Application of Intense Pulsed Light in the Treatment of Dermatologic Disease: A Systematic Review

Heidi Wat, BSc,* Douglas C. Wu, MD, PhD,† Jaggi Rao, MD, FRCPC,‡ and Mitchell P. Goldman, MD, FAAD

BACKGROUND  The Food and Drug Administration (FDA) has approved intense pulsed light (IPL) devices for the treatment of a variety of benign pigmentary and vascular lesions, but the range of disease amenable to IPL treatment continues to expand, and there are no evidence-based clinical guidelines for its use in FDA-approved and off-label indications.

OBJECTIVE  To provide evidence-based recommendations to guide physicians in the application of IPL for the treatment of dermatologic disease.

EVIDENCE REVIEW  A literature search of the CENTRAL (1991 to May 6, 2013), EMBASE (1974 to May 6, 2013), and MEDLINE in-process and nonindexed citations and MEDLINE (1964 to present) databases was conducted. Studies that examined the role of IPL in primary dermatologic disease were identified, and multiple independent investigators extracted and synthesized data. Recommendations were based on the highest level of evidence available.

FINDINGS  Level 1 evidence was found for the use of IPL for the treatment of melasma, acne vulgaris, and telangiectasia. Level 2 evidence was found for the treatment of lentiginous disease, rosacea, capillary malformations, actinic keratoses, and sebaceous gland hyperplasia. Level 3 or lower evidence was found for the treatment of poikiloderma of Civatte, venous malformations, infantile hemangioma, hypertrophic scars, superficial basal cell carcinoma, and Bowen’s disease.

CONCLUSIONS  IPL is an effective treatment modality for a growing range of dermatologic disease and in some cases may represent a treatment of choice. It is typically well tolerated. Further high-quality studies are required.

Dr. Goldman is a consultant and has stock options with Lumenis, Ltd.

Goldman, Fitzpatrick and Eckhouse conceived of intense pulsed light (IPL) as therapeutic treatment of vascular lesions in April 1992. Clinical studies on rabbit ears and then humans by Goldman commenced in October 1992, with the first presentation of research in February 1993 at the 6th Annual Congress of the American College of Phlebology by Goldman entitled “Clinical and Histologic Evaluation of the ESC Vascular Lesion, Pulsed Light Source on the Dorsal Marginal Rabbit Ear Vein.” Food and Drug Administration clearance occurred in August 1995, with the first major publication by Goldman and Eckhouse in 1996. Since then, more than 20 different laser companies have developed a wide variety of IPL devices, each with unique characteristics. Most IPLs have a single pulse, with the energy used determined by or proportional to the pulse duration. Some IPLs have multiple sequential pulsing, and some have the ability to independently vary the pulse duration, the energy fluence, or both in each pulse. Other variables include the cut-off wavelengths, spectral
output, and size of the delivered light, so it is difficult to group all IPLs into one entity when evaluating treatment efficacy, but a growing body of evidence has shown the effectiveness of IPL in the treatment of vascular abnormalities, acneiform conditions, adnexal disease, inflammatory dermatoses, pigmentary disorders, premalignant lesions, and a variety of other dermatologic disorders. In this systematic review, with the limitations described above, we analyze the current available data on the clinical use of IPL for the treatment of dermatologic disease and provide evidence-based recommendations regarding its effectiveness.

Methodology

This systematic review was designed according to the principles outlined in the Preferred Items for Systematic Reviews and Meta-Analysis and Meta-analysis of Observational Studies in Epidemiology recommendations. On May 19, 2013, a literature search of the CENTRAL (1991 to May 6, 2013), EMBASE (1974 to May 6, 2013), and MEDLINE in-process and nonindexed citations and MEDLINE (1964 to present) databases was conducted. The query term “intense pulsed light therapy” was used and mapped to Medical Subject Heading terms in MEDLINE and EMTREE headings in EMBASE.

A free-text search of key terms, including “intense pulsed light therapy,” “intense pulsed light treatment,” and other synonyms, was also executed. In each database, filters were used to identify articles restricted to human studies and the English language. An example of the search strategy used in EMBASE is outlined in Table S1.

Results from the three databases were compiled, and duplicates were removed. The titles and abstracts were screened to determine eligibility based on inclusion and exclusion criteria. Inclusion criteria required articles to assess therapy of dermatologic disease with IPL therapy. Treatments that involved combinations with other therapies, such as 5-aminolevulinic acid (ALA) for photodynamic therapy (PDT), were also included because of the frequent use of IPL in multitreatment regimens. Where applicable, these combination treatments are noted in the text.

Articles concerning the use of IPL for cosmetic or other nonmedical purposes were excluded. These included photorejuvenation, cosmetic hair removal, and other aesthetic purposes. Repeated data sets, nontherapy studies, review articles, commentaries, guidelines, letters, conference abstracts, and posters were also excluded from the analysis. Articles that did not include a complete description of results were also removed. Reference lists from review articles were screened, and no additional citations were identified. An overview of the literature search and selection is outlined in Figure 1.

Data Extraction and Analysis

The full text of 127 articles was analyzed to further assess for applicability. Study characteristics and outcomes were determined. The study characteristics extracted included type of study, study size, patient characteristics, intervention, comparison arm, outcome, adverse events, and follow-up period. Specific IPL parameters were identified, including wavelength, fluence, pulse duration, number of pulses, pulse delay, and number of treatment sessions. The primary outcome was degree of clinical improvement in skin lesions. Articles were classified into broader categories of disease based on pathogenesis and histologic features to facilitate interpretation. The characteristics and results of all included studies are outlined in Tables S2 through S6.

Dermatologic conditions described in more than one case report with a cumulative patient number of at least three were included in the results discussion. Diseases that were described in case reports with a cumulative total of fewer than three patients were noted for the sake of comprehensiveness. Because some are uncommon diseases with no effective treatment, these data may still be useful in treating refractory disease.
Available evidence for each dermatologic condition was assessed and synthesized, with emphasis on the highest level of study available. Levels of evidence were assessed according to modified criteria published by the Oxford Centre of Evidence-Based Medicine Levels of Evidence (Figure 2). A recommendation was made for a disease provided that it was associated with a level 1 study or three or more level 2 or 3 studies that independently arrived at concordant results.

Results by Disease

Pigmentary Disorders

Lentiginous Disease
One randomized right–left comparison trial, six uncontrolled open-label trials, and two case reports described the use of IPL for the treatment of solar lentigines and ephelides. Studies cumulatively depicted 199 patients. The study characteristics are summarized in Table S2A. All studies uniformly reported excellent efficacy in the treatment of solar lentigines and ephelides on the face and body after an average of three to five treatments. Kawada and colleagues paired video-microscopic technique and histologic analysis to show that microcrust formation was limited to pigmented spots and that these microcrusts contained melanin, as demonstrated by Fontana-Masson staining. Furthermore, there was less melanin in the basal layer than in untreated spots. Resolution of these crusts led to clinical clearing of the solar lentigines.

Individual case reports have also shown dramatic clinical improvement of prominent lentigines associated with Peutz-Jeghers syndrome (PJS) in a child and in 28-year-old woman with LEOPARD syndrome. Treatment of the PJS case required 12 sessions of small treatment areas to improve tolerability.

The highest-quality study retrieved was a randomized, observer-blind, right–left comparison trial of...
Figure 2. Levels of evidence. Evidence and recommendations were rendered based on modified guidelines of the Oxford Center for Evidence-Based Medicine, 2009.

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<tr>
<th>Level of Evidence</th>
<th>Types of Studies</th>
<th>Recommendation</th>
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<tr>
<td>1a</td>
<td>Systematic review of randomized controlled trials (RCTs) with homogeneity</td>
<td>A: Strong, consistent level 1 studies</td>
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<td></td>
<td>≥ 2 high quality RCTs (homogenous, consistent results)</td>
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<td></td>
<td>≥ 2 high quality prospective right-left comparison trials (PRLCs)</td>
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<tr>
<td>1b</td>
<td>Individual high quality RCT</td>
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<td></td>
<td>Individual high quality PRLC</td>
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<td>2a</td>
<td>PRLC with control being “no treatment”</td>
<td>B: Moderate, consistent level 2 studies</td>
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<td>Multiple low quality RCTs and/or PRLCs with concordant results</td>
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<tr>
<td>2b</td>
<td>Low quality RCT</td>
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<td></td>
<td>Low quality PRLC</td>
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<td></td>
<td>≥ 3 placebo-controlled open label trials (OLTs) with concordant results</td>
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<td>2c</td>
<td>Placebo-controlled OLT</td>
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<td>3a</td>
<td>OLT with controls being “no treatment”</td>
<td>C: Weak, consistent level 3 studies</td>
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<tr>
<td>3b</td>
<td>≥ 3 case series (homogeneity, consistent results)</td>
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<td>OLT with no controls, patients &gt;10</td>
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<tr>
<td>3c</td>
<td>Retrospective uncontrolled observational study</td>
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<td>4a</td>
<td>Individual case series</td>
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<td>OLT with no controls, patients &lt;10</td>
<td>D: Very weak, consistent level 4 studies</td>
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<tr>
<td>4b</td>
<td>Case reports (cumulative patient number ≥ 3) with homogenous patients, treatment and results</td>
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<td>5</td>
<td>Expert opinion without explicit critical appraisal</td>
<td>Inconclusive, no recommendations made</td>
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<td>Based on physiology, bench research or “first principles”</td>
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<th>Quality of Study</th>
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| *High quality randomized controlled trial (RCT) | Placebo-controlled  
| | Double blinded (or investigator blinded)  
| | Lack of significant unaccounted for drop-out subjects  
| | Free of selected reporting  
| | Matched treatment and control groups  
| | +/- follow-up |
| *Low quality RCT | Lack of high quality controls  
| | Or lack of 2 or more of above criteria  
| | Or inadequacy/obscurity in 3 or more of above criteria |
| *High quality prospective right-left comparison trials (PRLCs): each patient receives same treatment and control in split-face body method | Randomization  
| | Placebo-controlled  
| | Double-blinded (or investigator-blinded)  
| | Lack of significant unaccounted for drop-out subjects  
| | Free of selected reporting  
| | Matched left and right-sided lesions  
| | +/- follow-up |
| *Low quality PRLC | Lack of high quality controls  
| | Or lack of 2 of more of above criteria  
| | Or inadequacy/obscurity in 3 or more of above criteria |

* Modified according to the Oxford Centre of Evidence Based Medicine
32 women: 17 with ephelides and 15 with solar lentigines. The study aimed to compare the efficacy of IPL with that of quality-switched alexandrite laser (QSAL), an established therapeutic option for lentigines. The study showed that both modalities resulted in significant improvement in Pigmentation Area and Severity Index scores after one treatment with QSAL or two treatments with IPL \((p < .001)\). QSAL was more effective for ephelides, whereas IPL and QSAL were equivalent for solar lentigines, although postinflammatory hyperpigmentation (PIH) occurred in eight patients with ephelides and one with solar lentigines on the QSAL-treated side, whereas none occurred on the IPL treated side.

In conclusion, IPL has consistently been shown to be an effective modality for the treatment of solar lentigines and ephelides (level 2a evidence). IPL may be preferable to QSAL for the treatment of lentiginous disease in Asian patients because of a possible risk of PIH in the latter.

**Melasma**

Seven studies on melasma were included. These consisted of two randomized controlled trials, one prospective right–left comparison trial, two uncontrolled open-label trials, one retrospective comparison study, and one case series, for a total of 318 patients. The pertinent studies are summarized in Table S2B. Overall, IPL appears to show moderate efficacy for the treatment of melasma—a condition that is often refractory and recurrent. In a randomized controlled trial conducted by Wang and colleagues, IPL achieved significantly superior results than in a control group treated with topical hydroquinone and sunscreen. In this study, the IPL-treated group experienced 39.8% improvement in quantitative melanin index, compared with 11.6% improvement in the control group, although these results were only partially maintained at 24 weeks after cessation of therapy. A subsequent randomized controlled trial compared IPL treatment with a control group treated with triple combination (TC) cream (fluocinolone acetonide 0.01%, hydroquinone 4%, tretinoin 0.05%) and sunscreen. In this setting, the IPL treatment group achieved a Melasma Area and Severity Index reduction from 17.6 to 9.7, which was significantly superior to the control group \((p = .002)\). In complementary fashion, Goldman and colleagues demonstrated that the combination of IPL and TC cream was superior to IPL alone in a prospective right–left comparison trial. Na and colleagues performed a retrospective comparison study that suggested that the addition of IPL to low-fluence neodymium-doped yttrium aluminum garnet (Nd:YAG) laser was superior to use of low-fluence Nd:YAG laser alone in the treatment of melasma. These data by Na and colleagues were presented in three studies, all of which provided analysis on the same patient population and arrived at similar conclusions. In summary, the available evidence indicates that IPL is a reliable means of improving melasma hyperpigmentation (level 1b), although efficacy and sustainability depend on a variety of factors, including type of melasma and use of adjunctive topical treatments.

**Poikiloderma of Civatte**

Two uncontrolled open-label trials and one retrospective observational study describe the use of IPL in the treatment of 334 patients with poikiloderma of Civatte. These data are summarized in Table S2C. These studies unanimously showed marked to significant reduction in vascular, pigmented and atrophic skin changes in 81% to 82% of patients (\(n = 320\) cumulative) after three to five sessions of IPL. Skin biopsies before and after treatment showed that melanin distribution was more homogenized (85.7% of patients) and vessel diameter was decreased by more than 50% in the superficial vascular plexus (57.1% of patients), which may underlie the clinical improvement in dyspigmentation and telangiectasia. Histologic analysis further showed an increase in fibroblasts and nonfragmented elastic fibers and thickening and compaction of collagen fibres—
changes consistent with collagen remodeling, which may be the mechanism behind improved skin appearance.

In sum, the use of IPL for treatment of poikiloderma of Civatte has been consistently shown to be safe and effective based on uncontrolled studies of large numbers of patients (level 3a evidence).

Other Pigmentary Disorders

A variety of other pigmentary disorders have been treated with IPL, including nevus spilus, café-au-lait macule, Becker’s nevus, epidermal nevus, PIH, stasis dermatitis pigmentation, and Riehl’s melanosis (Table S2D).26–31 The majority of this evidence consists of small case series and case reports, and therefore definitive treatment recommendations cannot be given. Nevus spilus, café-au-lait macule, PIH, and Riehl’s melanosis appear to respond reasonably well to IPL treatment.26–29,31 Becker’s nevus may also respond well, although there are conflicting reports.27,32 Overall, more studies are required to evaluate the usefulness of IPL in these entities.

Acneiform, Adnexal, and Other Inflammatory Disorders

Acne Vulgaris

Twenty-one studies were identified: two randomized controlled trials, seven prospective right–left comparison trials, 11 uncontrolled open-label trials, and one retrospective observational study, for a total of 544 patients.33–53 These studies can be broadly categorized into those that investigated the efficacy of IPL alone in the treatment of acne and those that used IPL as an activator of PDT for the treatment of acne. The relevant data are summarized in Table S3A.

IPL Alone

Chang and colleagues conducted a split-face, open-label, prospective trial in 30 Korean women with mild to moderate acne and found that IPL treatment resulted in improvement of acne red macules, irregular pigmentation, and skin tone but did not affect inflammatory acne lesion counts.36 Similarly, Yeung and colleagues studied 30 Chinese patients and found that IPL treatment alone led to a significant reduction in noninflammatory acne lesions but had no benefit for inflammatory lesions.38 In contrast, Sami and colleagues reported that an average of four to eight IPL sessions achieved 90% or greater clearance of inflammatory acne lesions.39 Kawana and colleagues reported similar findings in 25 Japanese patients treated with five sessions of IPL.44 Choi and colleagues treated 20 patients in a split-face prospective trial and found that IPL was able to improve inflammatory and noninflammatory acne lesions within four treatment sessions but that recurrent flares were observed 8 weeks after the final treatment session.42 As shown in the above studies, treatment of acne vulgaris with IPL alone has the potential to achieve significant improvement in clinical severity and patient satisfaction (level 2b evidence). The reported efficacy ranged from 34% to 88.3% improvement depending on the type of acne lesion (inflammatory, noninflammatory), but most commonly fell between 40% and 60%.

IPL plus PDT

Although IPL monotherapy shows benefit in the treatment of acne vulgaris, the majority of the evidence supports greater efficacy when used in combination with PDT. Shaaban and colleagues performed a split-body prospective open-label trial in 30 patients comparing IPL alone with IPL as an activator of ALA PDT and found that, although all patients experienced improvement in acne lesions, the PDT side was significantly better and achieved longer-lasting results.49 In a randomized placebo-controlled trial, Mei and colleagues compared ALA-IPL-PDT with IPL alone in the treatment of moderate to severe facial acne and found the former to be superior in terms of reduction in global acne lesion counts and specific inflammatory and noninflammatory lesions. At 12-week follow-up, there was between 75% and 85% improvement in the PDT group, versus 50% to 60% improvement in the IPL-alone group.52 In an inter-
testing study comparing multiple light sources in the sequential activation of PDT for acne vulgaris, Friedmann and colleagues revealed that patients treated with a combination of blue light and IPL had a significantly lower rate of acne flares.\textsuperscript{50} Taken in sum, the above data suggest that IPL-PDT is a good treatment option for acne vulgaris (level 1b evidence). The most commonly reported efficacy ranged between 60\% and 80\%. Overall, IPL can be considered a safe and effective option for acne vulgaris, especially in the setting of patients who are intolerant of or resistant to oral retinoids and antibiotics.

Rosacea
Nine studies on the efficacy of IPL for the treatment of rosacea were identified: two prospective right–left comparison trials, three uncontrolled open-label trials, three uncontrolled retrospective observational studies, and one case report, for a total of 304 patients.\textsuperscript{54–62} The relevant data are summarized in Table S3B. Initial studies demonstrated the efficacy of IPL in reducing blood flow, telangiectasia, and severity of erythema in individuals with rosacea.\textsuperscript{58,62} These data were confirmed in a prospective trial involving 60 patients who underwent an average of 4.1 treatments to achieve a mean clearance of 77.8\%. These results were maintained during a 3-year post-treatment follow-up period.\textsuperscript{61} Papa-georgiou and colleagues found that IPL was effective in significantly reducing erythema and telangiectasia in erythematotelangiectatic rosacea after four treatments were delivered at 3-week intervals.\textsuperscript{60} In a head-to-head randomized, controlled, single-blind split-face trial comparing pulsed dye laser (PDL) with IPL in the treatment of erythematotelangiectatic rosacea, Neuhaus and colleagues found that both modalities were equally effective in reducing cutaneous erythema and telangiectasia and that both were significantly superior to untreated controls. Patient-reported satisfaction and symptoms were also comparable.\textsuperscript{59} In another prospective right–left comparison trial, Fabi and colleagues showed that the therapeutic benefit of IPL for rosacea could be further enhanced with the addition of 15\% topical azelaic acid.\textsuperscript{54} A case report involving a single patient demonstrated the effective treatment of granulomatous rosacea with IPL. In this patient, the disease had previously been refractory to topical clindamycin, metronidazole, azelaic acid, calcineurin inhibitor, and oral doxycycline.\textsuperscript{57} Overall, IPL appears to be an effective, well-tolerated treatment option for rosacea (level 2a evidence), with efficacy equal to that of PDL. Typical reported improvement was in the 50\% range.

Other Adnexal Disorders
Other adnexal disorders include pilonidal cyst, hidradenitis suppurativa, pseudofolliculitis barbae, keratosis pilaris atrophicans, and primary axillary hyperhidrosis.\textsuperscript{63–69} Where possible, the data for these studies are summarized in Table S3C. Small case series have suggested that IPL may be an effective treatment option for pilonidal cyst disease.\textsuperscript{64,67} Similarly, IPL was moderately effective in the treatment of pseudofolliculitis barbae, but required 10–12 sessions to achieve 50\% improvement, with the possibility of recurrence after treatment cessation.\textsuperscript{65} Rodriguez-Lojo and colleagues treated keratosis pilaris atrophicans in four patients in five to nine sessions and observed clinical improvement between 75\% and 100\%. The effect was sustained during a 10-month follow-up period.\textsuperscript{63} Highton and colleagues demonstrated statistically significant improvement in hidradenitis suppurativa over a 12-month period (level 2a evidence).\textsuperscript{63} These investigators delivered a fairly aggressive treatment regimen consisting of two sessions per week for 4 weeks. In a small, open-label, nonblinded prospective trial, Schweiger and colleagues reported that ALA-IPL-PDT may be of benefit in the treatment of hidradenitis suppurativa.\textsuperscript{68} Attia and colleagues conducted a prospective right–left comparison studying the effect of IPL-PDT on axillary hyperhidrosis and found a striking 90\% reduction in sweating on the treated side, versus 2.2\% on the untreated side.\textsuperscript{69} These data need to be confirmed in larger studies. Because of the paucity of high-level evidence associated with the treatment of
other adnexal disorders with IPL, no firm recommendations can be made at this stage. The possible exceptions are hidradenitis suppurativa and axillary hyperhidrosis, although larger randomized controlled trials are still required.

Other Inflammatory Dermatoses
The evidence for IPL in the treatment of other inflammatory dermatoses is limited to small open-label trials and case reports. These data are summarized in Table S3D. Oh and colleagues treated facial atopic dermatitis in 11 patients with IPL and found significant improvements in eczema severity score, scaling, edema, induration and papules, erythema, and lichenification. A single case report demonstrated the efficacy of IPL in the treatment of actinic lichen planus that had been refractory to acitretin, hydroxychloroquine, and cyclosporine. In this setting, IPL may have been most effective in resolving the residual PIH. Cutaneous sarcoidosis has been successfully treated using IPL in two case reports. Attia and colleagues treated 20 patients with bilateral finger and toenail psoriasis with IPL and achieved significantly improved Nail Psoriasis Severity Index scores. In a retrospective study of 16 patients with discoid lupus erythematosus, Triolius and colleagues reported that IPL and PDL may be useful adjunctive therapies to mitigate scarring and disfigurement. When dyspigmentation and scarring are sequelae of inflammatory dermatoses, IPL appears to have a useful role, but further study is needed on the potential therapeutic benefit of IPL when the dominant clinical feature is cutaneous inflammation.

Vascular Lesions
Capillary Malformations
Fourteen studies were retrieved describing the use of IPL in the treatment of capillary malformations: one randomized controlled trial, two prospective right–left comparison trials, eight uncontrolled open-label trials, two uncontrolled retrospective observational studies, and one case series, for a total of 368 patients. The pertinent studies are summarized in Table S4A. Raulin and Goldman reported the first successful treatment of an adult port wine stain (PWS) with IPL in 1997. In this study, the PWS had been previously refractory to PDL but resolved after four treatments with IPL. A subsequent, larger retrospective study found that 70% of patients with PWS achieved 70% to 100% clearance after one to four treatments. Bjerring and colleagues treated 15 patients with PWS that had previously been resistant to PDL and found that IPL was able to achieve 75% to 100% clearance in 46.7% of cases. In a prospective study of 22 patients with PWS treated with IPL, Ho and colleagues found that 90% achieved greater than 25% clearance, 50% achieved 25% to 50% clearance, 40% achieved greater than 50% clearance, and 9% achieved greater than 75% clearance. Nodular PWS were particularly resistant to treatment. A subsequent prospective trial involving 12 patients showed similar results. A randomized, controlled, single-blind head-to-head trial comparing PDL with IPL for the treatment of PWS showed that both modalities were effective but that PDL was superior in terms of median clinical improvement and patient preference. A later study reported that IPL was superior to short PDL (SPDL) and equivalent to long PDL (LPDL). Recently, Wang and colleagues confirmed the efficacy of IPL in the treatment of facial and extrafacial PWS in Chinese patients. In sum, there is reasonable evidence to suggest that IPL is an effective, safe modality for the treatment of capillary malformations (level 2a evidence). It may be especially useful for darker lesions that have greater vascularity but minimal nodularity. There are conflicting studies with regard to the relative efficacy of PDL and IPL.

Telangiectasia
Eleven studies were identified: three randomized controlled trials, six uncontrolled open-label trials, one case series, and one case report, for a total of 1291 patients. The telangiectasias found to be responsive to IPL treatment included benign essential telangiectasia, telangiectasia of the lower limbs, hereditary hemorrhagic telangiectasia, radiotherapy-induced telangiectasia, postsurgical
telangiectasia, and telangiectasia associated with systemic sclerosis. The pertinent studies are summarized in Table S4B.

Multiple, early, uncontrolled, open-label trials near the turn of the millennium demonstrated that IPL could be an effective method of treatment for multiple forms of telangiectasia. In the case of leg veins, Goldman and colleagues conducted a large multicenter open-label trial treating 159 patients with lower limb telangiectasia and found that 79% of patients achieved 75% to 100% clearance of vessels.1 The following year, Raulin and colleagues reported that 71% of patients achieved excellent clearance of leg veins (>90%) after an average of 4.4 treatments.92

A subsequent study analyzed the effect of IPL on facial telangiectasias and found that 79.2% of patients achieved greater than 50% reduction of vessels after one to four treatments.94 In the largest study to date, Clementoni analyzed 1,000 patients with telangiectasias treated using IPL and found that 89.7% experienced 75% to 100% improvement. These telangiectasias included leg veins that had no associated feeding reticular veins. The authors reported that positive results directly correlated with operator experience and proficiency.96,102 With the proven efficacy of IPL in the treatment of telangiectasia, further studies attempted to compare it with the criterion standard PDL. Three randomized, split-side controlled, investigator-blind trials compared IPL with LPDL for the treatment of telangiectasia.98–100 In the two that Nymann and colleagues conducted, the authors concluded that LPDL was superior in achieving vessel clearance (90% in the LPDL group vs 50% in the IPL group).98 Subgroup analysis revealed that IPL and LPDL both achieved greater than 50% clearance in 77% of patients but that LDPL achieved 75% to 100% clearance in 46% of patients, versus 28% of patients treated with IPL.99 A more recent study by Tangheiit and colleagues concluded that IPL and LPDL were equally efficacious and shared a similar side-effect profile.100

Because of the inhomogeneity of the above trials, direct comparisons are difficult to make. The differences in results and conclusions may be attributable to differences in device settings and operator proficiency. Overall, IPL appears to be an effective and well-tolerated treatment for telangiectasia of multiple varieties (level 1b evidence). It may be viewed as a viable alternative to LPDL. Optimization of treatment parameters and operator experience are essential in achieving good results.

Other Vascular Lesions

Intense pulsed light has been used in the treatment of venous malformations, infantile hemangioma (IH), angioma serpiginosum, tufted angioma, pyogenic granuloma, lymphangioma circumscriptum, angio-keratoma of Fabry, and multinucleate cell angiohistiocytoma.103–115 The pertinent studies are summarized in Table S4C. Other than the cases of venous malformations and IHs, the treatment of the above disorders is limited to solitary case reports, and therefore no further level of evidence or recommendation may be given at this time. Three studies on the efficacy of IPL in the treatment of venous malformations were included: an uncontrolled retrospective observational study, a case series, and a case report, for a total of 14 patients. Although the numbers were small, and the study designs did not achieve a high level of evidence rating, the results were uniformly favorable, with all study patients achieving 70% to 100% clearance of their lesions.103–105 Thus, IPL may be considered a reasonable treatment option for venous malformations (level 3c evidence). Two studies examined the role of IPL in the treatment of IH: an uncontrolled open label trial and a case report, for a total of 64 patients.110,113 In the open-label trial, Li and colleagues found that 61.3% of treated patients achieved 75% to 100% clearance at 6 months of follow-up.113 Although the results are favorable, IH is typically a self-resolving condition, and no untreated controls were included in the study. Further study is required to determine the effect of early IPL treatment on incidence of complications such as ulceration, rate of resolution, and resultant cutaneous scarring after lesion resolution.
Nevertheless, given the reported benign side-effect profile of IPL treatment, it may be considered an option for IH (level 3b evidence).

**Premalignant and Malignant Lesions**

**Actinic Keratoses**

Studies examining the use of IPL for actinic keratoses (AKs) have focused on whether it is an effective activator of photosensitizing agents for PDT. A compilation of one randomized controlled trial, one prospective right–left comparison trial, three uncontrolled open-label trials, and one retrospective observational study were included, for a total of 111 patients.\(^{116-121}\) These data are summarized in Table S5.

One right–left comparison study comparing IPL alone with IPL–methyl-aminolevulinate (MAL)-PDT showed that 60% of patients showed improvement on the combination side, whereas 55% responded on the IPL side.\(^{121}\) This suggests that IPL may be effective alone in the treatment of AKs, but is augmented by the use of a photosensitizer. Four other studies examining the use of ALA or MAL plus IPL reported clinical resolution of AKs in 50% to 91% of their patients after a single treatment.\(^{116,117,119,120}\) One of these studies also documented histological resolution in 42% of lesions.\(^{120}\) The combination of 5-fluorouracil plus IPL-PDT has also been successful in the treatment of AKs.\(^{118}\) The sole randomized controlled trial examining the optimal fluence for AKs found greater response in the 40-J/cm\(^2\) (20 J/cm\(^2\) \times 2 passes; \(p = .02\)) and 50-J/cm\(^2\) (25 J/cm\(^2\) \times 2 passes; \(p = .02\)) groups than with IPL alone, and 20 J/cm and 25 J/cm groups,\(^{119}\) although only 24% of patients overall had a marked response (>75% improvement), and 29% has a moderate response (50% to 75%).

A recent study by Goldman and colleagues further determined that the combination of IPL, PDL, and blue light was superior to blue light plus IPL for the treatment of AKs (\(p < .001\)). The study suggested that using multiple sequential laser combinations may be more effective and produce fewer adverse effects, including pain, erythema, and peeling.\(^{122}\)

The evidence for use of a photosensitizer with IPL for treatment of AKs is based on consistent results, albeit from small trials. Overall, the literature supports the use of IPL-PDT as an effective, reasonable alternative for treatment for AKs (level 2b evidence).

**Bowen’s Disease and Superficial Basal Cell Carcinomas**

Limited studies have examined the use of IPL for superficial malignant lesions. This review identified two open-label trials including 22 patients.\(^4,117\) One trial examined the use of MAL plus IPL in 30 patients with a combination of AKs, superficial basal cell carcinoma (BCC), and Bowen’s disease. After two sessions of IPL (6 pulses, 1–10 seconds apart), all 10 patients with superficial BCC and all nine with Bowen’s disease had complete resolution. Another small open-label trial (\(n = 3\)) found that all three patients had significant to complete resolution of lesions after two to five sessions administered every 2 weeks. The use of ALA plus IPL may be a worthwhile treatment for superficial BCC and Bowen’s disease, but the evidence is based on low-quality studies and small patient numbers (level 4a).

**Other Dermatologic Conditions**

**Hypertrophic Scars and Keloids**

A review of the literature identified five eligible studies: one prospective right–left comparison trial, one retrospective observational study, one open-label trial, and two case reports, with a cumulative 160 patients.\(^{123-127}\) The study characteristics and results are summarized in Table S6A.

Hyperpigmented, erythematous, and proliferative scars all demonstrated greater than 50% improvement after a mean of 2.97 sessions, whereas atrophic scars did not respond.\(^{123}\) Erol and colleagues showed in an investigator-blinded, open-label trial...
that scar height, erythema, and hardness were all reduced in 92.5% of patients with keloidal or hypertrophic scars, although six to 24 treatments were required. Excellent overall improvement in appearance was achieved in 31.2% of patients, and good responses were seen in 25.7%. A single case of hypopigmentation in peripheral skin was reported and was attributed to the lack of protective tape used around the scar periphery. These patients had previously failed other therapies including intralesional corticosteroids, silicone sheets, carbon dioxide laser, skin grafting, and scar tissue excision.

An investigator-blinded, right–left trial comparing LPDL with IPL on postsurgical breast and abdominal scars showed that both modalities were equally efficacious. IPL was reported to be more painful but was associated with lower rates of post-treatment purpura.

Based on uncontrolled, open-label trials and retrospective studies, IPL may be a worthwhile treatment modality to pursue in patients with keloidal, hypertrophic, proliferative, hyperpigmented, or erythematous scars (level 3a evidence), but a major limitation of the existing evidence is the lack of rigorous study design and controls.

**Verruca Vulgaris**
The use of IPL for the treatment of verruca vulgaris has been investigated in a limited number of trials. Two studies were reviewed: one randomized controlled trial and one case report, describing a total of 80 patients. The study characteristics and results are summarized in Table S6B. An investigator-blinded, randomized controlled trial of 79 patients conducted by Togsverd-Bo and colleagues showed that IPL after paring was no more effective than paring alone for the treatment of hand and foot warts and was associated with greater pain intensity \((p < .001)\). Nine of 41 (22%) in the paring plus IPL group and five of 37 (13.5%) in the paring alone group had a complete response. These results were not significantly different. Based on these data, IPL does not appear to be more efficacious than paring alone in the treatment of recalcitrant warts (level 1b evidence).

**Sebaceous Gland Hyperplasia**
A single randomized controlled, investigator-blinded trial of 12 patients showed that PDT with ALA plus blue light and PDT with ALA plus IPL were efficacious in reducing sebaceous gland hyperplasia counts by more than 50%. Both treatments were well tolerated, and no recurrence was seen at 12-week follow-up (level 2b evidence).

**Microstomia in Scleroderma**
A case series by Comstedt and colleagues \((n = 4)\) demonstrated that microstomia due to systemic sclerosis may be improved with IPL treatments. All patients experienced softening of perioral skin and better daily functioning because of increases in range of motion of the jaw after 35 treatments. Oral opening was increased by approximately 1 mm per treatment in three of four patients (level 4a evidence).

**Other**
Stand-alone case reports have also described the successful application of IPL in the treatment of colloid milium and disfigurement from Parry-Romberg syndrome. IPL was unsuccessful in the treatment of orofacial edema associated with Melkersson-Rosenthal syndrome.

**Discussion**

**Main Findings**

Intense pulsed light may be used as a standalone treatment modality or as an activator of PDT. When used alone, a strong to moderate recommendation was established for lentigines, melasma, rosacea, capillary malformations, and telangiectasia. In combination with PDT, a strong to moderate recommendation was established for acne vulgaris, AK, and sebaceous gland hyperplasia. A synopsis of the levels of evidence and associated recommendations is outlined in Figure 3.
<table>
<thead>
<tr>
<th>Disease Entity</th>
<th>Highest Level of Evidence</th>
<th>Recommendation</th>
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</thead>
<tbody>
<tr>
<td><strong>PIGMENTARY DISORDERS</strong></td>
<td></td>
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<tr>
<td>Lentiginous disease</td>
<td>Level 2a</td>
<td><strong>B: MODERATE</strong>&lt;br&gt;IPL is consistently effective for solar lentigines and ephelides. It may be preferred over QSL in the Asian population to decrease risk of post-inflammatory hyperpigmentation.</td>
</tr>
<tr>
<td>Melasma</td>
<td>Level 1b</td>
<td><strong>A: STRONG</strong>&lt;br&gt;IPL is a good therapeutic option for melasma. However, dermal-dominant melasma may be more refractory to treatment.</td>
</tr>
<tr>
<td>Poikiloderma of Civatte</td>
<td>Level 3a</td>
<td><strong>C: WEAK</strong>&lt;br&gt;IPL is effective in significantly improving skin changes associated with PoC, but there is a lack of high quality studies.</td>
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<tr>
<td><strong>ACNEIFORM</strong></td>
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<tr>
<td>Acne vulgaris</td>
<td>Level 2b (IPL)</td>
<td><strong>B: MODERATE</strong>&lt;br&gt;IPL can be a good option for acne (40-60% improvement)</td>
</tr>
<tr>
<td></td>
<td>Level 1b (IPL+PDT)</td>
<td><strong>A: STRONG</strong>&lt;br&gt;IPL+PDT is a good treatment option for acne</td>
</tr>
<tr>
<td>Rosacea</td>
<td>Level 2a</td>
<td><strong>B: MODERATE</strong>&lt;br&gt;IPL is effective in treating erythematotelangiectatic rosacea, with comparable efficacy to PDL</td>
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<tr>
<td><strong>VASCULAR LESIONS</strong></td>
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<tr>
<td>Capillary malformations</td>
<td>Level 2a</td>
<td><strong>B: MODERATE</strong>&lt;br&gt;IPL is a good treatment option for capillary malformations and may even be used in PDL-resistant cases</td>
</tr>
<tr>
<td>Telangiectasia</td>
<td>Level 1b</td>
<td><strong>A: STRONG</strong>&lt;br&gt;IPL is an excellent treatment option for a wide variety of telangiectasias and may be comparable to gold standard PDL</td>
</tr>
<tr>
<td>Venous malformation</td>
<td>Level 3c</td>
<td><strong>C: WEAK</strong>&lt;br&gt;IPL appears effective in treating venous malformations, but there is a lack of high quality studies</td>
</tr>
<tr>
<td>Infantile hemangioma</td>
<td>Level 3b</td>
<td><strong>C: WEAK</strong>&lt;br&gt;IPL may be considered in the treatment of infantile hemangioma</td>
</tr>
<tr>
<td><strong>MALIGNANCIES</strong></td>
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<tr>
<td>Actinic keratosis</td>
<td>Level 2b (IPL+PDT)</td>
<td><strong>B: MODERATE</strong>&lt;br&gt;When used as an activator of photodynamic therapy, IPL is a reasonable treatment option for actinic keratosis</td>
</tr>
<tr>
<td>Superficial basal cell carcinoma/Bowen’s</td>
<td>Level 4a (IPL+PDT)</td>
<td><strong>D: VERY WEAK</strong>&lt;br&gt;IPL may be a treatment consideration if surgery is not an option</td>
</tr>
<tr>
<td><strong>OTHER</strong></td>
<td></td>
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<tr>
<td>Hypertrophic scars and keloids</td>
<td>Level 3a</td>
<td><strong>C: WEAK</strong>&lt;br&gt;Multiple sessions of IPL may be effective for the treatment of scars, but less so for atrophic variants</td>
</tr>
<tr>
<td>Verruca vulgaris</td>
<td>Level 1b</td>
<td><strong>A: STRONG</strong>&lt;br&gt;IPL is no more effective than paring alone in the treatment of recalcitrant warts.</td>
</tr>
<tr>
<td>Sebaceous gland hyperplasia</td>
<td>Level 2b (IPL+PDT)</td>
<td><strong>B: MODERATE</strong>&lt;br&gt;ALA plus blue light or IPL are both effective in reducing numbers of sebaceous gland hyperplasias.</td>
</tr>
</tbody>
</table>

Figure 3. Summary of recommendations for the use of intense pulsed light in the treatment of dermatologic disease. Recommendations were made based on the highest level of evidence available.
In terms of pigmentary disorders, level 2a and level 1b evidence was found for the treatment of lentigines and melasma, respectively. In the reviewed studies, IPL was consistently effective in the treatment of lentigines and ephelides, even in the case of syndromic eruptions, with an efficacy generally comparable with criterion standard quality-switched laser therapy and one study suggesting that IPL may be preferable in Asian patients because a possible lower risk of PIH.

Acne vulgaris and rosacea also responded well to IPL therapy. When combined with PDT, level 1b evidence was found for the treatment of acne vulgaris. Level 2a evidence was found for rosacea. There were trends to suggest that the more-severe forms of acne benefited the most from IPL-PDT treatment. Virtually all of the studies on rosacea investigated the erythematotelangiectatic or papulopustular variants. Therefore, no firm conclusions can be given with regard to the efficacy of IPL treatment for phymatous, granulomatous, or other variants.

For vascular lesions, level 2a and level 1b evidence was found for the treatment of capillary malformations and telangiectasia, respectively. These vascular lesions consistently responded excellently to IPL treatment. In some reports, IPL was shown to be comparable in efficacy with criterion standard PDL, although there is conflicting evidence in this regard, and some evidence indicated the superiority of PDL over IPL in the treatment of vascular lesions.

For neoplasms, the combination of IPL plus PDT was shown to be associated with level 2b evidence for AK and sebaceous gland hyperplasia. The ability to perform field treatment with this modality is advantageous in patients who present with extensive and often ill-demarcated actinic damage to the face and scalp, although high-quality comparisons with other proven treatment modalities such as topical imiquimod, 5-fluorouracil, and ingenol mebutate are lacking.

A solitary study investigating the role of IPL for the treatment of common warts concluded that it was no more effective than paring (level 1b evidence). In contrast, PDL has shown reasonable efficacy for the treatment of verruca vulgaris. A possible explanation for this discrepancy is that PDL is used in multiple pulses to produce nonspecific thermal damage in addition to coagulation of blood vessels. In light of this study, the recommendation is against using IPL for treating verruca vulgaris.

**Adverse Events**

Generally speaking, IPL was found to be well tolerated, with a benign side-effect profile. The most common adverse effects reported in the literature were mild discomfort, erythema, purpura, edema, blistering, and crusting. These findings typically resolved within 1 to 48 hours but sometimes lasted up to 1 week. Post-treatment hyper- and hypopigmentation were also noted as possible adverse effects of IPL. This pigmentary alteration typically responded to conservative management but in rare cases could be long lasting (up to 18 months). Study dropout due to intolerance of side effects was rarely reported and was typically because of the use of overly aggressive treatment parameters. Serious adverse events were exceedingly rare and consisted of one case of prolonged ulceration (30 days), one case of herpes simplex labialis, and two cases of hypertrophic scarring. When IPL was used as an activator for PDT, the side-effect profile was similar although typically more severe. The degree of these side effects was in keeping with those found with other established light sources that have been used in the activation of PDT. Overall, adverse events secondary to IPL treatment were typically transient or could be managed with simple conservative strategies. Safety and efficacy with IPL devices relies on appropriate use of device settings and sufficient operator experience.

**Limitations**

The main limitation of this review was the general lack of high-quality studies. The majority of the
evidence reviewed consisted of nonrandomized, uncontrolled, open-label trials or retrospective reviews. These study designs tend to overestimate treatment efficacy and do not account for placebo effect. Many studies in this review were also right–left comparison trials, which have the advantage of accounting for interindividual variability by providing intrapatient (internal) controls, but the possibility of an intervention applied to one side of the patient also affecting the other side cannot be entirely excluded in this design. Almost all of the reviewed studies were limited by the number of patients enrolled (usually <100) and by the length of follow-up (typically ≤6 months). Long-term outcome analysis is needed. Additionally, the wide variety of IPL devices, device settings, patient demographic characteristics, and user expertise detracted from a completely homogeneous assessment of the data. On the other hand, heterogeneity across race, sex, and age may suggest applicability of these data to a broad patient demographic.

Clinical Research Implications

Further large-scale, high-quality studies are needed to optimally delineate exact treatment parameters for specific diseases. This review did not evaluate the separate efficacy of the multiple types of IPL devices available. Given the large range of programmable variables in current IPL devices, this study did not attempt to correlate efficacy with optimal treatment parameters, and further research is required in this area. A special note should also be made about the treatment of other inflammatory dermatoses, because the efficacy of IPL has not been properly explored in this group. These isolated case reports and small case series are included in this review for the sake of comprehensiveness, but no level of recommendation is attached to them. Nevertheless, there have been interesting successes reported, and further study is required to explore the effects of IPL on diseases that feature cutaneous inflammation as the primary pathophysiologic factor.

Conclusion

The available evidence strongly suggests that IPL is a useful treatment option in a variety of cutaneous disorders. In most cases, it should be considered alongside other, more-traditional therapies, although in some instances, it may be considered a treatment of choice. Further study is required to continue to broaden the applications of IPL and other energy-based systems in the treatment of dermatologic disease.

References

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APPLICATION OF INTENSE PULSED LIGHT


Supplementary Material

Additional Supporting Information may be found in the online version of this article:

Table S1. Search Strategy Used in EMBASE.

Table S2. Study Characteristics and Results for (A) Lentiginous Disease, (B) Melasma, (C) Poikiloderma of Civatte and (D) Other Pigmented Disorders.

Table S3. Study Characteristics and Results for (A) Acne Vulgaris, (B) Rosacea, (C) Adnexal Disease and (D) Other Inflammatory Dermatoses.

Table S4. Study Characteristics and Results for (A) Port Wine Stain (PWS), (B) Telangiectasias and (C) Other Vascular Lesions.

Table S5. Study Characteristics and Results for Premalignant and Malignant Lesions.

Table S6. Study Characteristics and Results for (A) Scars and (B) Other Dermatological Conditions.