IN THIS ISSUE

REVIEW ARTICLE INCENTIVE PROGRAM WINNERS

Immunostaining in Mohs Micrographic Surgery: A Review

Paradoxical Hypertrichosis After Laser Therapy: A Review

Fractionated Laser Skin Resurfacing Treatment Complications: A Review
Fractionated Laser Skin Resurfacing Treatment Complications: A Review

ANDREI I. METELITSKA, MD* AND TINA S. ALSTER, MD1

BACKGROUND Fractional photothermolysis represents a new modality of laser skin resurfacing that was developed to provide a successful clinical response while minimizing postoperative recovery and limiting treatment complications.

OBJECTIVES To review all of the reported complications that develop as a result of fractional ablative and nonablative laser skin resurfacing.

METHODS A literature review was based on a MEDLINE search (1998–2009) for English-language articles related to laser treatment complications and fractional skin resurfacing. Articles presenting the highest level of evidence and the most recent reports were preferentially selected.

RESULTS Complications with fractional laser skin resurfacing represent a full spectrum of severity and can be long-lasting. In general, a greater likelihood of developing post-treatment complications is seen in sensitive cutaneous areas and in patients with intrinsically darker skin phototypes or predisposing medical risk factors.

CONCLUSIONS Although the overall rate of complications associated with fractional laser skin resurfacing is much lower than with traditional ablative techniques, recent reports suggest that serious complications can develop. An appreciation of all of the complications associated with fractional laser skin resurfacing is important, especially given that many of them can be potentially prevented.

The authors have indicated no significant interest with commercial supporters.

The introduction of ablative laser skin resurfacing techniques with high-energy, pulsed carbon dioxide (CO2) and erbium-doped yttrium aluminum garnet (Er:YAG) devices in the mid-1990s was met with great enthusiasm because of their excellent clinical outcomes in the treatment of atrophic scars and photodamaged facial skin, including rhytides, lentigines, and dermal elastosis, but the prolonged recovery and risk of potential side effects eventually made them less attractive treatment alternatives.1,2

The subsequent development of nonablative laser devices improved recovery and tolerability, although limited clinical efficacy was associated with these less invasive treatments.1,2

The concept of fractional photothermolysis, coined in 2004 by Manstein and colleagues, has revolutionized the field of laser skin resurfacing by providing the ability to obtain significant clinical results with minimal post-treatment recovery.3 This technique generates microthermal treatment zones (MTZs) in the dermis, which are columns of thermally denatured skin of controlled width and depth. The small surface area of each wound results in rapid wound healing from a reservoir of viable keratinocytes in the untreated islands of surrounding skin.

Fractionated technology has led to the development of a number of nonablative and ablative devices, as reflected in Table 1.4,5 Initial reports on the nonablative fractionated devices emphasized almost complete absence of prolonged side effects,6,7 but more recent publications involving ablative fractionated lasers have shown that clinical complica-

*Division of Dermatology, University of Alberta, Edmonton, Alberta, Canada; 1Washington Institute of Dermatologic Laser Surgery, Washington, DC

© 2010 by the American Society for Dermatologic Surgery, Inc. • Published by Wiley Periodicals, Inc. • ISSN: 1076-0512 • Dermatol Surg 2010;36:299–306 • DOI: 10.1111/j.1524-4752.2009.01434.x
<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>System</th>
<th>Laser Type</th>
<th>Wavelength (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ablative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alma</td>
<td>Pixel Harmony</td>
<td>Er:YAG</td>
<td>2.940</td>
</tr>
<tr>
<td></td>
<td>Pixel CO₂</td>
<td>CO₂</td>
<td>10.600</td>
</tr>
<tr>
<td></td>
<td>Pixel CO₂ Omnifit</td>
<td>CO₂</td>
<td>10.600</td>
</tr>
<tr>
<td>Cutera</td>
<td>Pearl Fractional</td>
<td>YSGG</td>
<td>2.790</td>
</tr>
<tr>
<td>Cynosure</td>
<td>Affirm CO₂</td>
<td>CO₂</td>
<td>10.600</td>
</tr>
<tr>
<td>Eclipsomed</td>
<td>SmartXide DOT</td>
<td>CO₂</td>
<td>10.600</td>
</tr>
<tr>
<td>Ellipse Inc.</td>
<td>Juvia</td>
<td>CO₂</td>
<td>10.600</td>
</tr>
<tr>
<td>Focus Medical</td>
<td>Naturalase Er</td>
<td>Er:YAG</td>
<td>2.940</td>
</tr>
<tr>
<td>Fotona</td>
<td>SP Plus</td>
<td>Nd:YAG/Er:YAG</td>
<td>1.064/2.940</td>
</tr>
<tr>
<td></td>
<td>SP Dualis</td>
<td>Nd:YAG/Er:YAG</td>
<td>1.064/2.940</td>
</tr>
<tr>
<td></td>
<td>XS Dualis</td>
<td>Er:YAG</td>
<td>2.940</td>
</tr>
<tr>
<td></td>
<td>XS Fidelis</td>
<td>Er:YAG</td>
<td>2.940</td>
</tr>
<tr>
<td>Lasering</td>
<td>Mixto SX</td>
<td>CO₂</td>
<td>10.600</td>
</tr>
<tr>
<td>Lumenis</td>
<td>UltraPulse Active FX</td>
<td>CO₂</td>
<td>10.600</td>
</tr>
<tr>
<td></td>
<td>UltraPulse Deep FX</td>
<td>CO₂</td>
<td>10.600</td>
</tr>
<tr>
<td>Lutronic</td>
<td>eCO₂</td>
<td>CO₂</td>
<td>10.600</td>
</tr>
<tr>
<td>Matrix</td>
<td>LS-25</td>
<td>CO₂</td>
<td>10.600</td>
</tr>
<tr>
<td>Palomar</td>
<td>Lux 2.940</td>
<td>Er:YAG</td>
<td>2.940</td>
</tr>
<tr>
<td>Quantel</td>
<td>EXEL O₂</td>
<td>CO₂</td>
<td>10.600</td>
</tr>
<tr>
<td></td>
<td>FX4 and FX12</td>
<td>Er:YAG</td>
<td>2.940</td>
</tr>
<tr>
<td>Sciton</td>
<td>Profractional</td>
<td>Er:YAG</td>
<td>2.940</td>
</tr>
<tr>
<td>Sellas</td>
<td>Cis F1</td>
<td>CO₂</td>
<td>10.600</td>
</tr>
<tr>
<td>Solta Medical</td>
<td>Fraxel re:pair</td>
<td>CO₂</td>
<td>10.600</td>
</tr>
<tr>
<td>Nonablative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cynosure</td>
<td>Affirm</td>
<td>Nd:YAG</td>
<td>1.440 ± 1.320</td>
</tr>
<tr>
<td>Palomar</td>
<td>Lux 1,540</td>
<td>Er:Glass</td>
<td>1.540</td>
</tr>
<tr>
<td></td>
<td>Lux 1,440</td>
<td>Nd:YAG</td>
<td>1.440</td>
</tr>
<tr>
<td></td>
<td>Lux DeepIR</td>
<td>Infrared</td>
<td>880–1,350</td>
</tr>
<tr>
<td>Sellas</td>
<td>1,550</td>
<td>Erbium fiber</td>
<td>1.550</td>
</tr>
<tr>
<td>Solta Medical</td>
<td>Fraxel re:store</td>
<td>Erbium fiber</td>
<td>1.550</td>
</tr>
<tr>
<td>Syneron</td>
<td>Matrix RF</td>
<td>Diode/bipolar RF</td>
<td>915</td>
</tr>
</tbody>
</table>

CO₂, carbon dioxide; Er:YAG, erbium-doped yttrium aluminum garnet; Nd:YAG, neodymium-doped yttrium aluminum garnet; RF, radiofrequency; YSGG, yttrium scandium gallium garnet.

Tions can occur. Given that some of these complications are potentially avoidable, the importance of their recognition by health professionals cannot be overemphasized (Table 2).

**Prolonged Erythema**

Immediate post-treatment erythema is an expected consequence of fractionated laser skin resurfacing that usually resolves within 3 to 4 days. Prolonged erythema is defined as post-treatment erythema that persists longer than 4 days with nonablative resurfacing and beyond 1 month with ablative treatment. It has been reported in fewer than 1% of nonablative and more than 12.5% of ablative laser-treated patients, although erythema typically resolves in these latter cases within 3 months. Although traditional nonfractionated laser resurfacing tends to be associated with longer-lasting postoperative erythema, fractionated laser resurfacing treatments that use multiple laser passes or inadvertent stacking also increase the risk of prolonged erythema.

The intensity and duration of postfractional laser erythema can be decreased with the use of a 590-nm-wavelength light-emitting diode (LED) array.
TABLE 2. Complications of Fractional Laser Skin Resurfacing

<table>
<thead>
<tr>
<th>Degree of Severity</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
</table>
|                    | • Prolonged erythema  
|                    | • Acne and milia  
|                    | • Delayed purpura  
|                    | • Superficial erosions  
|                    | • Contact dermatitis  
|                    | • Recall phenomenon  | • Infection  
|                    |                        | • Pigmentary alteration  
|                    |                        | • Anesthesia toxicity  
|                    |                        | • Eruptive keratoacanthomas  | • Hypertrophic scarring  
|                    |                        |                        | • Ectropion formation  
|                    |                        |                        | • Disseminated infection |

split-face study of 20 patients, LED photomodulation was shown to reduce the intensity of erythema in all treated facial halves at the 24-hour postoperative visit. In six patients, total resolution of erythema was 24 to 48 hours faster after LED treatment than in untreated control facial halves. In addition, given its antiinflammatory properties, topical ascorbic acid should be considered because a previous study reported less severe and shorter postablative laser resurfacing erythema with its use.

Infection

Given that viral, bacterial, and fungal infections usually present during the first postoperative week, proper identification and treatment are essential to avoid further complications, including delayed wound healing, scarring, co-infection with other pathogens, and systemic dissemination.

The rate of herpes simplex virus (HSV) infection, the most common type of infection after fractional laser skin resurfacing, has been reported in 0.3% to 2% of cases. In contrast, infection rates with traditional (nonfractionated) laser treatment are higher, with 2% to 7% of cases developing HSV reactivation. Patients may not present with classic herpetiform vesicopustules but instead may demonstrate only superficial erosions that develop during the first week after treatment. To minimize the risk of HSV reactivation with fractional resurfacing, antiviral prophylaxis should be administered when a prior history of facial HSV is documented or if full-face ablative laser procedures are performed. In these patients, oral antiviral agents should be initiated concomitant with or 1 day before treatment and continued for 5 to 7 days. This approach can minimize the rate of patient complications to less than 0.5% in healthy individuals with no prior history of HSV, although in individuals who have had HSV before, 7% will show reactivation if prophylactic therapy is not initiated as outlined above. Furthermore, fractional skin resurfacing should not be performed on patients with active HSV infection, given the risk of HSV exacerbation.

In cases in which herpetic outbreak occurs despite prophylaxis, optimization of treatment doses or switching to another antiviral agent may be required, because viral resistance to the initially prescribed drug is possible, with a high risk of subsequent scarring. Although not yet reported with fractional skin resurfacing, in rare instances of herpetic dissemination, intravenous antiviral therapy and further hospitalization may be necessary.

The rate of bacterial infection with traditional laser vaporization tends to be low (0.5–4.5% of cases). It is even more rarely observed after fractionated skin resurfacing, with only 0.1% of all treated cases documented to develop impetigo. Excessive wound occlusion during the early postoperative period can enhance the likelihood of pathogen overgrowth, primarily Staphylococcus aureus and Pseudomonas aeruginosa. Given potential progression to scarring, documentation of
the causative agents and appropriate treatment are essential, especially in light of possible methicillin-resistant S. aureus.\textsuperscript{9} Notwithstanding, controversy remains with regard to the use of prophylactic systemic antibiotics in all patients but should be standard practice in patients at high risk, especially those who are immunosuppressed or have documented mitral valve prolapse with regurgitation or other valvular heart disease.

Increased pain, focal intense erythema, increased exudate, and erosions with crusting should alert the physician to the possibility of bacterial suprainfection that usually presents 1 to 3 days after treatment.\textsuperscript{9,16} After a wound culture, broad-spectrum empiric antibiotics should be initiated and further adjusted based on the culture results.

Although rarely seen, cutaneous candidiasis induced by Candida albicans is the most common fungal infection reported after fractional laser skin resurfacing (usually 7–14 days after treatment) and should be treated with antifungal medications to prevent scarring.\textsuperscript{9,16}

**Acne and Milia**

Transient acneiform eruptions and milia are relatively common after traditional nonfractionated laser resurfacing, with up to 80% of cases developing the former and more than 14% developing the latter. Although the rates of acneiform eruptions are significantly lower (2–10%) with fractional skin resurfacing, the incidence of milia development has been reported in as many as 19% of treated patients.\textsuperscript{6,7,21–23} Given that occlusive moisturizers and dressings can exacerbate such eruptions, most authors recommend their avoidance or a change to noncomedogenic equivalents.\textsuperscript{2,6,24} Disruption of follicular units during treatment and aberrant follicular epithelialization during healing may further contribute to acne exacerbation. One case of transient acneiform eruption was reported after nonablative fractionated treatment of acne scarring, presumably related to visible cracks on the laser tip that the authors purported triggered random scattering of the laser beam and subsequent bulk thermal injury of the skin.\textsuperscript{25}

In moderate to severe acne flares, short courses of oral tetracycline–based antibiotics have been advocated. Antibiotics also can be prescribed during subsequent treatments to prevent future outbreaks.\textsuperscript{22}

**Pigmentary Alteration**

Postinflammatory hyperpigmentation (PIH) is much less frequent with fractional laser skin resurfacing than with other ablative procedures but is observed in 1% to 32% of patients, depending on the system used, parameters applied, and skin phototypes treated.\textsuperscript{7,11,19,24,26–29} Patients with darker skin phototypes (Fitzpatrick III–VI) have a higher likelihood of developing PIH. In general, fractional resurfacing of darker skin should use higher fluencies, lower density settings, and longer treatment intervals.\textsuperscript{26,30} To further minimize the risk of PIH, patients should avoid sun exposure at least 2 weeks before and after fractional skin resurfacing.\textsuperscript{26,31} In contrast to traditional nonfractionated laser resurfacing, PIH is typically less intense and of shorter duration. Although it often resolves without treatment, application of topical bleaching and mild peeling agents (e.g., retinoic, azelaic, ascorbic, glycolic acid) and judicious use of sunblock can hasten its resolution.\textsuperscript{2}

Hypopigmentation is an extremely uncommon complication of fractional laser skin resurfacing. One reported case involved transient hypopigmentation 15 days after treatment that was attributed to the prophylactic use of topical tretinoin and hydroquinone.\textsuperscript{32} Subsequent resolution of the hypopigmentation was observed upon discontinuation of these medications. Hypopigmentation persisting several months after treatment was noted in two patients within areas of laser-induced hypertrophic scarring on the neck.\textsuperscript{9,10}

Hypopigmentation often has a delayed onset (6–12 months postoperatively), necessitating longer
patient follow-up for definitive conclusions regarding its overall risk to be made.

Scarring

Hypertrophic scarring is a known and rare complication of ablative skin resurfacing using CO² and Er:YAG lasers. Several recent reports provide further evidence that fractional ablative resurfacing can also induce such scarring. Focal areas of erythema and induration 2 to 4 weeks after treatment are the first signs of potential scar formation. Nine of 10 published cases involved fractional ablative skin resurfacing of the neck, resulting in multiple vertical and horizontal hypertrophic scars.

There are several potential explanations for hypertrophic scarring in this setting, including the use of excessively high energy densities, postoperative infection of the skin, and lack of technical finesse. The neck is also a well-recognized site that is especially susceptible to the development of scarring because of the small number of pilosebaceous units and poor vasculature in this region, which are essential for wound healing. In addition, the thin skin of the neck renders it more susceptible to thermal injury. Other scar-prone anatomic locations that also require more conservative treatment protocols include the periorbital and mandibular regions.

These cases highlight that only experienced physicians who are aware of potential scarring and have good understanding of postoperative wound care should perform fractional ablative resurfacing of the neck, using more cautious treatment parameters. In general, patients with a prior history of radiation or surgical procedures involving the neck or eyelids or those who have experienced postoperative wound infection, contact dermatitis, or keloid scarring have the highest risk of scarring. Early treatment of hypertrophic scarring in such settings often involves the use of topical corticosteroids or silicone gel products, intralesional corticosteroid injections, and pulsed dye laser therapy.

Ectropion Formation

Cicatricial ectropion is a rare and serious complication that has recently been reported after fractional CO² laser treatment. The lower eyelid is typically involved, with eversion of the eyelid away from the globe, resulting in exposure of the mucosal surface. Patients who have a previous history of eyelid surgery or limited preoperative skin elasticity in the periorcular area have the greatest risk of developing this complication. Careful intraoperative detection of excessive collagen contraction and use of lower energy density settings help to minimize ectropion formation.

Eruptive Keratoacanthomas

Keratoacanthomas are low-grade malignant skin tumors that are known to arise over sites of trauma. Although previously described in association with ablative laser treatment of the face, the development of multiple eruptive keratoacanthomas after fractional resurfacing has more recently been reported on the legs of two patients. Of note in the latest report is that both patients had a history of actinic keratoses in the treatment sites preoperatively. Four to 6 weeks after treatment, hyperkeratotic papules appeared in their place that were histologically proven to be keratoacanthomas. The authors speculated that trauma to the follicular unit during fractional laser treatment could have induced these low-grade tumors. This report reemphasizes that physicians should exercise caution when treating extensive and hypertrophic actinic keratoses on legs with fractional laser resurfacing.

Recall Phenomenon

Heat-induced recall phenomenon has been observed after skin resurfacing with a combination (1,320/1,440 nm) fractional laser. After resolution of transient post-treatment wheal-like erythema, some patients experience reappearance of eryhematous patches after a hot shower or prolonged exposure to direct sunlight, resulting in a "recall" phenomenon.
The exact mechanism has not been fully elucidated, but it appears that there is activation of neurogenic or histamine- or mast cell-dependent mechanisms responsible for high levels of molecules that produce erythema in the skin.\(^6\) Although this completely benign and transient phenomenon usually resolves within 48 hours and does not carry any long-term stig mata, treating physicians should forewarn patients of this potential side effect when using the combined fractional device.

**Anesthesia Toxicity**

Topical anesthesia-induced toxicity rarely occurs, but in a cohort of 1,000 patients, two cases were observed in which 30% lidocaine gel was not removed from the skin before fractional laser treatment.\(^4^0\) A number of symptoms suggestive of lidocaine toxicity were evident, including agitation, anxiety, light-headedness, palpitations, slight nausea, perioral tingling, and tachycardia. A theoretical increase in percutaneous absorption of lidocaine induced by fractional photothermolysis is a plausible explanation for this reaction. As a consequence, complete removal of topical anesthesia before laser treatment is advocated to minimize this risk.

**Delayed Purpura**

Delayed purpura arising more than 3 days after fractional laser skin resurfacing has been reported.\(^7\)\(^4^1\) Avoidance of nonsteroidal antiinflammatory drugs, aspirin, and other blood thinners in the immediate postoperative period are recommended to decrease the risk of purpura. Patients should also avoid traumatizing their skin through rubbing or scratching because of skin fragility during the recovery period.

**Superficial Erosions**

Small linear abrasions, ranging between 2 and 16 mm, have occurred after fractional laser treatment.\(^1^9\)\(^4^2\) The most susceptible body sites are the upper lip, lower orbital rim, and forehead, presumably because of incomplete contact of the handpiece with the skin.\(^6^7\) Newer modifications of the laser handpieces have reduced the incidence of this complication.\(^4^2\)

**Contact Dermatitis**

The incidence of postfractional laser dermatitis is rare and, in most cases, represents an irritant contact variant.\(^7\) Previously described allergic reactions to topical ointments (e.g., antibiotics) can occur, so their use should be avoided during the reepithelialization process. Patients should be instructed to refrain from using any nonprescribed topical natural or herbal remedies to prevent additional irritation.

**Summary**

There is little doubt that fractional laser skin resurfacing is here to stay, especially because it represents a better standard of safety than previous ablative technologies. Although clinical efficacy remains important, so is the risk of side effects and complications. As additional information is collected, more specific guidelines will be established to optimize laser selection, intraoperative technique, and post-treatment wound care. This review reemphasizes the need for a tailored approach that involves matching a particular treatment technique with the specific patient, especially taking into account all of the risk factors involved. Proper technique is even more essential with fractionated ablative resurfacing because of its higher incidence of severe side effects. The primary aim of fractional photothermolysis is to ensure the safe and effective treatment of patients while applying the principle of “primum nil nocere.”

**References**


38. Foster KW, Fincher EF, Moy RL. Heat-induced “recall” of treatment zone erythema following fractional resurfacing with


Address correspondence and reprint requests to: Tina S. Alster, MD, Washington Institute of Dermatologic Laser Surgery, 1430 K Street, NW Suite 200, Washington, DC 20005, or e-mail: talster@skinlaser.com