298-301, 2006
8. Rahman Z, Alam M, Dover JS: Fractional laser treatment for pigmentation and texture improvement. Skin Ther Lett 11:7-11, 2006
9. Weiss E: Nonablative 1927 nm fractional resurfacing effective for facial actinic keratoses. Abstract presented at: The American Dermatologic Surgery Conference; October 2010; Chicago, IL
10. Alster TS, Tanzi EL, Lazarus M: The use of fractional laser photothermolysis for the treatment of atrophic scars. Dermatol Surg 33:295-299, 2007
11. Ortiz A, Tremaine AM, Zachary CB: Long-term efficacy of a fractional resurfacing device. Abstract presented at: American Society for Laser Medicine and Surgery Conference; April 2009; National Harbor, MD
12. Tierney EP, Kouba DJ, Hanke CW: Review of fractional photothermolysis: Treatment indications and efficacy. Dermatol Surg 35:1445-1461, 2009
13. Lee HS, Lee JH, Ahn GY, et al: Fractional photothermolysis for the treatment of acne scars: A report of 27 Korean patients. J Dermatol Treat 19:45-49, 2008
14. Glaich AS, Goldberg LH, Friedman RH, et al: Fractional photothermolysis for the treatment of post-inflammatory erythema resulting from acne vulgaris. Dermatol Surg 33:842-846, 2007
15. Glaich AS, Rahman Z, Goldberg LH, et al: Fractional resurfacing for the treatment of hypopigmented scars: A pilot study. Dermatol Surg 33: 289-294, 2007
16. Tierney E, Mahmoud BH, Srivastava D, et al: Treatment of surgical scars with fractional photothermolysis versus pulse dye laser: Randomized control trial. Dermatol Surg 35:1172-1180, 2009
17. Lin JY, Warger WC, Izikson L, et al: A prospective, randomized controlled trial on the efficacy of fractional photothermolysis on scar remodeling. Lasers Surg Med 43:265-272, 2011
18. Rokhsar CK, Fitzpatrick RE: The treatment of melasma with fractional photothermolysis: A pilot study. Dermatol Surg 31:1645-1650, 2005
19. Blankenship CM, Alster TS: Fractional photothermolysis of residual hemangioma. Dermatol Surg 34:1112-1114, 2008
20. Izikson L, Anderson RR: Resolution of blue minocycline pigmentation of the face after fractional photothermolysis. Lasers Surg Med 40:399-401, 2008
21. Karsai S, Hammes S, Rütten A, et al: Fractional photothermolysis for the treatment of granuloma annulare: A case report. Lasers Surg Med 40:319-322, 2008
22. Chrastil B, Glaich AS, Goldberg LH, et al: Fractional photothermolysis: A novel treatment for disseminated superficial actinic porokeratosis. Arch Dermatol 143:1450-1452, 2007
23. Marra DE, Pourrabbani S, Fincher EF, et al: Fractional photothermolysis for the treatment of adult colloid milium. Arch Dermatol 143:572-574, 2007
24. Kineston D, Kwan JM, Uebelhoer NS, et al: Use of a fractional ablative 10.6-$\mu$m carbon dioxide laser in the treatment of a morphea-related contracture. Arch Dermatol 147:1148-1150, 2011
25. Graber EM, Tanzi EL, Alster TS: Side effects and complications of fractional laser photothermolysis: Experience with 961 treatments. Dermatol Surg 34:301-305, 2008
26. Metelitsa AI, Alster TS: Fractionated laser skin resurfacing treatment complications: A review. Dermatol Surg 36:299-306, 2010
27. Palm MD, Butterwick KJ, Goldman MP: Mycobacterium chelonae infection after fractionated carbon dioxide facial resurfacing (presenting as an atypical acneiform eruption): Case report and literature review. Dermatol Surg 36:1473-1481, 2010
28. Shamsaldeen O, Peterson JD, Goldman MP: The adverse events of deep fractional CO(2): A retrospective study of 490 treatments in 374 patients. Lasers Surg Med 43:453-456, 2011
29. Tanzi EL, Wanitphakdeedecha R, Alster TS: Fraxel laser indications and long-term follow-up. Aesthet Surg J 28:675-678, 2008
30. Rahman Z, MacFalls H, Jiang K, et al: Fractional deep dermal ablation induces tissue tightening. Lasers Surg Med 41:78-86, 2009
31. Tan KL, Kurniawati C, Gold MH: Low risk of post-inflammatory hyperpigmentation in skin types 4 and 5 after treatment with fractional CO2 laser device. J Drugs Dermatol 7:774-777, 2008
32. Chan HH, Manstein D, Yu CS, et al: The prevalence and risk factors of post-inflammatory hyperpigmentation after fractional resurfacing in Asians. Lasers Surg Med 39:381-385, 2007
33. Fife DJ, Fitzpatrick RE, Zachary CB: Complications of fractional CO2 laser resurfacing: Four cases. Lasers Surg Med 41:179-184, 2009
34. Goldman MP, Fitzpatrick RE, Manuskiatti W: Laser resurfacing of the neck with the erbium:YAG laser. Dermatol Surg 25:164-167, 1999
35. Haedersdal M, Sakamoto FH, Farinelli WA, et al. Fractional CO(2) laser-assisted drug delivery. Lasers Surg Med 42:113-122, 2010
36. Haedersdal M, Katsnelson J, Sakamoto FH, et al: Enhanced uptake and photoactivation of topical methyl aminolevulinate after fractional CO2 laser pretreatment. Lasers Surg Med 43:804-813, 2011
37. Lee WR, Shen SC, Al-Suwayeh SA, et al: Laser-assisted topical drug delivery by using a low-fluence fractional laser: Imiquimod and macromolecules. J Control Release 153:240-248, 2011
38. Weiss ET, Geronemus RG: Combining fractional resurfacing and Q-switched ruby laser for tattoo removal. Dermatol Surg 37:97-99, 2011
39. Ibrahimi OA, Syed Z, Sakamoto FH, et al: Treatment of tattoo allergy with ablative fractional resurfacing: A novel paradigm for tattoo removal. J Am Acad Dermatol 64:1111-1114, 2011
40. Leyden J, Stephen T: Multi-center clinical trials of home-use non-ablative fractional laser device for wrinkle reduction. Abstract presented at: American Society for Laser Medicine and Surgery Conference; April 2010; Phoenix, AZ