# The efficacy of pulsed dye laser treatment for inflammatory skin diseases: A systematic review

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***Background:*** The position of the pulsed dye laser (PDL) in the treatment of inflammatory skin diseases is still unclear. Evidence-based recommendations are lacking.

***Objectives:*** We sought to systematically review all available literature concerning PDL treatment for inflammatory skin diseases and to propose a recommendation.

***Methods:*** We searched for publications dated between January 1992 and August 2011 in the database PubMed. All studies reporting on PDL treatment for an inflammatory skin disease were obtained and a level of evidence was determined.

***Results:*** Literature search revealed 52 articles that could be included in this study. The inflammatory skin diseases treated with PDL consisted of: psoriasis, acne vulgaris, lupus erythematodes, granuloma faciale, sarcoidosis, eczematous lesions, papulopustular rosacea, lichen sclerosis, granuloma annulare, Jessner lymphocytic infiltration of the skin, and reticular erythematous mucinosis. The efficacy of PDL laser treatment for these inflammatory skin diseases was described and evaluated.

***Limitations:*** Most conclusions formulated are not based on randomized controlled trials.

***Conclusions:*** PDL treatment can be recommended as an effective and safe treatment for localized plaque psoriasis and acne vulgaris (recommendation grade B). For all other described inflammatory skin diseases, PDL seems to be promising, although the level of recommendation did not exceed level C. (J Am Acad Dermatol 2013;69:609-15.)

***Key words:*** inflammatory; pulsed dye laser; skin diseases; treatment.

The flash lamp pumped pulsed dye laser (PDL) was the first laser specifically developed for the treatment of vascular lesions. The mode of action of the PDL is based on the principle of selective photothermolysis,[1] a targeted damaging of specific structures in the skin without damaging the surrounding area and by direct cutaneous immunologic activation.[2,3] Omi et al[3] have shown acute inflammatory changes (neutrophils, monocytes, and mast cells) 3 hours after laser treatment. Four weeks later, many lymphocytes and fibroblasts were observed, still increasing in week 5, whereas the capillaries showed an almost normal structure at week 2.

*Abbreviations used:*

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| CDLE: | chronic discoid lupus erythematodes |
| GF: | granuloma faciale |
| LOE: | level of evidence |
| LT: | lupus tumidus |
| PDL: | pulsed dye laser |
| RCT: | randomized controlled trials |
| SCLE: | subacute cutaneous lupus erythematodes |
| SLE: | systemic lupus erythematodes |
| UVB: | ultraviolet-B |

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The current PDL is able to vary the different parameters such as the spot size (up to 12 mm), the pulse duration (ranging from 0.35-40 milliseconds), and the energy fluence, which has increased in recent years because of the development of protective cooling systems.[4] The most frequently used wavelengths are 585 and 595 nm allowing the penetration depth to a maximum of 1.5 mm. So, the fields of application are limited to superficial structures. Side effects during and after treatment with PDL are dependent of the chosen parameters, location, and skin type. They include erythema, purpura, edema, blistering, crusting, pigmentary changes, and, rarely, scarring.[5]

Today, the PDL is considered the laser of choice for most congenital and acquired vascular lesions.[6-8] In addition, it is used for the treatment of many other nonvascular or vascular-dependent indications, such as viral infections,[9,10] scars,[11] and stretch marks.[12] In 1992, Hacker and Rasmussen[13] described for the first time the treatment of an inflammatory skin disease, psoriasis, with the PDL.

To examine the position of PDL for the treatment of inflammatory skin diseases, we reviewed the current literature and provided updated information on the treatment of inflammatory skin diseases with PDL.

**CAPSULE SUMMARY**

- Although many inflammatory skin diseases have been treated with pulsed dye laser, evidence-based recommendations are lacking.
- In this review, the evidence published in the literature concerning the efficacy of PDL treatment for inflammatory skin diseases is discussed.
- Varying levels of evidence exist to support the efficacy of the PDL in the treatment of different inflammatory skin diseases.

## METHODS

The focus of attention was the use of PDL in patients with inflammatory skin diseases. We searched for peer-reviewed publications dated between January 1, 1992, and August 31, 2011, in the computerized bibliographic database PubMed. Selected languages were limited to English, German, and Dutch. The key terms used were "pulsed dye laser" and "pulsed dye lasers." The term "inflammatory skin diseases" includes an extensive range of different diagnoses. Therefore, the literature on PDL was systematically scanned by a dermatologist, to be sure that all possible inflammatory skin diseases were found. Full details on the search strategy are available upon request.

Exclusion criteria were: treatment of lesions other than inflammatory skin diseases, the use of laser systems other than the PDL, and the use of concomitant local therapies, except for keratinolytic pretreatment to reduce scale and enhance PDL penetration. The use of concomitant systemic therapy was allowed, if this was not started or altered more than 6 weeks before the study onset or during the study itself. Outcome measures depended on the investigated skin disease. Because the available literature about PDL for inflammatory skin diseases is limited, all found articles were reviewed, including case reports, case series, retrospective studies, open-label trials, and randomized controlled trials (RCT). The bibliographies of all articles identified were checked for additional relevant articles that were not identified in the PubMed search. After the initial search was performed, all abstracts were screened for suitability for inclusion. Full texts of the suitable abstracts were obtained. Articles were assigned a level of evidence (LOE) and afterward graded according to the Oxford Center for Evidence-based Medicine Levels of Evidence[14] (Tables I and II) by 3 dermatologists.

## RESULTS

### Trial flow

In total, 2215 articles regarding PDL were identified. After screening of titles, abstracts, and full-text articles if applicable, 52 of these articles were suitable to be used in the review. The publications of inflammatory skin diseases treated with PDL consisted of: psoriasis (13), acne vulgaris (9), lupus erythematosus (including systemic, chronic discoid, and subacute cutaneous) (8), granuloma faciale (GF) (7), sarcoidosis (5), chronic eczema (1), lichen sclerosis (3), granuloma annulare (2), Jessner lymphocytic infiltration of the skin (1), reticular erythematous mucinosis (1), and papulopustular rosacea (2). All results are shown in Table III (available at http://www.jaad.org). Because of limited space, however, the inflammatory skin diseases with 3 publications or less (chronic eczema, lichen sclerosis, granuloma annulare, Jessner lymphocytic infiltration of the skin, reticular erythematous mucinosis, and papulopustular rosacea) will not be discussed in detail, but are listed in Table III (available at http://www.jaad.org).

### Psoriasis

Literature search revealed 11 articles[13,15-24] describing PDL treatment for localized plaque-type psoriasis[15,16]; localized, chronic stable plaque psoriasis[17-20];

**Table I.** Level of evidence

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|---|
| 1a. Systematic review of RCTs |
| 1b. Individual RCT |
| 2a. Systematic review of cohort studies |
| 2b. Individual cohort study (including low-quality RCT) |
| 3a. Systematic review of case-control studies |
| 3b. Individual case-control study |
| 4. Case series |
| 5. Case reports, expert opinion |

*RCT*, Randomized controlled trial.
Data from Oxford Center for Evidence-based Medicine Levels of Evidence.[14]

**Table II.** Grades of recommendation

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|---|
| A. Studies with consistent LOE 1a and/or 1b |
| B. Studies with consistent LOE 2a, 2b, 3a, or 3b; or extrapolations from studies with LOE 1a or 1b |
| C. Studies with LOE 4 or extrapolations from studies with LOE 2a, 2b, 3a, or 3b |
| D. Studies with LOE 5 or troubling inconsistent or inconclusive studies of any level |

*LOE*, Level of evidence.
Data from Oxford Center for Evidence-based Medicine Levels of Evidence.[14]

and localized recalcitrant plaque psoriasis.[13,21-24] In most studies PDL treatment was limited to one single or a few lesions. Two articles described the treatment of nail psoriasis.[25,26] Outcome measures included clinical scores as (modified) Psoriasis Area and Severity Index (PASI), Psoriasis Severity Index (PSI), Physician Global Assessment (PGA), total plaque severity or sum score for erythema, scaling and thickness,[27,28] Nail Psoriasis Severity Index (NAPSI)[29] and more subjective parameters such as percentage of clearance obtained from photographs taken before and after treatment.

Taibjee et al[15] (LOE 2b) published a within-patient controlled prospective trial of treatment of localized plaque psoriasis in 22 patients. Every patient received 3 different treatments, applied to 3 different plaques: PDL treatment with salicylic acid pretreatment, excimer laser twice weekly, and salicylic acid alone. One plaque was left untreated to serve as control. The PDL-treated lesions showed complete clearance in 6 patients (27%) and improvement in 15 patients (68%). Clinical response to treatment was significantly greater for PDL. The PSI showed significant improvement of PDL-treated lesions compared with untreated lesions and there was an improvement compared with salicylic acid–treated lesions. A subset of patients responded better to PDL, although the excimer laser appears to be on average more efficacious.

De Leeuw et al[16] (LOE 2b) performed a single-blind, prospective paired randomized controlled study. In 27 patients 4 similar psoriasis lesions were divided into 2 halves and treated with PDL vs ultraviolet-B (UVB) (1), UVB vs no treatment (2), PDL vs no treatment (3), and PDL + UVB (4). The PGA score showed a significant improvement of the psoriasis lesions after both PDL treatment and UVB treatment. No significant differences were noted between the therapies. Hacker and Rasmussen[13] (LOE 3b) treated 20 patients using fluences of 5.0, 7.0, and 9.0 J/cm$^2$ in 3 quadrants within 1 lesion, leaving 1 quadrant as a control. In 11 of 19 patients clinical improvement was seen after 1 session in the area treated with 9.0 J/cm$^2$; no improvement was seen in the other areas. Katugampola et al[17] (LOE 3b) treated 8 patients with chronic symmetric plaque psoriasis with PDL on 1 side, leaving the contralateral plaques untreated. Complete clearance was seen in 1 patient and a reduction of more than 50% was seen in 5 patients after 3 PDL treatments. Another study[16] (LOE 3b) including 10 patients showed a significant decline of psoriasis severity score in 6 patients and minimal advantage in 1 patient after PDL treatment. Zelickson et al[18] (LOE 3b) achieved significant clearance in 2 to 5 sessions. In 13 patients a single psoriasis plaque was divided into two and treated unilaterally, leaving the other side as a control. In another 23 patients the plaque was divided into 4 quadrants. Different pulse durations (0.45 and 1.5 milliseconds), triamcinolone acetonide 0.1% ointment, and emollients were used in the separate quadrants. Significant clinical improvement was seen after PDL. Bjerring et al[19] (LOE 4) compared 1 PDL treatment with dermabrasion in 11 patients. The PDL-treated lesions showed a complete response in 3 patients and a partial response in 6 patients. Two studies[20,23] (LOE 3b) compared PDL treatment with an active comparator and both studies showed significant reduction of psoriasis after PDL treatment, although the effect compared with the comparator varied in both studies because of the difference in laser parameters and chosen active comparator. Two studies investigated PDL treatment in nail psoriasis[25,26] (LOE 4). One study[26] showed a significant decrease in the NAPSI score.

**Conclusion.** *Grade B for localized plaque psoriasis (2 studies with LOE 2b[15,16] and 6 studies with*

*LOE 3b*[13,17,18,20,21,23]*).* PDL proved to be an effective treatment for localized psoriasis.

*Grade D for nail psoriasis (2 studies with LOE 4*[25,26]*).* No solid conclusion could be drawn for the treatment of nail psoriasis with PDL.

### Acne

Literature search revealed 9 studies on PDL treatment for acne vulgaris.[30-38] Outcome measures included the Leeds grading system, revised Leeds grading system, acne lesion counting, and percentage of clearance scored on photographs taken before and after treatment.[39-42]

Seaton et al[30] (LOE 1b) performed a randomized double-blind study in 41 patients with mild to moderate facial acne. They randomly assigned patients to PDL or sham treatment. Twelve weeks after a single PDL treatment, with 2 different fluences given at each side of the midline, they reported clinically and statistically significant reduction in acne lesions on both sides of the face. Orringer et al[31] (LOE 1b) did a single-blind split-face RCT in 26 patients. At 12 weeks changes in lesion count were not significantly different for treated versus nontreated sites. A trend toward improvement in inflammatory acne was described. Jasim et al[32] (LOE 3b) did a split-face study in 10 patients, in which one half was treated with PDL and the untreated site served as a control side. On the treated site, 50% of the patients showed visible improvement of their acne lesions. Another study[33] (LOE 3b) compared PDL treatment with regular acne treatments. One group of 15 patients was treated with PDL, and compared with 2 other groups who received regular topical treatments (topical vitamin A acid, benzoyl peroxide) or chemical peels (trichloroacetic acid 25%). Significant decrease in all 3 groups was seen, although in the follow-up period remission was significantly higher in the PDL group. PDL treatment was also compared with other, less established, treatments for acne[34-37] (LOE 4). These studies are not described in detail, but can be found in Table III (available at http://www.jaad.org), as well as in one other study.[38]

**Conclusion.** *Grade B for acne vulgaris (1 study with LOE 1b*[30] *and 2 studies with LOE 3b*[32,33]*).* PDL seems to be an effective treatment for acne vulgaris.

### Chronic discoid lupus erythematodes, systemic lupus erythematodes, subacute cutaneous lupus erythematodes, and lupus tumidus

PDL treatment was given for chronic discoid lupus erythematodes (CDLE) lesions (27 patients),[43-46] for telangiectasia and erythematous patches in patients with systemic lupus erythematodes (SLE) (12 patients),[43,46-49] for subacute cutaneous lupus erythematodes (SCLE) lesions (3 patients),[43,45,50] and for lupus tumidus (LT) (2 patients).[45] Outcome measures included estimated clearance rate and modified Cutaneous Lupus Erythematosus Disease Area and Severity Index.[51]

### Chronic discoid lupus erythematodes

Raulin et al[43] (LOE 4) described PDL treatment of 8 patients with CDLE in a retrospective study and showed a clearance rate of 57.5% after an average of 4 treatments (ranging from 1-6). One study[44] described a significant improvement of CDLE lesions after PDL treatment. A recently published study[45] confirmed these findings.[50]

**Conclusion.** *Grade C for CDLE (3 publications with LOE 4*[43-45]*).* PDL seems an effective therapeutic option for localized CDLE.

### Systemic lupus erythematodes

Nunez et al[47] (LOE 4) described for the first time the treatment of 4 patients with SLE using PDL and showed a clearance rate of 75%. Similar results were founded by Baniandres et al[48] (LOE 4) describing an average clearance of 68.0% (range 50%-80%) after 4.2 (range 1-10) treatments in 5 patients. Another case series[43] (LOE 4) confirmed these findings. One case report[46] (LOE 5) described complete clearance after 3 PDL treatments.

**Conclusion.** *Grade C for SLE (3 publications with LOE 4*[43,47,48]*).* PDL seems an effective therapeutic option for SLE.

### SCLE and LT

Three patients with SCLE (LOE 5)[43,45,50] showed marked improvement after PDL treatment and 2 patients with LT (LOE 5)[45] showed a significant reduction of erythema and scaling after PDL treatment.

**Conclusion.** *Grade D for the treatment of SCLE (3 patients)*[43,45,50] *and LT (2 patients).*[45] PDL in SCLE and LT seems effective in a small number of patients.

### PDL in GF

The treatment of GF with PDL was described in 2 case series[52,53] and 5 case reports.[54-58]

Cheung and Lanigan[52] (LOE 4) reported 4 cases of GF treated with PDL. Two patients achieved a significant cosmetic improvement of their GF, whereas the GF lesions in the other 2 patients stayed unaltered. No complications were recorded. A recently published case series[53] (LOE 4) of 4 patients described complete flattening and bleaching of all treated lesions in 3 patients, whereas 1 treated lesion

remained bright red-brown. Four case reports[54-57] (LOE 5) described a complete remission of GF after PDL treatment, whereas 1 case report[58] (LOE 5) described a marked improvement.

**Conclusion.** *Grade C for GF (2 case series with LOE 4[51,53]).* Treatment of GF with PDL seems to be promising, but the number of patients is too small to draw a firm conclusion.

### PDL in cutaneous sarcoidosis

Five case reports of PDL treatment for cutaneous sarcoidosis/lupus pernio[59-63] were identified. An improvement of 75% to complete remission was described in 4 cases.[59-62] One case report described a limited effect.[63]

**Conclusion.** *Grade D for cutaneous sarcoidosis (5 case reports with LOE 5[59-63]).* PDL seems to be an effective treatment to improve cutaneous sarcoidosis lesions; however, a solid conclusion could not be drawn based on 5 patients.

## DISCUSSION

Initially, PDL was used for the treatment of vascular indications. Two decades ago, PDL treatment of a psoriasis plaque lesion[14] showed promising results and therefore triggered the attention to optimize the treatment parameters for this disease and to explore PDL treatment for other inflammatory skin diseases.

Literature concerning treatment efficacy and safety of PDL for inflammatory skin diseases is diverse. Overall, most studies have shown limitations in small patient numbers, inconsistent treatment parameters, and a relatively short follow-up period. Large RCT with consistent laser parameters, validated outcome measures, and long follow-up periods are lacking.

Psoriasis was the most investigated inflammatory skin disease. All studies described the treatment of localized psoriasis, which mostly concerned chronic, stable plaque psoriasis, sometimes explicitly described as recalcitrant, not responding to conventional therapy such as potent topical steroids, UVB, psoralen plus UVA, and tar. The results of treatment with PDL on various sites of the body were highly variable, therefore no recommendation can be made about which anatomic site will respond best. Despite the currency of this skin disease, no large RCT on the efficacy of PDL for psoriasis were identified. Practically, PDL treatment is limited for a few psoriasis plaque lesions resistant to conventional therapy. According to our opinion, it should be considered, based on evidence, for solitary recalcitrant psoriasis lesions.

Two large RCT[31,32] were performed for acne treatment with PDL. The statistically significant improvement of acne lesions after PDL treatment in the first study could not be confirmed by the second study, possibly because of different laser parameters and different treatment regimens. Despite the positive finding of the first study and the promising results found in other studies, it is still unclear whether PDL treatment for acne will become a standard treatment in the future. No large intrapatient, split-face comparative studies were done with PDL treatment in comparison with other well-established, easily accessible treatments, so the added value to conventional forms of therapy is still unclear. One could hypothesize that it can be an alternative when topical therapies have failed or are contraindicated, before starting systemic therapy. Recommendation grade B was given for the PDL treatment of both localized psoriasis and acne vulgaris.

Evidence for SLE, CDLE, SCLE, GF, chronic eczema, papulopustular rosacea, cutaneous sarcoidosis, lichen sclerosis, granuloma annulare, Jessner lymphocytic infiltration of the skin, and reticular erythematous mucinosis is of a low level, ie, grade C and D. Although the incidence of these skin diseases, except for eczematous lesions and rosacea, is quite low, it is unlikely that large randomized trials will be performed in the near future to position the PDL for these skin diseases. Most of these lesions are located in the facial area/chest and can be recalcitrant to conventional therapies, thereby giving a lot of emotional distress. Therefore, despite the low level of recommendation, treatment with PDL is still worth consideration, especially when topical and/or systemic therapies have failed or are contraindicated. Because of the light sensitivity of some of these diseases, one should be extra cautious when treating these lesions with PDL. One study described the treatment of eczema with PDL and showed good results.[64] This promising result should be further investigated, with the emphasis, as in psoriasis, on localized recalcitrant eczema with failure or contraindication to topical and/or systemic therapies.

PDL treatment for inflammatory skin diseases was shown to be effective for localized psoriasis and acne vulgaris and can be recommended if conventional therapies have failed, are contraindicated, or both. For other inflammatory skin it can be considered as an alternative or supplementary treatment. Long-term studies in large groups of patients are clearly needed.

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**Table III.** PDL treatment of inflammatory skin diseases

| | | | | Laser parameters | | | | Treatment parameters | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Author** | **LOE** | **Study type** | **No. of patients** | **λ (nm)** | **ø (mm)** | **Pulse duration (ms)** | **Fluence (J/cm²)** | **No. of treatments** | **Treatment interval** | **Follow-up** |
| **Psoriasis** | | | | | | | | | | |
| Hacker and Rasmussen,[13] 1992 | 3b | OL | 19 | 585 | 5 | 0.45 | 5.0, 7.0, and 9.0 Divided over 4 quadrants, leaving 1 quadrant untreated | 1 | — | 8 wk |
| Katugampola et al,[17] 1995 | 3b | OL | 8 | 585 | 5 | 0.45 | 8.5 | 3 | 2 wk | 10 mo |
| Ros et al,[21] 1996 | 3b | CS | 10 | 585 | 5 | 0.36-0.45 | 6.5-8.0 | 1-3 | 2-3 wk | 2-9 wk |
| Zelickson et al,[18] 1996 | 3b | OL | 36 | 585 | 5 | 0.45; 1.5 | 7.5-8.5 | 2-5 | 2-3 wk | 4-13 mo |
| Bjerring et al,[19] 1997 | 4 | CS | 11 | 585 | 5 | 0.2 | 2.0-7.0 | 1 | — | 4-9 mo |
| Taibjee et al,[15] 2005 | 2b | OL | 22 | 595 | 7 | 1.5 | 10.0-12.0 | 2-4 | 4 wk | 12 mo |
| Ilknur et al,[20] 2006 | 3b | CS | 19 | 585 | 5 | 0.35 | 7.0-8.5 | 3 | 3 wk | 9 wk |
| de Leeuw et al,[22] 2006 | 4 | CS | 41 | 585 | 7 | 0.45 | 5.0-6.5 | 4.2 | 4-6 wk | 36 mo |
| Erceg et al,[23] 2006 | 3b | OL | 8 | 585 | 5 | 0.45 | 8.5 | 1-3 | 2 wk | 3 mo |
| de Leeuw et al,[16] 2009 | 2b | OL | 27 | 585 | 7 | 0.45 | 5.5-6.5 | 4 | 3 wk | 13 wk |
| Noborio et al,[24] 2009 | 4 | CS | 11 | 585 | 10 | 0.45 | 8.0 | 4.5 (1-9) | 4 wk | 1 mo |
| Fernández-Guarino et al,[25] 2009 | 4 | CS | 14 | 595 | 7 | 6.0 | 9.0 | 6 | 4 wk | 6 mo |
| Oram et al,[26] 2010 | 4 | CS | 5 | 595 | 7 | 1.5 | 8.0-10.0 | 3 | 4 wk | 3 mo |

| Location | Control side | Pretreatment | Tool assessment | Results | Side effects |
|---|---|---|---|---|---|
| Trunk/sacral/extremities | 1 Quadrant in lesion | No | Erythema, scaling, thickness on 1-7 scale, Photo | 11 (57%) of 19 Patients had clinically positive effect in quadrant treated with 9.0 J/cm$^2$; no complete clearance; negligible improvement in 5.0 J/cm$^2$ and 7.0 J/cm$^2$ quadrant | None |
| Knee/elbow | Yes | Emollient | Erythema, scaling, thickness on 0-4 scale, PASI, histologic examination | 5 Patients had >50% reduction of plaque severity score; 1 patient had complete clearance; decrease of vessel diameter; no discernible trend in cell infiltrate (polymorphs, lymphocytes) | Hemorrhagic crusts |
| Arm/leg/trunk | Yes | Emollient | Erythema, scaling, infiltration/induration on 0-3 scale, Photo, histologic examination | Significant decline of psoriasis severity score in 6 patients; minimal advantage in 1 patient; no advantage in 3 patients; epidermal thinning and regeneration without signs of psoriasis | Hypopigmentation, hyperpigmentation |
| Arm/trunk | Patients divided into 2 groups. Group A: Psoriasis lesions were divided in 2 parts. One part was treated with PDL; the other part was left untreated (polysporine cream could be used). Group B: Psoriasis lesions were divided in 4 parts, 2 parts were treated with PDL (with different pulse duration), 1 part with a corticosteroid ointment group II, and 1 part left untreated (polysporine cream could be used). | No | Erythema, scaling, infiltration/induration on 0-4 scale, Photo, histologic examination | Significant clinical improvement; no significant difference in 0.45 ms vs 1.5 ms; histologic normalization after treatment | Mild hyperpigmentation/hypopigmentation |
| Elbow/leg/trunk | Dermabrasion | Emollient | ECR, Photo, histologic examination | 3 (of 11) Patients treated with laser showed complete remission vs 5 (of 6) treated with dermabrasion; partial response in 6 patients with laser; 2 patients showed no response; histology in 1 patient was without characteristics of disease | Slight hyperpigmentation, hypopigmentation |
| Trunk/limbs | Untreated lesions, SA, excimer laser | SA 1 wk before every treatment | PASI, PSI, Photo, spectrophotometric intracutaneous analysis | 6 Patients showed complete clearance; 15 patients showed improvement; 9 patients had same or better response compared with excimer laser | Hypopigmentation, blistering |
| Trunk/limbs | SA and PDL; SA and clobetasol propionate | No/SA before every treatment | Modified PASI, Photo | Modified PASI score decreased in all groups when compared with baseline; no statistically significant difference for PDL vs PDL with SA | Mild to moderate hyperpigmentation |
| Hands/feet | No | Calcipotriol or SA before each treatment | ECR, Photo | 76% Good to very good improvement; average duration of remission 11 mo | Transient hyperpigmentation, hypopigmentation |
| Trunk/limbs | vs Calcipotriol/betamethasone dipropionate | SA before initial treatment | Erythema, infiltration/induration, scaling on 0-4 scale, Photo | Significant difference in sum score in favor of PDL; pain scores declined although not statistically significant | Hyperpigmentation |
| Unknown | vs UVB vs PDL + UVB vs no treatment | SA before each treatment | PGA score | Significant improvement in both PDL and UVB treatment; no significant differences for PDL vs UVB; no synergism of both therapies observed | Transient hyperpigmentation |
| Trunk/arm | No | 7% Lidocaine creme | Erythema, scaling, thickness on 0-4 scale, histologic examination | Significant decline in plaque severity score; significant decrease in microvessel count; downward trend in mean microvessel diameter | |
| Nails | Methyl-ALA, PDL | No | NAPSI, Photo | Decrease in NAPSI for both treatments; no statistical difference between treatment | |
| Nails | No | No | NAPSI | Significant decrease in NAPSI score | |

Continued

**Table III.** Con'd

| Author | LOE | Study type | No. of patients | Laser parameters | | | | Treatment parameters | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | λ (nm) | ø (mm) | Pulse duration (ms) | Fluence (J/cm$^2$) | No. of treatments | Treatment interval | Follow-up |
| **Acne** | | | | | | | | | | |
| Seaton et al,[30] 2003 | 1b | RCT, double blind | 41 (36 Completed) | 585 | 5 | 0.35 | 1.5 and 3.0 | 1 | — | 12 wk |
| Orringer et al,[31] 2004 | 1b | RCT, single blind | 40 (26 Completed) | 585 | 7 | 0.35 | 3.0 | 1 (group1); 2 (group 2) | 0 (group 1, single treatment); 2 wk (group 2) | 12 wk |
| Jasim et al,[32] 2005 | 3b | OL, intrapatient | 10 | 595 | 10 | 6.0 | 7.0 | 1 | — | 6 wk |
| Harto et al,[38] 2007 | 4 | OL | 36 (30 Completed) | 585 | ? | 0.35 | 2.5 | 3 | 4 wk | 12 wk |
| Haedersdal et al,[34] 2008 | 4 | Intrapatient comparative trial | 15 (12 Completed) | 595 | 10 | 10 | 7.5 (2 Passes) | 3 | 2 wk | 12 wk |
| Sami et al,[35] 2008 | 4 | Comparative study | 15 (30 Other patients were treated with IPL or LED) | 585 | 7 | 0.35 | 3.0 | 4.1 | | |
| Jung et al,[36] 2009 | 4 | Randomized prospective, double blind | 18 (16 Completed) | 585 | 7 | 40 | 7.0 | 3 | 2 wk | 12 wk |
| Leheta,[33] 2009 | 3b | Randomized trial | 15 (30 Treated with topical treatment or chemical peels) | 585 | 7 | 0.35 | 3.0 | 6 | 2 wk | 8 mo |
| Choi et al,[37] 2010 | 4 | Split-face, single-blind RCT | 20 | 585 | 10 | 40 | 8.0-10.0 | 4 | 2 wk | 12 wk |
| **Lupus erythematodes** | | | | | | | | | | |
| Nunez et al,[49] 1995 | 5 | CR | 1 (SLE) | 585 | 5 | 0.45 | 7.25-8.75 | 5 | | 16 wk |
| Nunez et al,[47] 1996 | 4 | CS | 4 (SLE) | 585 | 5 | 0.45 | 6.75-8.75 | 3-6 | | 16 wk |
| Maushagen-Schnaas and Raulin,[46] 1997 | 5 | CR | 1 (CDLE) | 585 | 7; 10 | | 5.5 and 3.5 | 2 | 4 wk | 12 mo |
| | 5 | CR | 1 (SLE) | 585 | 7; 10 | | 5.5-6.0 and 3.2 | 3 | 1-5 mo | 12 mo |
| Raulin et al,[43] 1999 | 4 | CS | 8 (CDLE) | 585 | 5; 7; 10 | 0.45 | 3.4-7.0 | 3.8 (1-9) | 2 wk-5 mo | 14.3 (5-32) mo |
| | 5 | CR | 1 (SCLE) | 585 | 7 | 0.45 | 3.0-7.0 | 6 | 4 wk | Interrupted |
| | 4 | CS | 2 (SLE) | 585 | 5; 7 | 0.45 | 5.5-6.5 | 7.5 (7-8) | 1-5 mo | 3-6 mo |
| Gupta and Roberts,[50] 1999 | 5 | CR | 1 (SCLE) | 585 | 5 | 0.45 | 5.3 | 4 | 1 mo | |
| Baniandres et al,[48] 2003 | 4 | CS | 5 (SLE) | 585/595 | 5; 7 | 0.45-10.0 | 5.0-8.75/6.0-12.0 | 3.8 (1-10) | 2.8-12.0 mo | 2.7 y (8 mo-6 y) |

| Location | Control side | Pretreatment | Tool assessment | Results | Side effects |
|---|---|---|---|---|---|
| Face | Parallel group | No | Leeds grading system,[39] lesion count | After 12 wk, decline in acne severity (Leeds scale) 3.8 (SD 1.5) to 1.9 (1.5) in PDL and 3.6 (1.8) to 3.5 (1.9) in controls ($P = .007$); total lesions decreased by 53% in PDL and 9% in controls ($P = .023$); inflammatory lesions decreased by 49% in PDL and 10% in controls ($P = .024$); no differences between 2 fluence levels | |
| Face | Yes | No | Lesion count, Photo | No significant differences for laser-treated vs untreated skin for reductions in mean papule counts (38% vs 25%, $P = .08$), mean pustule counts (0% vs 35%, $P = .12$), or mean comedone counts (9% vs 6%, $P = .63$); no significant difference in overall acne severity for treated vs untreated skin | Postinflammatory hyperpigmentation |
| Face | Yes, intrapatient | No | Modified Leeds acne score,[50] Photo | Significant reduction in modified Leeds acne score: 4.1 to 2.8 (treated site); 3.7 to 3.5 (untreated site) ($P < .05$) | |
| Face | No | No | Lesion count, Photo | Inflammatory lesions: reduction of 57% after 12 wk; noninflammatory lesions: reduction of 27% after 12 wk | |
| Face | MAL cream on 1 side of face according to randomization | No | Lesion count, Photo | Inflammatory lesions were reduced more on MAL-LPDL—treated than on LPDL-treated sides alone (wk 4: 70% vs 50%, $P = .03$; wk 12: 80% vs 67%, $P = .04$); noninflammatory lesions reduced similarly | Erythema, edema, and pustular eruption from MAL incubation |
| Face | No | No | ECR | $\geq$ 90% Clearance of inflammatory lesions after 4.1 $\pm$ 1.39 sessions in PDL group; after 6.0 $\pm$ 2.05 sessions in IPL group; and after 10.0 $\pm$ 3.34 sessions in LED group | |
| Face | No; other side treated with PDL and Nd:YAG | No | Cunliffe grading system,[52] lesion count, Photo, histologic examination | Significant reduction for inflammatory and noninflammatory acne lesions after both PDL and PDL/Nd:YAG; no significant difference between both treatments at end of study; both treatments decreased inflammation and IL-8 expression, and increased TGF-$\beta$ | No significant adverse reactions |
| Face | No; other patients received either topical treatment | No | Leeds acne scoring system, Photo | Significant decrease in all 3 groups; no significant difference was detected among 3 groups; remission in follow-up period was significantly higher in PDL group | |
| Face | No; IPL treatment on other half | No | Cunliffe grading system, lesion count, Photo, histologic examination | After 8 wk, inflammatory lesions were reduced to 14% of baseline (vs 45% in IPL group); noninflammatory reduced to 41% (PDL) and 57% (IPL); reduction of acne grade from 2.5 to 1.0 (PDL) and from 2.5 to 1.2 (IPL); patient satisfaction scores 5.2 (PDL) and 4.7 (IPL); amelioration in inflammatory reactions and increase in TGF-$\beta$ expression after both treatments more prominent for PDL site | |
| Face | No | No | ECR | Excellent | |
| Face | No | No | ECR, Photo, histologic examination | 75% Clearance of lesions; reduction in diameter of blood vessels; no changes in dermal infiltrate and direct immunofluorescence (CR[49] included in this CS) | Slight transient hyperpigmentation in 1 patient |
| Cheek/back | No | No | ECR | Complete clearance | |
| | No | No | ECR, histologic examination | Complete clearance, decrease in IgG and C3 | Slight hyperpigmentation |
| Face/trunk | No | No | ECR, Photo | Median 57.5% clearance (varying from no visible improvement to total clearance); 1 patient was excluded because of concomitant *local* treatment | Transient hyperpigmentation in 2 patients |
| | No | No | ECR, Photo | Clearance rate 50% | |
| | No | No | ECR, Photo | 75% Clearance (70% and 80%) | |
| Face, neck, arms | No | No | ECR, Photo | Marked improvement | |
| Face, cheeks, trunk | No | No | ECR, Photo, histologic examination | Average clearance rate 68.0% (range 50%-80%); histology for lupus negative, IFD similar to pretreatment biopsy; 1 patient with SLE, 7 with CDLE, and 1 with LT were excluded because of concomitant *local* treatment | 1 Patient developed hyperpigmentation, hypopigmentation |

Continued

**Table III.** Con'd

| Author | LOE | Study type | No. of patients | Laser parameters | | | | Treatment parameters | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | λ (nm) | ø (mm) | Pulse duration (ms) | Fluence (J/cm$^2$) | No. of treatments | Treatment interval | Follow-up |
| Erceg et al,[44] 2009 | 4 | OL | 12 (CDLE) | 585 | 7 | 0.45 | 5.5 | 1-3 | 6 wk | 6 wk |
| Díez et al,[45] 2011 | 4 | OL | 6 (CDLE) | 595 | 7 | 2 | 11 | 1 | — | 4 wk |
| | 4 | CS | 2 (LT) | 595 | 7 | 2 | 11 | 1 | — | 4 wk |
| | 5 | CR | 1 (SCLE) | 595 | 7 | 2 | 11 | 1 | — | 4 wk |
| **Granuloma faciale** | | | | | | | | | | |
| Ammirati and Hruza,[54] 1999 | 5 | CR | 1 | 585 | 5 | 0.45 | 8.0; 8.5 | 2 | 2 mo | 6 y |
| Welsh et al,[55] 1999 | 5 | CR | 1 (3 Lesions) | 585 | 7 | 0.45 | 6.5-7.25 | 9 | | 4 mo |
| | | | | 585 | 3 | 0.45 | 7.0-7.5 | | | |
| | | | | 595 | 7 | 1.5 | 12.0 | 3 | 6 wk | |
| Elston,[56] 2000 | 5 | CR | 1 | 595 | | | 6.5-7.0 | 3 | 1 mo | 1 mo |
| Chatrath and Rohrer,[57] 2002 | 5 | CR | 1 | 595 | 7 | 3.0 | 9.5-12.0 | 3 | 6 wk | 9 mo |
| Cheung and Lanigan,[52] 2005 | 4 | CS | 4 | 595 | 7 | 1.0-3.0 | 10.0-14.0 | ? | 2-4 mo | |
| Fikrle and Pizinger,[53] 2011 | 4 | CS | 4 | 595 | 7 | 1.5 | 9.0-10.0 | 3-8 | 6-8 wk | 6 mo |
| Leite et al,[58] 2011 | 5 | CR | 1 | 585 | | 20 | 5.8-8.3 | 5 | | 6 mo |
| **Cutaneous sarcoidosis** | | | | | | | | | | |
| Goodman and Alpern,[59] 1992 | 5 | CR | 1 | 585 | 5 | 0.46 | 5.0-8.0 | 2 | 7 mo | 6 mo |
| Cliff et al,[60] 1999 | 5 | CR | 1 | 585 | 5 | 0.45 | 5.6-7.3 | 6 | 6 wk | 2 mo |
| Ekbäck and Molin,[63] 2005 | 5 | CR | 1 | 585 | ? | 0.45 | 6.75-7.0 | 10 | | |
| Holzmann et al,[61] 2008 | 5 | CR | 1 | 595 | 7 | 0.5 | 7.6-7.8 | 3 | 6 wk | 12 mo |
| Roos et al,[62] 2009 | 5 | CR | 1 | 585 | 12 | 0.5 | 6.0 | 1 | — | 4 wk |
| **Eczematous skin lesions** | | | | | | | | | | |
| Syed et al,[64] 2008 | 3b | OL | 12 | 595 | 7 | | 4.0; 4.5; 5.0 | 1 | — | 6 wk |
| **Papulopustular rosacea** | | | | | | | | | | |
| Berg and Edström,[68] 2004 | 3b | OL | 14 (10 Completed study) | 585 | 5 | 0.5 | 5.75-7.75 | 2.4 (1-4) | | 10 mo |
| Bernstein and Kligman,[69] 2008 | 4 | CS | 20 (17 Completed study) | 595 | 3 × 10<br>12 | 40<br>3 | 17-19<br>6.0-7.0 | 4 | 4 wk | 2 mo |
| **Lichen sclerosis** | | | | | | | | | | |
| Rabinowitz,[70] 1993 | 5 | CR | 1 | 585 | 5 | | 5.75-6.25 | 4 | | |
| Greve et al,[71] 1999 | 5 | CR | 1 | 585 | 7 | 0.3-0.45 | 5.3-6.0 | 4 | 4-6 wk | 7 mo |
| Passeron et al,[72] 2009 | 5 | CR | 1 (2 Lesions) | 595 | 10 | | 10.0 | 2 | | 1 mo |
| **Granuloma annulare** | | | | | | | | | | |
| Sniezek et al,[73] 2005 | 5 | CR | 1 | 585 | 5 | 0.45 | 6.75 | 3 | 5 mo; 8 mo | 3 y |
| Sliger et al,[74] 2008 | 5 | CR | 1 | 595 | 7 | 1.5 | 8.0 | 1 | — | 36 wk |
| **Jessner lymphocytic infiltration** | | | | | | | | | | |
| Borges da Costa et al,[75] 2009 | 5 | CR | 1 | 595 | 10 | 0.5 | 8.0 | 1 | — | ? |

| Location | Control side | Pretreatment | Tool assessment | Results | Side effects |
|---|---|---|---|---|---|
| Face, scalp, trunk, limbs | No | No | Modified CLASI, Photo | Baseline CLASI score was 4.4 ± 0.2 (mean ± SEM), reaching 1.3 ± 0.3 after follow-up ($P < .0001$); damage CLASI score did not show any significant change during and after therapy; observed clinical improvement was confirmed by photo assessment by 2 additional independent observers | 1 Patient developed slight hyperpigmentation |
| Face, back, arm, hand | No | No | Modified CLASI, histologic examination | Significant reduction of erythema and scaling after treatment; significant reduction of dermal lymphocytic infiltrate and important reduction of basal damage; ICAM-1 and VCAM-1 expression was reduced | |
| Face, back | No | No | Modified CLASI, histologic examination | Significant reduction of erythema and scaling after treatment; no epidermal change, no basal cell damage, decline of infiltrate in 1 patient; significant decline of both ICAM-1 and VCAM-1 | |
| Face, back, arm, hand | No | No | Modified CLASI, histologic examination | Absence of erythema and scaling after treatment; no biopsy data available after treatment | |
| Nose | No | No | ECR, Photo | Persistent clinical eradication | |
| Nose, cheek | No | No | ECR, Photo | Complete remission in all lesions | Mild epidermal atrophy |
| | No | No | ECR, Photo | | |
| | No | No | ECR, Photo | | |
| Face | No | No | ECR, Photo | Complete clearing | |
| Nose | No | No | ECR, Photo | Significant flattening of lesions after 2 treatments, complete clearing after third treatment | |
| Temporal, cheek, nose | No | No | ECR, Photo | 2 Patients achieved significant cosmetic improvement; lesions remained unchanged in other 2 patients | |
| Face | No | No | ECR, Photo | Complete flattening and bleaching in 3 patients (excellent), 1 lesion remained bright red-brown after treatment (very good) (*local steroid if no improvement after 2 sessions*) | |
| Scalp | No | No | ECR, Photo | Marked improvement | |
| Nose | No | No | ECR, Photo | Improvement of 75% after 2 treatments | |
| Nose | No | No | ECR, Photo, histologic examination | Considerable cosmetic improvement; presence of noncaseating granulomas in dermis; paucity of papillary dermal blood vessels | |
| Cheek | | No | ECR, Photo | Less reddish and somewhat thinner (after treatment with other laser there was complete healing) (*after 10 PDL and 2 frequenced-double YAG laser treatments*) | |
| Cheek | No | No | ECR, Photo | Clinical remission after 3 treatments | |
| Back | No | No | ECR, Photo | Slight reddening, but lesions had completely resolved | |
| | No | No | ESS, VAS | Significant decrease in ESS score and significant difference in eczema severity assessed by VAS | 1 Patient has superinfection with *Candida albicans* at treated site |
| Face | No | No | ECR | Markedly less (n = 2); slightly less (n = 3); unchanged (n = 3); worsened (n = 2) | Hyperpigmentation in 5 patients |
| Face | No | No | ECR | Significant overall improvement | Slight pain, edema |
| Genital | No | No | ECR | Very good results | |
| Neck/arm/arm | No | No | ECR, histologic examination | Complete clearance; no residue of LSA | |
| Abdomen/breast | Methyl-ALA in breast lesion | No | ECR | Moderate effect on abdominal lesion (PDL); marked improvement in breast lesion (PDL-PDT) | |
| Wrist | No | No | ECR | Reduction in erythema and almost complete flattening | |
| Trunk/limbs | No | No | ECR | Complete flattening and lighting | Slight transient hypopigmentation |
| Limbs | No | No | ECR, histologic examination | Complete clearing of all lesions; regression of histologic findings | |

Continued

**Table III.** Con'd

| Author | LOE | Study type | No. of patients | Laser parameters | | | | Treatment parameters | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | λ (nm) | ø (mm) | Pulse duration (ms) | Fluence (J/cm$^2$) | No. of treatments | Treatment interval | Follow-up |
| **Reticular erythematous mucinosis** | | | | | | | | | | |
| Greve and Raulin,[76] 2001 | 4 | CS | 1 | 585 | 7 | 0.3-0.45 | 5.4-6.9 | 5 | 2.8 mo (2-7) | |
| | | | 1 | 585 | 7 | | 6.0 | 3 | 1 mo; 3 mo | 2 mo |

*ALA*, Aminolevulinic acid; *CDLE*, chronic discoid lupus erythematodes; *CLASI*, Cutaneous Lupus Erythematosus Disease Area and Severity Index[51]; *CR*, case report; *CS*, case series; *ECR*, estimated clearance rate; *ESS*, Eczema Severity Score[65-67]; *ICAM*, intercellular adhesion molecule; *IFD*, direct immunofluorecent; *IL*, interleukin; *IPL*, intense pulsed light source; *LED*, light-emitting diode; *LOE*, level of evidence; *LPDL*, long-pulsed dye laser; *LSA*, lichen sclerosus et atrophicans; *LT*, lupus tumidus; *MAL*, methylaminolevulinic; *NAPSI*, Nail Psoriasis Severity Index[29]; *Nd:YAG*, neodymium:yttrium-aluminium-garnet; *OL*, open-label trial; *PASI*, Psoriasis Area and Severity Index[27,28]; *PDL*, pulsed dye laser; *PDT*, photodynamic therapy; *PGA*, Physician Global Assessment[27,28]; *Photo*, photograph before and after treatment; *PSI*, Psoriasis Severity Index; *RCT*, randomized controlled trial; *SA*, salicylic acid; *SCLE*, subacute cutaneous lupus erythematodes; *SLE*, systemic lupus erythematodes; *TGF*, transforming growth factor; *UV*, ultraviolet; *VAS*, visual analog score; *VCAM*, vascular cell adhesion molecule; *YAG*, yttrium-aluminium-garnet.

| Location | Control side | Pretreatment | Tool assessment | Results | Side effects |
|---|---|---|---|---|---|
| Chest/abdomen | No | No | ECR, histologic examination | Only minimal residues visible; regularly structured skin without acute inflammation; no significant lymphocytic infiltrates or mucin deposits | |
| Inframammary | No | No | ECR | Skin almost completely healed | Slight transient hypopigmentation |