STUDY

# Targeted UV-B Phototherapy for Plaque-type Psoriasis

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**Objective:** To determine whether targeted UV-B phototherapy is efficacious and safe in the treatment of localized psoriasis and whether there is a dose-response relationship.

**Design:** Randomized, evaluator-blind, controlled study.

**Setting:** Dermatology clinic in a large university-based hospital in Bangkok, Thailand.

**Patients:** Fourteen patients with stable, localized, plaque-type psoriasis.

**Interventions:** Patients were randomized to receive different fluences of targeted UV-B phototherapy 3 times weekly based on predetermined minimal erythema doses (MEDs). Treatment fluences were constant throughout the study period of 4 weeks. Follow-up was carried out until lesions returned to original state.

**Main Outcome Measures:** Modified psoriasis area and severity index.

**Results:** All fluences of UV-B produced some clinical improvement and were very well tolerated. Fluences ranging from 1 to 6 multiples of MEDs resulted in clearance of lesions in some patients with 6 MEDs producing clearance in 77% of patients. The number of treatments required to clear psoriatic lesions when 2 to 6 MEDs were used was 5.0 to 6.1 treatments. The only adverse events observed were erythema, which was asymptomatic in most subjects, and hyperpigmentation.

**Conclusions:** Incoherent, targeted UV-B phototherapy is a safe and efficacious treatment modality for localized psoriasis. Its value in other UV-B responsive conditions should be further investigated.

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PARRISH AND JAENICKE[1] DEMONstrated that the action spectrum for psoriasis clearing lies within the 300- to 313-nm range. Based on that conclusion, phototherapy using longer wavelengths of UV-B has been developed. For more than a decade now, narrowband UV-B phototherapy emitting light in the 311- to 313-nm spectra has been used successfully for the treatment of psoriasis. This is associated with more effective clearing of psoriasis compared with conventional broadband UV-B. However, the normal, uninvolved skin is unavoidably exposed to UV radiation, resulting in several adverse effects. It is also known that psoriatic plaques can tolerate higher fluences of UV radiation, compared with uninvolved skin.[2] Most recently, efforts have been made to develop therapeutic devices that deliver light, be it laser or incoherent, selectively to the psoriatic plaques.

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The use of 308-nm excimer laser to specifically treat psoriatic lesions has been reported since 1997.[3] Since that time several other studies with modifications of protocols appeared in the literature, confirming the usefulness of this treatment modality.[4-9]

*See also pages 1527, 1537, 1549, 1556, 1580, and 1589*

However, the excimer machine is rather costly; thus, a more economical device may be more suitable for use in the less developed nations. Our study objectives were to determine whether the use of the high-intensity, broadband UV-B device would result in clinical improvement and to determine the number of treatments and doses of UV-B needed to improve localized psoriatic plaques.

## METHODS

### PATIENTS

Patients 18 years or older with stable, plaque-type psoriasis, who had not received any systemic therapies, including photochemotherapy for the past 8 weeks and topical treatments or UV-B phototherapy within the past 4 weeks, were eligible for the study. All patients were recruited from dermatology clin-

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**Table 1. Patient Characteristics**

| Patient No./ Sex/Age, y | Skin Type | Duration, y | Previous Treatments | MED, mJ/cm$^2$ | Location of Treated Plaques |
|---|---|---|---|---|---|
| 1/M/23 | IV | 1 | Topical corticosteroids | 120 | Back |
| 2/M/44 | III | 9 | BB-UV-B | 120 | Buttock |
| 3/M/44 | IV | 6 | BB-UV-B, MTX | 180 | Back |
| 4/M/31 | IV | 3 | NB-UV-B | 300 | Buttock |
| 5/M/38 | III | 6 | Topical corticosteroids, LCD | 90 | Buttock |
| 6/M/33 | IV | 4 | Topical corticosteroids, LCD, anthralin | 210 | Buttock |
| 7/F/41 | IV | 7 | BB-UV-B | 270 | Back |
| 8/M/52 | IV | 20 | BB-UV-B | 390 | Buttock |
| 9/M/49 | III | 4 | NB-UV-B | 210 | Leg |
| 10/M/39 | IV | 11 | BB-UV-B | 210 | Buttock |
| 11/F/53 | III | 6 | Topical corticosteroids, LCD | 180 | Back |
| 12/M/41 | IV | 3 | Acitretin | 210 | Back |
| 13/F/44 | IV | 3 | Topical corticosteroids, LCD | 300 | Back |

Abbreviations: BB-UV-B, broadband UV-B phototherapy; LCD, liquor carbonis detergens; MED, minimal erythema dose; MTX, methotrexate; NB-UV-B, narrowband UV-B phototherapy.

ics at King Chulalongkorn Memorial Hospital, Bangkok, Thailand. Exclusion criteria were pregnancy, lactation, and photosensitive disorders. The study protocol was approved by the Ethics Committee of King Chulalongkorn Memorial Hospital/Faculty of Medicine, Chulalongkorn University. Informed consent was obtained from each participant.

### PHOTOTHERAPY DEVICE

The irradiation source used in this study, DuaLight (TheraLight Inc, Carlsbad, Calif), was a high-pressure mercury lamp capable of emitting either UV-B or UV-A. The UV-B spectral output of this light source includes peaks at 302 nm and 312 nm, with an average weighted erythemal wavelength of 304 nm. The high output of this device allows irradiation of 100 mJ/cm$^2$ of UV-B to take place within approximately 0.7 second. UV radiation is delivered through a square aperture sized 1.9 × 1.9 cm.

### TECHNIQUE

Prior to the start of the study, minimal erythema dose (MED) was determined on each subject using untanned, uninvolved skin of the buttocks or the lower back. The dose ranges were dependent on skin types, namely 90, 120, 150, 180, 210, and 240 mJ/cm$^2$ for skin type III and 120, 150, 180, 210, 240, and 270 mJ/cm$^2$ for skin type IV. If no erythema developed, the doses were further increased, so that the MED could be detected in all subjects.

Treatment was delivered 3 times per week for 4 weeks or until lesions cleared. Patients were then followed up every 4 weeks until lesions returned to their baseline state. The first treatment was started in October, and the last follow-up was in February of the following year. Doses of UV-B used for the treatment were 0.5, 1, 2, 4, and 6 multiples of MED. Fluences of UV-B delivered to each spot remained constant throughout the study. Mapping of lesions was performed using clear plastic sheets to ensure that the following doses were delivered to the very same areas treated previously. If blistering developed, treatment was to be withheld until reaction subsided. An untreated plaque in the same area served as control.

### EVALUATION OF EFFICACY

Psoriasis severity index (PSI) scores, also known as modified PASI scores, which took into account erythema, induration, and scaliness of the plaques,[4,7] were given at baseline and every 2 weeks of treatment by an investigator blinded to the dose assignment (P.A.). Scores of 0 to 4 were assigned to each of the 3 clinical aspects; thus, the maximum score possible was 12. Clearance was defined as greater than 95% improvement. Photographs were taken at each visit. Statistical analysis was carried out with SPSS version 11.0 (SPSS Inc, Chicago, Ill) software. Repeated-measure analysis of variance was used to determine the overall treatment effect.

## RESULTS

A total of 14 patients (10 men and 4 women), whose ages ranged from 23 to 53 years, were enrolled in the study. Only 1 patient failed to complete the study because her psoriasis flared up and oral methotrexate was prescribed. Of the remaining 13 patients who completed the study, 4 were of skin type III, while the other 9 were of skin type IV. **Table 1** gives the characteristics of patients who completed the study.

The body surface area involved in each patient was less than 10%. The mean PSI score of the 13 patients at baseline was 7.38, with a range of 3 to 10. Minimal erythema doses for patients with skin type III ranged from 90 to 240 mJ/cm$^2$, while those of skin type IV ranged from 120 to 390 mJ/cm$^2$.

All fluences produced some clinical improvement. Psoriasis severity index scores improved in 12 subjects. Only 1 subject (patient 9) had worsening of the treated plaques. This is probably because his psoriatic lesions elsewhere

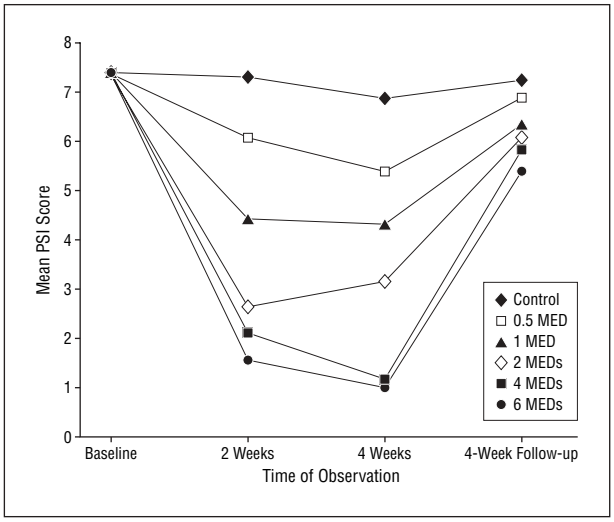


**Figure 1.** Dose-response relationship of targeted UV-B phototherapy. MED indicates minimal erythema dose; PSI, psoriasis severity index.

**Table 2. PSI Scores of Treated Plaques Compared With Controls***

| Time Point | Difference in PSI Score From Control, Mean ± SE (95% CI) | *P* Value† |
|---|---|---|
| 2 Weeks | | |
| 0.5 MED | 1.231 ± 0.486 (–0.542 to 3.003) | .39 |
| 1MED | 2.885 ± 0.825 (–0.124 to 5.894) | .07 |
| 2 MEDs | 4.654 ± 0.861 (1.512 to 7.796)‡ | .002 |
| 4 MEDs | 5.192 ± 0.458 (3.520 to 6.865)‡ | <.001 |
| 6 MEDs | 5.731 ± 0.657 (3.334 to 8.128)‡ | <.001 |
| 4 Weeks | | |
| 0.5 MED | 1.462 ± 0.526 (–0.459 to 3.382) | .25 |
| 1 MED | 2.538 ± 0.781 (–0.312 to 5.389) | .11 |
| 2 MEDs | 3.629 ± 0.756 (0.932 to 6.453)‡ | .006 |
| 4 MEDs | 5.654 ± 0.624 (3.378 to 7.930)‡ | <.001 |
| 6 MEDs | 5.846 ± 0.697 (3.304 to 8.388)‡ | <.001 |
| 4-Week follow-up | | |
| 0.5 MED | 0.346 ± 0.274 (–0.653 to 1.345) | >.99 |
| 1 MED | 0.885 ± 0.651 (–1.490 to 3.259) | >.99 |
| 2 MEDs | 1.154 ± 0.783 (–1.704 to 4.012) | >.99 |
| 4 MEDs | 1.385 ± 0.789 (–1.494 to 4.263) | >.99 |
| 6 MEDs | 1.846 ± 0.783 (–1.1012 to 4.704) | .54 |

Abbreviations: MED, minimal erythema dose; PSI, psoriasis severity index.
*Based on estimated marginal means.
†Bonferroni adjustment for multiple comparison.
‡The mean difference is significant at the .05 level.

on the body also worsened, as reflected by the increase in the PSI score of the control plaque. Also of note is that the assigned plaques of this patient were located on the lower leg, an area notoriously recalcitrant to most forms of treatment.

**Figure 1** shows the PSI scores at baseline, at weeks 2 and 4, and at 4-week follow-up, which clearly demonstrate a dose-response relationship. The mean PSI score at 2 weeks for all UV-B doses combined was 3.37 (range, 0-10). At 4 weeks, this mean global score was further reduced to 3.01 (range, 0-10). Compared with controls, no statistically significant improvement was seen at any time points when 0.5 to 1.0 MED fluences

**Table 3. Number of Treatments and Cumulative UV-B Doses Received by Patients**

| MED | Mean No. of Treatments | Mean Cumulative Doses of UV-B* |
|---|---|---|
| 0.5 | 9.31 | 4.65 |
| 1 | 9.00 | 9.00 |
| 2 | 7.54 | 15.08 |
| 4 | 7.31 | 29.23 |
| 6 | 7.15 | 42.92 |

Abbreviation: MED, minimal erythema dose.
*Cumulative doses of UV-B are expressed as multiples of MED.

**Table 4. Number of Treatments and Cumulative UV-B Doses Necessary to Clear Psoriasis**

| MED | No. of Patients | Mean No. of Treatments | Mean Cumulative Doses of UV-B* |
|---|---|---|---|
| 0.5 | 0 | NA | NA |
| 1 | 3 | 7.67 | 7.67 |
| 2 | 5 | 5.00 | 10.00 |
| 4 | 7 | 5.71 | 22.86 |
| 6 | 10 | 6.10 | 36.60 |

Abbreviations: MED, minimal erythema dose; NA, not applicable.
*Cumulative doses of UV-B are expressed as multiples of MED.

were used (**Table 2**). Fluences ranging from 2 to 6 MEDs produced statistically significant improvements when compared with controls at 2 weeks ($P=.002$ for 2 MEDs; $P<.001$ for 4 and 6 MEDs). These significant improvements were maintained at week 4 (Table 2). However, when mean PSI scores obtained from 1, 2, 4, and 6 MEDs were compared, there were no statistically significant differences among the doses (data not shown).

The average total number of treatments and cumulative doses of UV-B received by patients for each particular dose are outlined in **Table 3**.

A fluence of 0.5 MED did not clear any psoriatic plaques. Fluences as low as 1 MED were able to clear psoriasis at some time points in 3 patients and 2 MEDs cleared 5 lesions, while 4 MEDs cleared 7 lesions. As expected 6 MEDs, the highest fluence, cleared the most lesions (ie, 10 plaques) (**Table 4**). The mean number of treatments necessary to clear psoriasis was lowest for 2 MEDs. However, this is not significantly different from fluences of 4 and 6 MEDs, for which 5.71 and 6.10 treatments, respectively, were needed (Table 4). The clearing of psoriasis following this treatment, unfortunately, is followed by rapid relapse. Most psoriatic plaques returned to their original state within 4 weeks after treatment was discontinued. Only in 2 patients were remissions maintained past 4 weeks at doses at or above 2 MEDs.

Adverse effects observed were limited to asymptomatic erythema at higher fluences and hyperpigmentation in some patients. Interestingly, painful erythema, but not blistering, was seen in 2 subjects. This was seen only when treatment was delivered to the elbow area and not elsewhere on the body.

## COMMENT

High-dose UV-B phototherapy, whether delivered by laser or broadband light source, seems promising in the treatment of localized, recalcitrant psoriatic lesions. The higher fluences delivered through these devices result in fewer numbers of treatments compared with the conventional stand-up units used in most centers. Another major benefit from such treatment lies within the fact that only psoriatic lesions are treated. Thus, normal skin is not at increased risk of developing photoaging or skin cancers.

We have demonstrated that using higher fluences of broadband UV-B, psoriasis can be cleared even with the darker skin types. Similar to previous studies using 308-nm excimer laser, UV fluences less than 6 multiples of MED can be safely delivered without causing any significant phototoxic effects. Recently, Trehan and Taylor[5] reported that medium dose excimer laser delivered 3 times weekly results in clearance of psoriasis, defined as greater than 95% improvement, after a mean of 10.6 treatments and mean cumulative dose of 6.1 J/cm$^2$. When higher doses of excimer laser, namely, 8 and 16 times the MED, were used, as few as 1 treatment may clear psoriasis.[6]

In a multicenter study involving 116 evaluable patients, Feldman et al[7] found that 72% (66 of 92) of the participants who completed the 10 treatments as planned or had clearance before the 10 treatments could achieve at least 75% clearance after an average of 6.2 treatments, and 35% (28 of 80) of the participants achieved at least 90% clearance by 7.5 treatments. With Kaplan-Meier analysis, Feldman et al[7] concluded that the median time to achieve 75% improvement was 8 treatments. Overall, 84% of patients reached improvement of 75% or better after 10 or fewer treatments; 50% of patients reached improvement of 90% or better after 10 or fewer treatments.[7]

The results from our study are similar to the aforementioned excimer studies in that patients who received comparable doses of UV light, between 2 and 6 MEDs, cleared after receiving 5 to 6 treatments (Table 4). This has been confirmed in a study published recently in which Tanghetti and Gillis[9] demonstrated equivalent outcomes when excimer laser was compared with incoherent UV-B light source. However, a direct comparison regarding cumulative UV doses cannot be made because the dosimetry for excimer laser and incoherent UV-B light is different. Given the now wider varieties of available high-intensity light sources, it might be more logical to compare in terms of equi-erythemogenic doses, for instance, multiples of MEDs.

The therapeutic effect of targeted UV-B phototherapy should be similar to that of broadband UV-B,[10] narrowband UV-B,[11] and 308-nm excimer laser,[12] whereby apoptosis of infiltrating lymphocytes and reduction in proliferation of keratinocytes are the main mechanisms of action.

One major advantage of the device used in our study is the ease and efficiency for MED determination, which takes less than a minute. After that, UV-B fluences in the multiples of MEDs can be delivered in a reasonable time similar to excimer laser. Moreover, as mentioned by Tanghetti et al,[9] the beam profile is more uniform than that of excimer laser, making treatment in tile mode much easier to perform. This results in very homogeneous clearance of lesions (**Figure 2**).

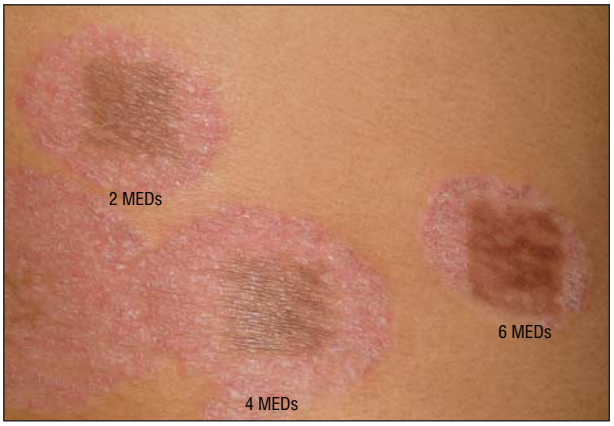


**Figure 2.** Clinical improvement observed at different fluences (4 weeks). MEDs indicates minimal erythema doses.

The remission time obtained in the present study is relatively short, with most patients having a relapse within 4 weeks of the last treatment. This might have resulted from the fact that our study time was limited to 4 weeks as opposed to 8 weeks in other studies[5] because we believe that for a novel phototherapy/laser device to appeal to patients with psoriasis, it needs to produce more rapid improvement compared with the median time of 40 days for clearing psoriasis that one gets with narrowband UV-B.[13] Trehan and Taylor[5] reported a mean remission time of 3.5 months after an 8-week course of medium-dose excimer laser treatment. For the high-dose excimer laser treatments, nearly half the treated subjects could maintain remission for more than 4 months after a single treatment.[6] In the multicenter study by Feldman,[14] data from the participants who cleared and were available for follow-up revealed a median remission time of 8.7 weeks.[14] We strongly believe there are several modifications that may improve the therapeutic outcomes; for instance, it would be interesting to see whether use of higher fluences at longer intervals will result in improved remission time. Also, Trehan and Taylor[6] demonstrated that induration and scaliness of lesions are more important predictors of outcome than erythema. In fact, basing the dose purely on induration of the lesions has proved very effective in the treatment of recalcitrant localized psoriasis.[8]

We did not observe any serious adverse events associated with this treatment modality. In fact, most patients tolerate the light doses very well. Only mild burning sensation at the higher fluences was observed. Bullae, which occurred with excimer laser treatment, even at medium doses,[5] were not observed in our study. However, long-term safety of such high-dose irradiation is difficult to predict at the moment. It is well accepted that sunburn,[15,16] especially in the earlier years of life, is associated with the development of melanomas in later years. Extended follow-up is thus warranted.

In summary, targeted UV-B phototherapy is a safe and convenient way to deliver light specifically to psoriatic lesions and will be of great benefit to patients who have localized, recalcitrant disease for which other conventional treatments have failed. Also, it may be useful for psoriasis

in certain areas, for example, the scalp and for inverse psoriasis.[17] However, because UV-B penetrates rather superficially into the dermis, it might be of limited use when nail and palmoplantar psoriasis are the concern. The other indications for which targeted UV-B phototherapy may be used should be similar to those for excimer laser, namely, vitiligo,[18-20] eczema, mycosis fungoides, and theoretically intraoral lesions such as oral lichen planus. In fact, after submission of this manuscript, we have had success with some patients with patch-stage mycosis fungoides.

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## *News and Notes*

**First Congress of the International Dermoscopy Society.** Naples, Italy, April 27 to 29, 2006. The recently founded International Dermoscopy Society organizes a meeting designed for all colleagues interested in the diagnosis and management of pigmented skin lesions. Special emphasis is given on guidelines for management, standardization of reports, and, particularly, on the development of machine vision in dermoscopy. In addition, seminars in discussion format and half-day workshops with special emphasis on pertinent issues in dermoscopy will be conducted.

The detailed program is presented on the Web site: http://www.dermoscopy-ids.org.

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