Optimal Frequency of Treatment with the 308-nm Excimer Laser for Vitiligo on the Face and Neck

ZHU SHEN, M.D., Ph.D., TIAN-WEN GAO, M.D., Ph.D., LING CHEN, M.D., LI YANG, M.D., YAN-CHUN WANG, M.D., LIN-CHAO SUN, M.D., Ph.D., CHUN-YING LI, M.D., Ph.D., YAN XIAO, M.D., and YU-FENG LIU, M.D.

ABSTRACT

Objectives: This study was designed to determine the optimal treatment frequency with the 308-nm excimer laser for vitiligo and identify key clinical variable(s) associated with treatment efficacy at the optimal frequency. Background Data: Optimal clinical parameters for excimer laser treatment of vitiligo have not been fully determined. Data about the influence on treatment frequency of different clinical variables of vitiligo are needed to facilitate effective treatment regimens. Methods: A total of 187 patients were treated with the 308-nm excimer laser for 20 sessions at different frequencies (0.5, 1.0, 2.0, and 3.0 per week). The repigmentation rate was graded on a six-point scale and was blindly evaluated by independent physicians. Results: The final percentage of repigmentation for group 0.5 was statistically lower than those for group 1.0, 2.0, and 3.0, and percentages of final levels of repigmentation among these three groups were not statistically different. The clinical variables showed no statistical differences in the final repigmentation effect. Repigmentation occurred fastest with treatment frequencies of 2.0 and 3.0 and there was no statistically significant difference between them. The onset of repigmentation correlated with the area of vitiliginous patches treated, not with the other clinical variables. Conclusions: The 308-nm excimer laser is effective for therapy to treat vitiligo on the face and neck. The ultimate laser-induced repigmentation effect does not correlate with treatment frequency and repigmentation occurs faster with treatment frequencies of 2.0 and 3.0 than that of 1.0. It appears that the onset of repigmentation correlates with the total area of vitiliginous patches and the optimal treatment frequency. Monitored studies on a larger population with long-term follow-up would be needed to confirm and extend our findings.

INTRODUCTION

The 308-nm excimer laser represents the latest advance in the concept of selective phototherapy. It emits a wavelength in the ultraviolet B (UVB) spectrum and thus shares the same indications as conventional phototherapy. Like other laser devices, the 308-nm excimer laser emits a monochromatic and coherent beam of light. It can selectively treat lesions while sparing surrounding healthy skin and can deliver adequate treatment results. Clinicians have taken advantage of these properties to treat dermatologic disorders since 1997, with vitiligo treatment attracting the most attention.1

1Department of Dermatology, Xijing Hospital, Fourth Military Medical University, Xi’an, China.
2Department of Dermatology, Institute of Battle Surgery, Daping Hospital, Third Military Medical University, Chongqing, China.
reduction of the risk of tumorigenesis. An effective and well tolerated treatment regimen (including proper treatment frequency) may contribute to the effective management of the disease. Optimal clinical parameters for excimer laser treatment have not been fully determined. Prospective data about the influence of treatment frequency on different clinical variables of vitiligo are needed to allow effective and well tolerated treatment regimens. Therefore we performed this study to evaluate the optimal treatment frequency of 308-nm excimer laser energy for vitiligo on the face and neck, and to identify the key clinical variable(s) affecting treatment efficacy with optimal treatment frequency.

MATERIALS AND METHODS

Materials

The 308-nm xenon-chloride excimer laser was manufactured by PhotoMedex, Inc. (XTRA; Carlsbad, CA, USA). The fixed technical variables were: pulse frequency, 200Hz; pulse width, 30 nanoseconds; and distal pulse energy, 18 mJ per cm². Beam transmission was performed by an arm with moveable joints, with a 20-mm diameter for the spot size.

Patients

Inclusion criteria included: age >2 years and vitiliginous patch stability for >3 months with surface area of at least 4 cm². For all participants, a written consent form was signed by the patient or the patient’s parent or legal guardian. Exclusion criteria included: pregnant or breast-feeding women; personal history of a hypertrophic scar or skin cancer; those on immunosuppressive or photosensitizing drugs; and those who had undergone phototherapy during the past 3 months. For each patient, age, sex, the total area of the vitiliginous patches, and the duration of disease were noted. This study comprised 187 patients (93 females and 94 males), with mean age of 22.9 (range 2–66) years, mean disease duration of 40.4 months (range 2–240 months), and mean area of vitiliginous patches was 20.3 cm² (range 4–400 cm²).

Treatment

Our treatment protocols adapted the dose to the lesions present in each patient, and not to the minimal dose that caused erythema, as is the case for conventional phototherapies. Initial energy levels were 100 mJ per cm² for the orbits and 150 mJ per cm² for the remainder of the face, ears, and neck. Energy levels were increased by 50 mJ per cm² every two sessions. In the presence of a vesicle, bulla, or erythema lasting 24–48 h in the treated areas, energy levels remained the same. When such sequelae lasted 48–60 h, energy levels were decreased by 50 mJ per cm², and when they lasted more than 60 hours, treatment was withheld and resumed after their resolution, and the last dose was reduced to 100 mJ per cm². The energy level was increased by 100 mJ per cm² at each session if there was no erythema over the treated lesions. Each lesion was treated once (group 1.0), twice (group 2.0), or three times (group 3.0) per week, and the final group had a session every 2 weeks (group 0.5), for a total of 20 sessions. The patients each decided which group to enter according to their distance from our hospital, the time period between treatment sessions, and other factors. Protective eyewear was worn by all patients, as well as by the operators, during the phototherapy sessions.

Assessment and statistical analysis

Efficacy and secondary events were recorded at each session. Efficacy was blindly evaluated using a grid system (0.25 × 0.25 cm) by two independent physicians. The onset of repigmentation of vitiliginous lesions was evaluated after five

![Graph](https://via.placeholder.com/150)

**FIG. 1.** Repigmentation rates in the different groups. See text for details. Repig, repigmentation.

![Graph](https://via.placeholder.com/150)

**FIG. 2.** Percentages of repigmentation rates in the four groups. See text for details. Repig, repigmentation.
**Table 1. Statistical Results of the Percentages of Different Repigmentation Rates in the Four Groups**

<table>
<thead>
<tr>
<th></th>
<th>≥25% Repigmentation</th>
<th>≥50% Repigmentation</th>
<th>≥75% Repigmentation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.5×</td>
<td>1.0×</td>
<td>2.0×</td>
</tr>
<tr>
<td>0.5×</td>
<td>χ² = 9.76</td>
<td>p = 0.002</td>
<td>χ² = 4.72</td>
</tr>
<tr>
<td>1.0×</td>
<td>χ² = 1.44</td>
<td>p = 0.230</td>
<td>χ² = 0.09</td>
</tr>
<tr>
<td>2.0×</td>
<td>χ² = 1.02</td>
<td>p = 0.311</td>
<td>χ² = 1.16</td>
</tr>
<tr>
<td>3.0×</td>
<td>χ² = 3.92&lt;sup&gt;a&lt;/sup&gt;</td>
<td>p = 0.047</td>
<td>χ² = 4.05&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Correction for continuity (Yates’ correction).
treatment sessions, and the repigmentation rate was graded on a six-point scale: grade 0 = no repigmentation; grade 1 = 1%–24% repigmentation; grade 2 = 25%–49% repigmentation; grade 3 = 50%–74% repigmentation; grade 4 = 75%–99% repigmentation; and grade 5 = total repigmentation.\(^5\) In case of disagreement between the two physicians, a second evaluation was done by both together. If the disagreement persisted, the lower of the two evaluation grades was chosen. The differences between group 0.5, 1.0, 2.0, and 3.0 were assessed by chi-square testing using SPSS statistical software (SPSS V11.0; SPSS Inc., Chicago, IL, USA). The level of significance was set to \( p < 0.05 \).

RESULTS

A total of 187 subjects were treated with the 308-nm excimer laser for 20 sessions at different weekly frequencies as described above. All the patients completed the study. The degree of concordance between the two observers was excellent, and disagreement was noted for only five patients.

The effect of treatment frequency on the ultimate level of repigmentation

In group 0.5 (17 patients in all), 11 patients (65%) achieved 0% repigmentation, 3 (18%) achieved 1%–24% repigmentation, 2 (12%) achieved 25%–49% repigmentation, 1 (5%) achieved 50%–74% repigmentation, and 0 achieved ≥75% repigmentation. In group 1.0 (108 patients in all), 35 patients (32%) achieved 0% repigmentation, 10 (9%) achieved 1%–24% repigmentation, 17 (16%) achieved 25%–49% repigmentation, 19 (18%) achieved 50%–74% repigmentation, and 27 (25%) achieved ≥75% repigmentation. In group 2.0 (46 patients in all), the corresponding numbers were 13 (28%), 11 (24%), 6 (13%), 4 (9%), and 12 (26%), respectively. In group 3.0 (16 patients total), the corresponding numbers were 4 (25%), 2 (12%), 3 (15%), and 5 (32%), respectively (Fig. 1).

At end of the treatment, the numbers of patients with repigmentation percentages ≥25% for treated lesions were 18% (3/17), 58% (63/108), 48% (22/46), and 63% (10/16), after 0.5, 1.0, 2.0, and 3.0 weekly treatments, respectively (Fig. 2). The number of patients with ≥50% and 75% repigmentation among groups 0.5 was lower than those for groups 1.0, 2.0, and 3.0. In group 0.5, 3 patients (18%) achieved repigmentation after fewer than 5 sessions. In groups 1.0, 2.0, and 3.0, the corresponding numbers were 52 (48%), 33 (72%), and 12 (75%), respectively. Repigmentation occurred slowest with 0.5 weekly treatment (statistically significant, as shown in Table 2). Repigmentation occurred faster for groups 2.0 and 3.0 compared with group 1.0 (statistically significant, as shown in Table 2). Repigmentation occurred fastest with 2.0 and 3.0 weekly treatments, and the onset of repigmentation between them was not statistically different (\( \chi^2 = 0.005, p = 0.941 \), as shown in Table 2).

The effect of treatment frequency on the onset of repigmentation

In group 0.5, 3 patients (18%) achieved repigmentation after fewer than 5 sessions. In groups 1.0, 2.0, and 3.0, the corresponding numbers were 52 (48%), 33 (72%), and 12 (75%), respectively. Repigmentation occurred slowest with 0.5 weekly treatment (statistically significant, as shown in Table 2). Repigmentation occurred faster for groups 2.0 and 3.0 compared with group 1.0 (statistically significant, as shown in Table 2). Repigmentation occurred fastest with 2.0 and 3.0 weekly treatments, and the onset of repigmentation between them was not statistically different (\( \chi^2 = 0.005, p = 0.941 \), as shown in Table 2).

In group 1.0, 40 patients (56%) achieved repigmentation after 5 sessions in the ≥20-cm\(^2\) subgroup, in contrast to 12 patients (35%) in the >20-cm\(^2\) subgroup (statistically significant: \( \chi^2 = 5.57, p = 0.018 \)). In group 2.0, these figures were 27

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TABLE 2. STATISTICAL ANALYSES OF THE ONSET OF REPIGMENTATION AFTER FIVE TREATMENT SESSIONS AMONG THE FOUR GROUPS

<table>
<thead>
<tr>
<th>Group</th>
<th>( \chi^2 )</th>
<th>df</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5×</td>
<td>5.55</td>
<td>2</td>
<td>0.018</td>
</tr>
<tr>
<td>1.0×</td>
<td>14.83</td>
<td>2</td>
<td>0.001</td>
</tr>
<tr>
<td>2.0×</td>
<td>7.26</td>
<td>2</td>
<td>0.007</td>
</tr>
<tr>
<td>3.0×</td>
<td>4.02</td>
<td>2</td>
<td>0.044</td>
</tr>
</tbody>
</table>

\( ^a \) Correction for continuity (Yates’ correction).

FIG. 3. The influence of the clinical variable (the area of vitiliginous patches) on the onset of repigmentation. See text for details. Repig, repigmentation.
menting vitiligo patches. Selective phototherapy with this kind of laser in treating vitiligo was first reported in 2001. Since then, many studies have shown the efficacy of this laser for repigmentation on UV-sensitive areas. Surgical treatment (mini-}

DISCUSSION

Vitiligo is an acquired cutaneous depigmentation disorder affecting approximately 1%–2% of the world population with no predilection for age, gender, or racial background. The clinical presentation is characterized by well circumscribed white cutaneous patches with an absence of melanin. Although not life threatening, people affected by vitiligo have a vastly reduced quality of life and psychological problems caused by the color contrast between healthy pigmented skin and the depigmented vitiliginous patches.

Although current therapeutic modalities are targeted to increasing melanocyte melanin production, to our knowledge few treatment modalities address the immunologic nature of the disease and provide truly satisfactory results. Because of its relatively good efficacy and excellent tolerance, narrow band UVB (NB-UVB) therapy is considered the best treatment for extensive vitiligo vulgaris. The mechanism of action of UVB therapy on vitiligo is not fully understood. Stimulation of melanocyte migration and proliferation starting from the outer root sheath of the hair follicles are certainly the leading factors. This stimulation probably involves the direct action of UV therapy on the melanocytes, and the action of the cytokines secreted by the keratinocytes. Recent studies on the autoimmune origin of vitiligo emphasize the probable implication of the immunomodulatory mechanisms in the treatment of vitiligo. This immunomodulating photobiological action involves the depletion of Langerhans cells and the decrease of their antigen presentation function, the keratinocytic cytokines, and also the apoptosis of the activated T lymphocytes.

The excimer laser represents the latest advance in the concept of selective phototherapy. It delivers high energy monochromatic UVB at 308 nm and shares the physical properties of lasers: a monochromatic and coherent beam of light and selective treatment of the target. The use of the 308-nm excimer laser in treating vitiligo was first reported in 2001. Selective phototherapy with this kind of laser is more effective than NB-UVB phototherapy in the treatment of vitiligo, and this is attributed to more immunomodulatory mechanisms, representing a new treatment modality for the management of stable vitiligo, especially on UV-sensitive areas (e.g., the face and neck).

Optimal clinical parameters for the excimer laser treatment have not yet been fully determined. Among the factors that can influence the clinical response to the treatment, the location of the lesions seems to play a crucial role. There was a statistically significant difference between results obtained on UV-resistant areas (e.g., extremities and bony prominences) and those on UV-sensitive areas, in which repigmentation rates were much higher. Treatment frequency was also an important factor in how effective and well tolerated the treatment regimens were. Treatment sessions can be performed once, twice, or three times a week, or once every 2 weeks. Recently Hofer et al. reported that the repigmentation rate seems to be linked to the total number of sessions and not to their frequency (they had 14 patients enrolled). More information about the influence of treatment frequency on different clinical variables of vitiligo were needed, and this could be gained through further investigation. Therefore we performed this study (with 187 patients enrolled) to determine the optimal treatment frequency with the 308-nm excimer laser for treating vitiligo (in UV-sensitive areas), and to identify the key clinical variable(s) affecting treatment efficacy.

At end of treatment, those with ≥75% repigmentation were 0% (0/17), 25% (27/108), 26% (12/46), and 32% (5/16) for 0.5, 1.0, 2.0, and 3.0 weekly treatments, respectively. Those with ≥50% repigmentation were 6% (1/17), 43% (46/108), 35% (16/46), and 50% (8/16), and those with ≥25% repigmentation were 18% (3/17), 58% (63/108), 48% (22/46) and 63% (10/16), after 0.5, 1.0, 2.0, and 3.0 weekly treatments, respectively. The percentage of those with total repigmentation for group 0.5 was significantly lower than those for the other groups, and rates of repigmentation among groups 1.0, 2.0, and 3.0 were not statistically different. The clinical variables (age, sex, skin type, the area of vitiliginous patches, and duration of disease) showed no statistical differences in the final repigmentation effect. It was shown that 308-nm excimer laser therapy is effective for vitiligo on the face and neck (Figs. 4, 5, 6, and 7), as was shown in another clinical trial. It seems that the final rates of laser-induced repigmentation does not correlate with treatment frequency, which was consistent with the results of the study by Hofer et al.

In groups 0.5, 1.0, 2.0, and 3.0, 3 (18%), 52 (48%), 33 (72%), and 12 (75%) patients achieved repigmentation after five treatment sessions, respectively. Repigmentation occurred fastest with treatment frequencies of 2.0 and 3.0 per week, and there was no statistically significant difference between them (p > 0.05). In group 1.0, 40 patients (56%) achieved repigmentation after five sessions in the ≥20-cm² subgroup versus 12 patients (35%) in the >20-cm² subgroup (p < 0.05). In group 2.0, these figures were 27 patients (82%) versus 6 patients (46%) (p < 0.05), and in group 3.0, 11 patients (92%) versus 1 patient (25%) (p < 0.05). The other clinical variables showed no statistical influence on the rate of repigmentation. It can be concluded that the onset of repigmentation correlates with the area of vitiliginous patches treated by the laser. Repigmentation occurs faster in ≥20-cm² subgroup than in the >20-cm² subgroup, no matter the treatment frequency.

Thus, the comparison of the above treatment regimens suggests a statistically significant superiority of 2.0 and 3.0 weekly treatments over 1.0 and 0.5 weekly treatments, and those with more weekly sessions saw earlier and more satisfying achievement of repigmentation on UV-sensitive areas. Surgical treatment (mini-
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FIG. 4. Vitiliginous patches on the face treated by the 308-nm excimer laser at a rate of 0.5× per week (i.e., once every 2 weeks).
FIG. 5. Vitiliginous patches on the face treated by the 308-nm excimer laser at a rate of 1.0× per week.
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FIG. 6. Vitiliginous patches on the face treated by the 308-nm excimer laser at a rate of 2.0× per week.
FIG. 7.  Vitiliginous patches on the face treated by the 308-nm excimer laser at a rate of 3.0× per week.
grafting, thin split-thickness grafting, or suction blister grafting) could be performed to reduce the area of vitiliginous patches. It appears that 308-nm excimer laser treatment, combined with surgical treatment, would be more feasible for large vitiliginous patches on the face and neck. It should be noted in our study that the range of age, disease duration, and area requiring treatment was high, and that the lack of follow-up was a limitation. Thus a larger, well monitored study (with controls) performed on a larger and more homogenous population, with extensive follow-up would be needed to confirm and extend our findings.

CONCLUSION

The 308-nm excimer laser is effective for treating vitiligo on the face and neck. The final repigmentation results do not correlate with treatment frequency, and repigmentation occurs fastest with treatments carried out 2.0 and 3.0 times per week. It also appears that the timing of the onset of repigmentation correlates with the total area of vitiliginous patches requiring treatment.

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REFERENCES


Address correspondence to:
Dr. Tian-Wen Gao
Department of Dermatology
Xijing Hospital
Fourth Military Medical University
Xi’an 710032, China

E-mail: gaotw@fmmu.edu.cn