

# Laser and Light-Based Treatments for Acne Vulgaris

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Acne vulgaris is the most common disease of the skin. Numerous medical therapies exist but have limitations. Laser and light-based procedures provide physicians and patients with options for treating active acne lesions as well as cosmetic improvement of hyperpigmentation and scarring. Various light-based therapies exist and target various factors that contribute to the pathogenesis of acne vulgaris. In general, light-based treatments target *Propionibacterium acnes* or the pilosebaceous unit. Treatment options that are currently available include blue light and red light therapies, pulsed dye lasers (PDLs), intense pulsed light (IPL), photodynamic therapy (PDT), photopneumatic therapy (PPX), and fractional photothermolysis (FP). These light-based treatment options can be effective as monotherapy or in combination with traditional medical therapies for the treatment of most patients with acne vulgaris.

Acne vulgaris is the most common disease of the skin with a prevalence of 70% to 87% of adolescents.<sup>1</sup> Over 17 million individuals in the United States are affected, and approximately one-third seek medical treatment.<sup>2</sup> The pathogenesis of acne is attributed to increased and altered sebum production, androgen activity, inflammation, follicular hyperkeratinization, and proliferation of *Propionibacterium acnes* in the pilosebaceous unit.<sup>3</sup> Clinically, patients present with comedones and/or inflammatory papules, pustules, or cysts most commonly affecting the face, chest, and back. These lesions may resolve with minimal or no residual effects, but in severe cases they can cause long-lasting postinflammatory hyperpigmentation and

scarring. Acne has a well-recognized potential to cause considerable morbidity, most commonly manifesting as negative effects on the psychosocial functioning of affected patients. In fact, acne is the second most common skin disease associated with suicide.<sup>4</sup>

Numerous medical therapies exist to treat acne vulgaris. These include topical benzoyl peroxide, antibiotics, and retinoids as well as systemic antibiotics, retinoids, and antihormonal therapies. Pharmacotherapy addresses the underlying pathophysiology of acne and effectively manages most cases. However, these treatment regimens have limitations. First, they can be time-consuming, cumbersome, and have a slow onset of action, which all lead to patient non-compliance. In addition, patients may not tolerate medication side effects. Some patients are refractory to treatment or develop frequent recurrences. Finally, pharmacotherapy does not address scarring and may be ineffective in treating postinflammatory pigmentation, which often develops in patients with moderate to severe acne vulgaris. By combining medical treatments with laser and light-based procedures in the office, dermatologists can provide patients

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with more options for treating acne and preventing long-term sequelae as well as provide cosmetic improvement of pigmentation or scarring that has already developed.

Laser and light-based therapies can treat active acne vulgaris as well as improve hyperpigmentation and scarring.<sup>5</sup> Also, compared with traditional pharmacotherapy some of these modalities can give patients a faster response.<sup>6</sup> The mechanism of action of light-based therapies depends on the particular device used as well as its wavelength. In general, lights may target *P. acnes* or damage the pilosebaceous unit directly.<sup>7</sup> Treatment options currently available include blue light, red light, pulsed dye lasers (PDLs), photodynamic therapy (PDT) with adjuvants such as 5-aminolevulinic acid (ALA) and methyl aminolevulinate acid (MAL), intense pulsed light (IPL), photopneumatic therapy (PPX), and fractional photothermolysis (FP). These treatment options can be effective in conjunction with pharmacotherapy or as monotherapy for most cases of acne vulgaris.

### BLUE LIGHT THERAPY

Blue light therapy can be used specifically to target and kill *P. acnes*. The bacteria produces protoporphyrin IX and coproporphyrin III, which selectively absorb light within the visible spectrum.<sup>8</sup> This results in the development of reactive oxygen radicals, which are toxic to *P. acnes*.<sup>9</sup> A broad range of wavelengths within the visible light spectrum produce this effect, but peak absorption occurs at 415 nm, in the blue light spectrum.<sup>7</sup> Two blue light devices approved by the US Food and Drug Administration (FDA) are the ClearLight Acne Photoclearing System and the Blu-U.<sup>10</sup> Other blue light systems, including the Omnilux blue, are available outside the United States.

The efficacy of blue light therapy has been demonstrated in several clinical trials. Performing blue light treatments 4 times weekly showed an improvement in acne lesions as early as 2 to 3 weeks.<sup>9</sup> Blue light therapy also has provided improvement equivalent to that of benzoyl peroxide 5%.<sup>11</sup> Mild to moderate inflammatory acne is most responsive to blue light therapy,<sup>12</sup> while patients with only comedonal acne or a predominance of nodulocystic lesions are poor candidates for this treatment. In patients with mild to moderate inflammatory acne, blue light therapy has proved to be superior to topical clindamycin solution 1%.<sup>13</sup>

The side-effect profile of blue light therapy is excellent and the treatment generally is very safe. Local irritation, dryness, and pruritus occur over 10 times less frequently with blue light therapy than with topical

benzoyl peroxide.<sup>11</sup> Moreover, visible blue light administration does not cause DNA damage or early photoaging as UV radiation does. Histologic effects observed in skin biopsy specimens after exposure to blue light were limited to transient melanogenesis and vacuolization without related cell death.<sup>14</sup> Given the low frequency of adverse effects, blue light therapy may be incorporated into therapeutic regimens either as an adjuvant therapy or as a safe replacement for pharmacotherapy for some patients with mild to moderate inflammatory acne.<sup>12</sup>

### RED LIGHT THERAPY

Visible light in the red spectrum (640–750 nm) has been shown to be beneficial in treating acne vulgaris. Red light has a longer wavelength than blue light, penetrates deeper into the skin, and reaches sebaceous glands better.<sup>15</sup> Unlike blue light, red light does not exhibit its effect through toxicity to *P. acnes*. Rather, red light is anti-inflammatory with direct inhibitory effects on macrophages, which ultimately leads to a decrease in the secretion of proinflammatory cytokines.<sup>16,17</sup> There also is evidence to suggest that a downstream effect of red light treatment is a decrease in transepidermal water loss.<sup>18</sup> Approved red light devices in the United States include the CureLight BroadBand and narrowband Aktelite CL128.

Red light therapy is newer than blue light, and it has not been studied as thoroughly as blue light. However, data thus far have been reassuring. In 2007, the first trial evaluating red light monotherapy for the treatment of acne vulgaris was published reporting efficacy with minimal adverse events.<sup>19</sup> These results were reproduced in a second study the following year.<sup>18</sup> Red light also is commonly used as the light source for PDT, but some argue that monotherapy with red light may be just as efficacious as PDT.<sup>20</sup> Finally, combination phototherapy with both blue light and red light has been demonstrated to be safe and efficacious in the treatment of mild, moderate, and severe acne.<sup>11,21,22</sup> In the United States, Acelamp is one such device that emits both blue light and red light.<sup>23</sup>

### PULSED DYE LASERS

Pulsed dye lasers are devices that emit yellow light in the wavelength range of 585 to 595 nm. The target chromophore for light of this wavelength is oxygenated hemoglobin, and PDL is effective in treating acne vulgaris as well as cutaneous vascular lesions including port-wine stains, telangiectases, hemangiomas, and scars.<sup>10,24</sup> Levels of oxygenated hemoglobin are increased in inflammatory lesions of acne vulgaris, so PDL can selectively target the affected skin. Pulsed dye

lasers also are thought to release anti-inflammatory mediators, decrease *P acnes* levels, and stimulate pro-collagen formation.<sup>25</sup> The use of PDL to decrease the number of inflammatory acne lesions was initially validated in 2003.<sup>6</sup> Pulsed dye lasers also have been found to be superior to IPL in a head-to-head comparison.<sup>26</sup> Other trials have shown mixed results on the effectiveness of PDL for acne.<sup>27,28</sup>

The most common complication of PDL therapy is the development of transient purpura. Less common side effects include skin dyspigmentation, crusting, bleeding, and scarring.<sup>24</sup> These side effects tend to be more frequent in darker-skinned patients. Given its side-effect profile and lack of clinical studies, PDL is generally not recommended as a first-line therapy for the treatment of acne vulgaris.<sup>12</sup>

### PHOTODYNAMIC THERAPY

Photodynamic therapy is a process that uses light to activate a photosensitive chemical. Photodynamic therapy is approved in the United States for the treatment of actinic keratoses (AKs) but has been used off-label for acne vulgaris. Topical sensitizers such as ALA, MAL, and indocyanine green (ICG) are applied and allowed to incubate so they can be absorbed into the skin. The use of a light source subsequently selectively activates the chemical.<sup>7</sup> Side effects such as erythema, edema, crusting, and desquamation may take several days to 1 week to heal.<sup>29</sup> In some cases, patients also may experience pain during the procedure.<sup>30</sup>

Photodynamic therapy is effective in treating acne vulgaris because it has both antibacterial and anti-inflammatory properties. Specifically, ALA is a precursor to protoporphyrin IX that penetrates the stratum corneum and is selectively absorbed into cells affected by solar damage, as well as sebaceous glands.<sup>31</sup> Once it accumulates in these cells, ALA is converted into protoporphyrin IX, and subsequent exposure to light results in the production of reactive oxygen radicals that are toxic to *P acnes*.<sup>32</sup> Other hypothesized mechanisms of action include a reduction in sebum production due to damage of the pilosebaceous unit and an anti-inflammatory effect from inhibition of infiltrating leukocytes.<sup>12</sup> Methyl aminolevulinic acid, the methyl ester of ALA, may penetrate the skin faster and deeper than ALA, is subsequently enzymatically converted to ALA, and requires a shorter incubation time than ALA.<sup>33</sup> The mechanism of action of ICG is less well understood. Indocyanine green has been shown to selectively accumulate in the sebaceous gland following topical absorption,<sup>34,35</sup> and its efficacy may be due to destruction of *P acnes* through local

photothermal reactions and modification of sebaceous gland function.<sup>36</sup>

Photodynamic therapy with ALA (ALA-PDT) using a variety of light sources (including blue light and IPL) has been gaining wider acceptance as an off-label therapy for moderate to severe inflammatory acne.<sup>10</sup> In the United States, ALA is commercially available only in the form of Levulan Kerastick. In 2000, ALA-PDT was initially published as a therapeutic option for acne vulgaris, establishing efficacy with a 550- to 570-nm broadband light source.<sup>37</sup> Since then, numerous studies have proven the efficacy of ALA-PDT for the treatment of acne vulgaris with a variety of light wavelengths, including a 600- to 700-nm halogen light source.<sup>38,39</sup> In 2003, Goldman and Boyce<sup>40</sup> demonstrated both safety and efficacy in the treatment of moderate to severe acne with ALA-PDT with a blue light source. Treatment of acne vulgaris with ALA-PDT with IPL has also been successful.<sup>41,42</sup>

Photodynamic therapy with MAL (MAL-PDT) is becoming increasingly popular after initially being approved by the FDA for the treatment of AKs. While currently not approved for use in the United States for acne treatment, MAL is available in the United States as Metvixia and internationally as Metvix, and several randomized controlled trials have demonstrated its efficacy in the treatment of acne vulgaris.<sup>43</sup> Activation of MAL-PDT with red light has shown efficacy in treating moderate to severe acne vulgaris compared to placebo.<sup>44</sup> In a head-to-head trial versus ALA-PDT, MAL-PDT had similar efficacy with better patient tolerability.<sup>45</sup> However, issues with the topical preparations used and the source of light for PDT in this study lead some experts to question this claimed superiority.<sup>29</sup> Specifically, the use of a locally produced ALA cream, long incubation time with ALA-PDT, and red light as the light source for ALA-PDT were mentioned as possible confounding factors in the study.

Photodynamic therapy with ICG (ICG-PDT) has not been evaluated extensively by clinical trials for use in the treatment of acne vulgaris. Indocyanine green is a dye commonly used to evaluate blood flow, cardiac output, and liver function.<sup>46</sup> It has a peak absorption at 805 nm and can be photoactivated with a diode laser.<sup>23</sup> In 2002, a study introduced ICG-PDT as an option for face and back acne.<sup>34</sup> The following year, improvement of acne was reported with multiple treatments of ICG-PDT activated by a 803- to 810-nm diode laser.<sup>36</sup>

### INTENSE PULSED LIGHT

Intense pulsed light devices deliver light over a broad spectrum of near-infrared wavelengths (500–1200 nm)

## Fractional Photothermolysis Systems

Device	Type	Company	Description
Affirm	Ablative	Cynosure, Inc	Dual-wavelength 1320- and 1440-nm laser
Fraxel re:pair	Ablative	Reliant Technologies, Inc	10,600-nm CO <sub>2</sub> laser
Fraxel re:store	Nonablative	Reliant Technologies, Inc	Dual-wavelength deep-penetrating erbium fiber laser (1550 nm) and superficial thulium fiber laser (1927 nm)
Lux 1540	Nonablative	Palomar Medical Technologies, Inc	1540-nm laser
UltraPulse	Ablative	Lumenis Aesthetic	10,600-nm CO <sub>2</sub> laser

by nonlaser high-energy flashlamps. Intense pulsed light commonly is used to treat a variety of dermatologic conditions such as hyperpigmentation, telangiectasia, and fine lines and wrinkles.<sup>47</sup> Various chromophores are targeted by IPL, including melanin (250–1200 nm), hemoglobin (418 nm, 542 nm, 577 nm), and collagen (400–600 nm), and filters are used to select wavelength ranges. The use of IPL as monotherapy for acne has not been extensively studied. A 2007 study comparing IPL plus benzoyl peroxide with benzoyl peroxide alone showed similar results between the 2 treatment groups.<sup>48</sup> Other studies, however, have demonstrated that IPL had a measurable effect on the treatment of acne.<sup>49</sup> When used to treat acne, IPL is most commonly employed as the light source for PDT with a photosensitizing agent.<sup>33</sup>

### PHOTOPNEUMATIC THERAPY

Photopneumatic therapy utilizes simultaneous vacuum suction and pulsed broadband light (400–1200 nm) to irradiate the skin and induce pilosebaceous damage, ultimately improving acne vulgaris.<sup>50</sup> In the United States, this technology is available as the Isolaz Photopneumatic system. Aside from its novel use for the treatment of acne vulgaris, PPX previously has been used for hair removal and solar

dyspigmentation.<sup>51</sup> The mechanism of action of PPX for acne treatment is thought to be the removal of sebum from comedones prior to delivery of the pulsed light.<sup>50</sup> Photopneumatic therapy has been shown to be efficacious for the treatment of mild, moderate, and severe acne vulgaris.<sup>52,53</sup> One of the adverse effects of PPX therapy is mild erythema.<sup>54</sup> While PPX has not been extensively evaluated, current results are promising.<sup>52,53</sup>

### FRACTIONAL PHOTOTHERMOLYSIS

Fractional photothermolysis increasingly is being used to treat the sequelae of acne, such as acne scarring. In FP, a fractionated emission of light creates microscopic zones of thermal damage in the skin.<sup>55</sup> Fractional photothermolysis systems are currently approved by the FDA for the treatment of pigmented lesions, periorbital wrinkles, skin resurfacing, melasma and soft tissue coagulation, acne and surgical scars, and AKs.<sup>56</sup> Fractional photothermolysis systems used include the combined deep-penetrating 1550-nm erbium fiber laser and superficial 1927-nm thulium fiber laser, nonablative 1540-nm laser, and 10,600-nm CO<sub>2</sub> laser (Table).

Both fractionated ablative and nonablative laser systems have been used to improve the appearance

of acne scarring. Ablative FP is more aggressive, disrupting the integrity of the epidermis, while damage caused by nonablative FP is confined to the dermis. Acne scarring was first treated with nonablative technology in 2006.<sup>57</sup> Several studies have since confirmed that nonablative FP is effective, though several treatment sessions may be necessary to achieve maximal results.<sup>58,59</sup> Ablative FP lasers (CO<sub>2</sub>, Er:YAG) also are efficacious and commonly used for this purpose. They may require fewer treatment sessions but result in longer downtime.<sup>60-62</sup> A recent head-to-head split-face study by Cho et al<sup>63</sup> evaluating nonablative versus ablative FP determined that ablative FP was more effective but associated with a less desirable side-effect profile.

Fractional photothermolysis involves the emission of light to limited focal areas of tissue, leaving surrounding tissue unaffected. This allows for rapid healing and reepithelialization and is accompanied by collagen and elastic tissue remodeling.<sup>55</sup> The targeted chromophore for ablative FP devices is water, which ensures selective thermal damage to collagen, blood vessels, and epidermal keratinocytes.<sup>64</sup> An increase in type 3 collagen in treated skin has been demonstrated histologically, and the improvement of atrophic scars such as acne scars following FP treatment is likely secondary to new collagen formation and reorientation.<sup>56</sup> Nonablative FP leaves the epidermis intact while targeting the dermis and is associated with fewer side effects and less healing time than ablative FP, but the wound-healing response is not as complete and the resurfacing effects are not as dramatic as the ablative procedures.<sup>65</sup>

Fractional photothermolysis is associated with fewer and milder side effects compared with nonfractionated counterparts, largely because of the limited focal treatment delivered by FP in comparison with other traditional laser treatments. Side effects from nonablative FP tend to be milder than those of ablative FP. These include, pain during the procedure as well as posttreatment erythema and edema.<sup>56</sup> Compared with ablative FP, nonablative FP has a lower risk of postprocedure dyspigmentation and appears to be an excellent option for darker-skinned patients with acne scars.<sup>55</sup> Recovery from ablative FP procedures is longer than that from nonablative FP, with a week of erythema and edema, and a higher risk of posttreatment dyspigmentation and scarring.<sup>66</sup> Ablative FP has been used successfully to treat acne vulgaris in patients with skin of color,<sup>62</sup> but further studies are needed to evaluate the risk of postinflammatory hyperpigmentation in this group.

## SUMMARY

Proven efficacy, minimal to no systemic side effects, and the convenience of in-office administration make laser and light therapies an exciting option for patients with acne vulgaris. These devices can be utilized either as monotherapy or as an adjuvant treatment to medical therapies. In addition, they provide alternatives for patients in which topical or systemic medicines are contraindicated or are not tolerated. There are a variety of different lasers and light sources available for the treatment of acne vulgaris, but only large clinical trials in the future will validate their efficacy.

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