The Safety and Efficacy of the 308-nm Excimer Laser for Pigment Correction of Hypopigmented Scars and Striae Alba

Macrene R. Alexiades-Armenakas, MD, PhD; Leonard J. Bernstein, MD; Paul M. Friedman, MD; Roy G. Geronemus, MD

Objective: To assess the safety and efficacy of the 308-nm excimer laser in pigment correction of hypopigmented scars and striae alba.

Design: Institutional review board–approved randomized controlled trial.

Setting: Private research center.

Patients: Volunteer sample of 31 adult subjects with hypopigmented scars or striae alba distributed on the face, torso, or extremities.

Interventions: Lesions were randomized to receive treatment or not, with site-matched normal control areas. Treatments were initiated with a minimal erythema dose minus 50 mJ/cm² to affected areas. Subsequent treatments were performed biweekly until 50% to 75% pigment correction, then every 2 weeks thereafter until a maximum of 10 treatments, 75% increase in colorimetric measurements, or 100% visual pigment correction.

Main Outcome Measures: Pigment correction by visual and colorimetric assessments compared with untreated control lesions and site-matched normal skin before each treatment and at 1-, 2-, 4-, and 6-month follow-up intervals. Occurrence of erythema, blistering, dyspigmentation, or other adverse effects was monitored.

Results: The percentage pigment correction by both assessments increased in direct proportion to the number of treatments. The mean percentage pigment correction by visual assessment relative to control of 61% (95% confidence interval [CI], 55%-67%) for scars and 68% (95% CI, 62%-74%) for striae was achieved after 9 treatments. The mean percentage pigmentation by colorimetric measurements relative to control of 101% (95% CI, 99%-103%) for scars and 102% (95% CI, 99%-104%) for striae was achieved after 9 treatments. Both sets of values gradually declined toward baseline levels during the 6-month follow-up. No blistering or dyspigmentation occurred.

Conclusions: Therapy with the 308-nm excimer laser is safe and effective in pigment correction of hypopigmented scars and striae alba. Mean final pigment correction rates relative to control sites of approximately 60% to 70% by visual assessment and 100% by colorimetric analysis were observed after 9 treatments administered biweekly. Maintenance treatment every 1 to 4 months is required to sustain the cosmetic benefit.

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HYPOPIGMENTED SCARS AND striae alba have long been a therapeutic challenge for which a highly effective, low-risk treatment modality has been lacking. A scar or cicatrix is a skin defect resulting from the inflammatory, granulation, and matrix formation phases of repair after trauma or disease. As dermal remodeling progresses, the final scar becomes hypocellular, with collagen bundles parallel to the epidermis, effacement of the rete ridges, lack of skin appendages, and absence of the reticular dermal layer. At maturity, the scar is often hypopigmented. Although it has often been assumed that the hypopigmentation is due to a decrease in melanocytes and melanin, recent data suggest that vascular and optical factors may account for the hypopigmentation. Although erythematous scars are safely and effectively treated with the pulsed dye lasers, prior treatments of hypopigmented scars have met with limited efficacy and variable safety profiles. These prior treatment options include cosmetic tattooing, medium-depth chemical peels, carbon dioxide resurfacing, dermabrasion, skin grafting, and cosmetic camouflage. Therefore, a safe and effective treatment modality for hy-
popigmentation is needed. A treatment that increases melanin production could theoretically correct hypopigmentation regardless of whether it is caused by hypomelanocytosis, hypomelanosis, or optical factors.

Striae distensae, or stretch marks, are linear atrophic plaques that are initially erythematous (striae rubra), then hypopigmented (striae alba). They may result from mechanical stress, such as weight changes and weight lifting, or from hormonal factors, such as puberty, pregnancy, oral contraceptive use, and corticosteroid therapy or excess. On histopathologic analysis, a stria alba is similar to a scar: a thin, flattened epidermis overlies thin, densely packed collagen bundles parallel to the skin surface and abundant elastic fibers in a random array. Effective therapy of striae rubra has included topical tretinoin9 and 385-nm pulsed dye laser11 treatment. In contrast, striae alba have been notoriously difficult to treat. Striae alba may be amenable to a treatment that increases pigment levels and corrects the hypopigmentation.

Phototherapy has been used to treat vitiligo, a chronic disorder of cutaneous hypopigmentation and depigmentation, since ancient times. Phototherapy with UV-A radiation and oral or topical psoralens, broadband UV-B, and narrowband UV-B has been shown to be effective in repigmenting vitiligo. Narrowband UV-B, which has a wavelength spectrum of 311 to 312 nm and a peak emission of 311 nm, is as effective as topical psoralen–UV-A, with fewer adverse effects. Based on these findings, a single-wavelength 308-nm UV-B laser has been used to effectively and safely treat vitiligo. A prior case study showed that the 308-nm excimer laser may be used to treat postresurfacing leukoderma. In the present randomized, blinded, controlled study, we assessed the effects of a 308-nm excimer laser in pigment correction of hypopigmented scars and striae alba.

### METHODS

#### PATIENTS

The study was approved by the Essex Institutional Review Board, Inc. (Lebanon, NJ), and verbal and written informed consent was obtained from each subject. A volunteer sample of 31 adult subjects with hypopigmented scars (22 patients) and striae alba (9 patients) distributed on the face, torso, or extremities was enrolled.

#### INTERVENTIONS

Lesions were randomized by alternate allocation to receive treatment or not, with site-matched normal control areas. Pretreatment photographs, colorimetric analyses, and minimal erythema dose tests were performed. Before each treatment and at each follow-up, photographic direct visual assessment relative to control areas, as well as colorimetric analyses of the treated and site-matched control areas, were repeated.

Lesions were treated with a xenon chloride excimer laser (Xtrac [308 nm, 3.2 cm², 30 nanosecond]; Photomedex, Radnor, Pa). Minimal erythema dose tests were performed at 100, 150, 200, 250, 300, and 350 mJ/cm². A patient’s minimal erythema dose minus 50 mJ/cm² was initially applied to affected areas. The surrounding normal skin was protected with a UV-B-blocking template, consisting of a plastic shield (Photomedex) or wooden tongue depressors. Subsequent treatments were performed at biweekly intervals until 50% to 75% pigment correction was obtained and were repeated every 2 weeks thereafter until a maximum of 10 treatments, 75% increase in colorimetric measurements relative to baseline, or 100% visual pigment correction. If there was no erythematous or colorimetric response, the dosage was increased by 50 mJ/cm² per treatment; otherwise, the dosage was maintained. If blistering or burning occurred, the dosage was decreased by 50 J/cm² after healing. After completion of treatment, subjects returned for 1-, 2-, and 4-month evaluations.

### MAIN OUTCOME MEASURES

Visual assessment of pigment correction relative to untreated control lesions was performed by 3 blinded observers (including M.R.A.-A.) on a discrete scale of 0% to 100% improvement to the nearest 5% before each treatment and at each follow-up visit. Quantitative measurements of pigmentation compared with site-matched normal skin were made using a tristimulus colorimeter (Spectrophotometer; Topix Pharmaceuticals, Amityville, NY). This system measures spectrometric reflectance data and uses the Commission Internationale de l’Eclairage L*a*b* color system, in which values L*, a*, and b* are plotted at right angles to one another to form a 3-dimensional coordinate system. Equal distances in the space approximately represent equal color differences. Value L* represents lightness; a*, the redness or greenness axis; and b*, the yellowness or blueness axis. This system is popular for use in measuring reflective and transmissive objects. The L*/a* and b* variables correlate with melanin indexes and the degree of epidermal melanin, whereas the a* value correlates with erythema and the amount of hemoglobin in the superficial vascular plexus. Percentages of L*/a* and b* relative to matched control sites were used to quantify degree of pigmentation. Percentages of a* relative to matched control sites were used to quantify erythema. Patients were monitored at each visit for the occurrence of erythema, blistering, or dyspigmentation.

### STATISTICAL ANALYSIS

The results of the colorimetric analysis at baseline and following each treatment were evaluated by t tests. A comparison was also performed of the colorimetric values among patients with single vs multiple treatment sites at baseline.

### RESULTS

The mean percentage (95% confidence interval [CI]) pigmentation relative to matched untreated control lesions by visual assessment for scars and striae alba are presented in Table 1 and Figure 1. Mean pigmentation of 61% (95% CI, 55%-67%) for scars and 68% (95% CI, 62%-74%) for striae alba after 9 treatments were presented in Table 2 and Figure 2). The mean percentage (95% CI) pigmentation relative to matched control sites was calculated as [(1/(L*les) - 1/L*control)] × 100; values of 101% (95% CI, 99%-103%) for scars and 102% (95% CI, 99%-104%) for striae alba were achieved after 9 treatments. These values declined gradually during the follow-up (Figure 2 and Table 2).

Representative photographic examples of hypopigmented scars and striae alba treated with the 308-nm ex-
cimer laser are presented in Figures 3, 4, and 5. Figure 3 demonstrates visible pigment correction of facial scars after 5 treatments (A and B), which began to decline toward baseline levels at the 2-month (C) and 6-month (D) follow-ups. Figures 4 and 5 demonstrate excellent pigment correction of striae alba (A and B), which was maintained to the 1- to 2-month follow-ups (C).

The results of treatment by colorimetric analysis were statistically evaluated by $t$ tests. A significant difference ($P < .05$) between the colorimetric values associated with the treated vs site-matched control lesions at baseline and after the first treatment was identified. This difference disappears after treatment 1 (before treatment 2) and is not present at any subsequent treatment. No statistically significant difference in colorimetric values at baseline was found between patients with single vs multiple treatment sites, indicating that bias was not introduced by including patients with multiple treatment sites.

No cases of blistering or dyspigmentation were observed. Transient erythema, which is the desired end point, was noted.

**COMMENT**

The study presented herein demonstrates that treatment with the 308-nm excimer laser is safe and effective in pigment correction of scars and striae alba. Mean final pigment correction rates relative to control sites of approximately 60% to 70% by visual assessment and approximately 100% by colorimetric analysis were achieved after 9 treatments administered biweekly. These gradually declined toward baseline values during a 6-month follow-up, indicating the need for maintenance treatments.

The 308-nm excimer laser has been used in the repigmentation of vitiligo\textsuperscript{18,22} and postresurfacing leukoderma.\textsuperscript{19} In one study,\textsuperscript{18} treatment of vitiligo 3 times a week for 12 treatments resulted in repigmentation scores of 1% to 25% in 4 patients, 26% to 75% in 3, and 76% to 100% in 2, among 9 patients who completed the study. Another study\textsuperscript{22} extended twice weekly treatments of vitiligo to 6 months and achieved higher (50%-95%) repigmentation rates in the 4 patients who completed the study. In the treatment of postresurfacing leukoderma, 50% to 75% improvement was noted in 2 patients after 10 treatments.\textsuperscript{19}

The potential weaknesses in the present study include the small sample size. This may introduce some bias or sampling error in the study. An analysis was carried out to compare colorimetric values at baseline between patients with single vs multiple sites selected for treatment. No statistically significant difference was noted between these patients, indicating that bias was not introduced by the inclusion of patients with multiple treatment sites. Visual assessment and colorimetric analysis

| Table 1. Pigmentation Relative to Untreated Control Lesions by Visual Assessment\textsuperscript{*} |
|-----------------------------------------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|
| Lesion Type     | Treatment No. | Follow-up Interval, mo |
|-----------------|---------------|------------------------|---------------|---------------|---------------|---------------|---------------|---------------|
| Scars           | 1   | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9   |
| 3 (1-4)         | 31 (22-39)    | 17 (7-26)              | 41 (28-54)    | 25 (15-35)    | 10 (6-14)     | 1   |
| 9 (6-12)        | 58 (44-71)    | 40 (12-68)             | 20 (12-40)    | 0   |
| 17 (12-23)      | 36 (29-50)    | 20 (12-40)             | 0   |
| 24 (18-30)      | 31 (22-39)    | 17 (7-26)              | 41 (28-54)    | 25 (15-35)    | 10 (6-14)     | 1   |
| 29 (23-35)      | 58 (44-71)    | 40 (12-68)             | 20 (12-40)    | 0   |
| 34 (27-40)      | 36 (29-50)    | 20 (12-40)             | 0   |
| 43 (36-50)      | 31 (22-39)    | 17 (7-26)              | 41 (28-54)    | 25 (15-35)    | 10 (6-14)     | 1   |
| 54 (50-59)      | 58 (44-71)    | 40 (12-68)             | 20 (12-40)    | 0   |
| 61 (55-67)      | 58 (44-71)    | 40 (12-68)             | 20 (12-40)    | 0   |

*Data are given as mean percentage (95% confidence interval). Ellipses indicate data not available.

Figure 1. Mean percentage (95% confidence interval) pigmentation relative to matched untreated control lesions by visual assessment.

Figure 2. Mean percentage (95% confidence interval) pigmentation relative to matched normal skin by colorimetric analysis.
were included in the study to control for subjective bias. Although the sensitivity of the human retina exceeds that of the colorimetric device used herein, the latter serves as a quantitative measure that is free of potential subjectivity on the part of the evaluator.

A major limitation of this new therapeutic intervention for pigment correction of scars and striae alba is the need for maintenance treatments. Although the frequency of maintenance treatment was not formally evaluated, the pigment levels gradually declined toward baseline values during the 6-month follow-up. It is estimated that skin phototypes I and II, as illustrated in Figures 3 and 4, would require maintenance treatments on the order of once per 1 to 2 months. Darker skin types (III-VI), such as in Figure 5, appear to require less frequent maintenance treatments, on the order of once per 2 to 4 months. The practitioner should inform patients of the need for maintenance treatments for durable results. A newer localized, high-dose UV-B phototherapy device, the ReLume (Lumenis, Pleasanton, Calif), has recently been evaluated for the pigment correction of hypopigmented scars and striae alba.23 The pigment correction rates and duration of response with this device appear to be similar to those of the excimer laser.

Another important concern in the cutaneous use of UV-B–based laser or light devices is the theoretic increased risk of skin carcinogenesis. Ultraviolet-B radiation is more carcinogenic than UV-A radiation in experimental induction of squamous cell carcinoma, with UV-B causing characteristic point mutations in p53.24 A com-

Table 2. Pigmentation Relative to Site-Matched Normal Skin by Colorimetric Analysis*

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>Baseline</th>
<th>Treatment No.</th>
<th>Follow-up Interval, mo</th>
</tr>
</thead>
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<tr>
<td></td>
<td></td>
<td>1 2 3 4 5 6 7 8 9</td>
<td>1 2 3 4 5 6</td>
</tr>
<tr>
<td>Scars</td>
<td>98 (96-99) 99 (96-101) 100 (97-102) 100 (98-103) 102 (99-105) 100 (98-103) 101 (99-103) 102 (99-105)</td>
<td>102 (99-104) 97 (96-98) 98 (97-100) 97 (96-100) 94 (94-95) 94 . . . 98 (96-100)</td>
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<tr>
<td>Striae</td>
<td>95 (92-98) 99 (98-101) 98 (96-101) 98 (97-100) 100 (97-103) 100 (99-102) 100 (99-101) 99 (98-100)</td>
<td>98 (95-102) 99 (99-99) . . . . . . . . 99 (96-101)</td>
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</table>

*Data are given as mean percentage (95% confidence interval). Ellipses indicate data not available.
prehensive literature review regarding long-term UV-B exposure for psoriasis and nonmelanoma skin cancer found 4 results ranging between −0.6% and 1.8% excess incidence of skin cancers per year.25 The major problems in assessing risk from these results are the lack of information regarding cumulative UV-B dose and the concomitant use of coal tar by all the patients, which carries its own carcinogenic risk.26 Therefore, these data were insufficient for quantifying the excess incidence of skin cancer in UV-B–treated patients. Inconsistent results regarding squamous cell carcinoma25,27 and other nonmelanoma skin cancer28 rates in UV-B–treated patients have been reported; nevertheless, the calculated increased risk appears to be low.29

An inherent problem with retrospective studies of skin cancer risk among patients treated with broadband UV-B phototherapy for psoriasis during the 1980s to 1990s is that any small increased incidence of skin cancer must be compared with the incidence in the general population. Increases in melanoma incidence have been reported in retrospective investigations of the Surveillance, Epidemiology, and End Results program of the US National Cancer Institute of 1973 and 1987.30 Because squamous cell carcinoma and basal cell carcinoma are not reportable to this program, comparisons to those data for nonmelanoma skin cancer are not possible. Increases in nonmelanoma skin cancer incidence in the general population between the 1970s and 1990s have been reported from some central pathology laboratories31 but not others.32 Therefore, it is unclear whether any increases in skin cancer incidences among UV-B phototherapy–treated patients are equal to or greater than those reported in the general population.

Given the possibility that exposure to UV-B or a single wavelength in the UV-B range may result in a small excess skin cancer risk, a comparison of the cumulative doses delivered for routine psoriasis treatment vs the excimer laser treatment of scars and striae alba was performed. Because the excimer laser emits a single wavelength at 308 nm, it would be most appropriate to compare cumulative doses with narrowband UV-B, which emits a single wavelength at 311 nm. A minimal clearing course for psoriasis would involve 3 treatments per week for a minimum of 8 weeks (24 treatments), followed by twice weekly for 4 weeks and then once weekly for 4 weeks. Estimating a mean of 300 mJ/cm² of narrowband UV-B per treatment, this would yield a cumulative dose of approximately 11.1 J/cm² at the end of a minimal 4-month clearing and taper course. In contrast, a typical course of excimer laser treatment for hypopigmentation would require twice weekly treatments for 5 weeks (10 treatments), followed by monthly maintenance treatments. If one considers an estimated mean fluence of 200 mJ/cm² delivered per laser treatment, it would take roughly 4 years to achieve a cumulative dose of 11.6 J/cm². Therefore, the cumulative dose from excimer laser treatment for hypopigmentation is much lower than that delivered by narrowband UV-B phototherapy and would theoretically pose a lower excess skin cancer risk.

An important and interesting question regarding the ability to repigment hypopigmented scars and striae alba...
is whether the perceived hypopigmentation in these conditions is due to decreased pigment levels in the first place. Immunohistochemical investigations using melanocyte markers and Fontana-Masson silver stain to compare scars with normal skin demonstrated normal numbers of melanocytes and normal melanin transfer to keratinocytes, suggesting that vascular and optical factors may account for the hypopigmentation.\(^2,3\) This is supported by our observations that the hypopigmentation in most striae alba and some scars fails to enhance or fluoresce on Wood (black) light examination. The enhancement of hypopigmented lesions following irradiation with the light is due to the lack of absorption of the UV light by melanin, which results in the subsequent fluorescence of epidermal proteins. Quantitative support for this observation comes from the colorimetric data presented herein. Increased L\(^*\) values in the scars and striae alba relative to control sites (Figure 2 and Table 2) may be accounted for by differences in pigment (ie, melanin) or dermal factors, such as the degree of vasculature and collagen orientation, resulting in increased reflected light. The b\(^*\) values were lower for scars than for striae alba (data not shown), which is in keeping with Wood light findings. The a\(^*\) values were diminished equally in both conditions. Together, these data suggest that the increased lightness in scars has a greater relative contribution from diminished melanin, whereas in striae alba, dermal factors such as collagen distribution and decreased vascularity likely play a larger role. We are examining melanin levels by Fontana-Masson silver stain before and during treatment of hypopigmented scars and striae alba with a localized UV-B device. Comparing these levels with those of normal skin and control lesions will test this interesting hypothesis.

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Correspondence: Macrene R. Alexiades-Armenakas, MD, PhD, 880 5th Ave, New York, NY 10021 (dralexiades@nyderm.org).

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