

## Procedural Treatments for Acne Vulgaris

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**BACKGROUND** Simple procedural treatments such as comedone extraction and intralesional steroids have been utilized for many years as adjunctive therapy for acne. In the past 5 years, new technologies and procedures have become available that present new options for the treatment of acne.

**OBJECTIVES** The objective was to review, summarize, and evaluate the key studies of procedural therapies for the treatment of acne as well as place them in perspective with current clinical practice.

**METHODS** Studies selected for evaluation had at least 10 patients and clear statements of purpose, acne severity, patient selection, follow-up evaluations, previous and concurrent medications, treatment parameters, methods for evaluating results, and adverse effects. All studies were complete and published (in English) in peer-reviewed journals.

**RESULTS AND CONCLUSIONS** Earlier procedural therapies were adjunctive to medical therapy, such as intralesional steroids, chemical peels, and microdermabrasion. Newer methods include radiofrequency, light or laser, and photodynamic therapy that represent treatment alternatives for systemic medications. Still early in their development, these new procedures provide an important, novel set of options for the treatment of acne. The most developed and studied therapies are blue or blue/red light combinations, 1,450-nm diode laser, and photodynamic therapy with 5-aminolevulinic acid or indocyanine green. Review of the literature of more up-to-date physical procedures provides a starting point for physicians seeking to treat their acne patients safely and effectively with these new methods.

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Because the pathogenesis of acne vulgaris involves multiple factors, physicians often prescribe agents in combination in an effort to attack as many factors as possible. For example, in mild acne, topical retinoids, and antimicrobial agents are often prescribed together because the combination more effectively reduces comedones and inflammatory lesions than antimicrobial agents alone.<sup>1</sup>

Even before the advent of light, laser, and radiofrequency treatment modalities, physical therapies have been employed to complement medical therapy. Light cautery<sup>2-4</sup> and aspiration followed by in situ injection of cortisone, respectively, are useful adjunctive therapies.<sup>5</sup> Other adjunctive therapies include extraction, chemical peels, and cryotherapy.

More recently, light, heat, and radiofrequency energy devices and modalities as well as photodynamic therapy (PDT) have emerged as useful cotherapies or, in some cases, replacements for systemic medications.

The purpose of this review is to summarize and evaluate the key studies of physical therapies for acne vulgaris, as well as attempt to put them into perspective with what is accepted in current clinical practice. Old favorites such as comedone extraction and intralesional injection of cortisone live on in everyday practice due to their immediate impact. Newer therapies relying on light, heat, radiofrequency, and PDT are becoming more commonly utilized due to an increasing body of evidence that

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they are safe and effective as well as concerns and scrutiny over adverse events occurring with pharmacologic agents.

### Early Physical Methods

Physical removal of individual comedones provides immediate improvement and patient satisfaction. Disadvantages include the potential for incomplete extraction, tissue damage, and refilling.<sup>1</sup> Although comedo extraction<sup>6</sup> is widely used (light cautery and fulguration less commonly so), articles describing their use are scarce in peer-reviewed dermatology journals (Table 1).

### Intralesional Injections

Corticosteroids are injected intralesionally to provide a high concentration of steroid within the lesion with minimal systemic absorption. This modality is indicated when a quick response is required.<sup>7,8</sup> Corticosteroid injections flatten most acne nodules in 48 to 72 hours.<sup>7</sup> Marked improvement in nodular and cystic acne after intralesional steroid injections has been reported.<sup>9</sup> Preparations usually come as triamcinalone acetonide in 10 mg/mL multiple-use vials that may be diluted with sterile normal saline to 5 or 3.3 mg/mL, two commonly used dilutions.

Leeming<sup>10</sup> cited five advantages with intralesional injection of corticosteroids: (1) rapid resolution of lesions; (2) low cost; (3) fewer side effects than systemic corticosteroid therapy; (4) simple, easy technique; and (5) patient comfort in knowing that new cystic lesions can be easily and rapidly resolved. Corticosteroids injected intralesionally, however, do have potential complications. Local overdose can result in atrophy, pigmentary changes, and telangiectasias,<sup>11</sup> and repeated injections can clinically suppress the hypothalamic-pituitary-adrenal axis,<sup>12–14</sup> the duration of which depends on dose.<sup>13</sup>

Corticosteroids should be injected at the smallest concentrations possible, which can be determined by experience with the types of lesions and the patient's

response.<sup>15</sup> Using this as a primary or regular form of treatment for someone with multiple lesions is not an effective treatment strategy, due to the need for frequent visits and the increased risk for potential side effects. As a “quick fix” for an occasional or particularly stubborn cystic lesion, however, this treatment method excels.

### Superficial Exfoliation

#### Cryotherapy

*Controlled Trial* Liquid nitrogen has been evaluated and reported to be effective against pustular but not comedonal and papular acne.<sup>16</sup> In a split-face study of 25 patients, liquid nitrogen was applied to lesion areas on one side and other topical therapies were used on the other side. Liquid nitrogen was most effective against superficial cystic lesions and least effective against deeper lesions. The treatment was painful and caused stinging and burning for up to 4 hours.

*Case Series Studies* Cryotherapy for the treatment of acne and acne scars was introduced in 1939 by Karp and colleagues.<sup>17</sup> In their 50-patient study, these investigators mixed solid carbon dioxide, acetone, and precipitated sulfur and applied the yellow paste first to the lesions and then to the entire face for 20 minutes during which the treated skin “froze.” Erythema and edema appeared immediately and lasted for several days before mild epidermal exfoliation occurred.

One year later, Dobes and Keil<sup>18</sup> reported a modification in which a similar mixture with more acetone was applied as a “slush” once weekly. The authors reported improvement in papulopustular acne (3–24 treatments) and cystic acne (21 treatments) with a few cases of recurrence in 95 patients. Comedonal acne responded poorly. Severe edema, depigmentation (in patients with Type VI skin) and purpurallike patches resulted in a few instances.

Although there are still individual practitioners who use cryotherapy and find it to be helpful for their

**TABLE 1. Reports Evaluating the Efficacy and Safety of Extraction and Light Cautery for the Physical Removal of Open and Closed Comedones**

<i>Reference</i>	<i>Method</i>	<i>Number of patients</i>	<i>Comedo types treated</i>	<i>Number of treatments/ intervals (weeks)</i>	<i>Results</i>
<i>Controlled trial</i>					
Bottomley et al. <sup>3</sup>	Fulguration* vs. topical tretinoin	11	Closed	2/2	Number of noninflamed lesions reduced more, cosmetic improvement greater by fulguration
Bottomley et al. <sup>3</sup>	Fulguration vs. electrocautery*	12 <sup>†</sup>	Closed	2/2	Electrocautery better for large closed comedones. Fulguration comparable to electrocautery with anesthesia for small lesions. Patients prefer fulguration
<i>Case series studies</i>					
Lowney et al. <sup>6</sup>	Comedone extraction of the forehead	20	Noninflamed, closed	4–10/1–2	Reduces number of future inflamed lesions and recurrence rate of comedones; inflamed cystic lesions made worse
Pepall et al. <sup>2</sup>	Light cautery	14	Large whiteheads <sup>†</sup> (macrocomedones)	1–5/2	>95% lesions cleared; no recurrence, scarring, pigmentation 6–14 months later

\*Topical anesthesia (EMLA<sup>®</sup>).

<sup>†</sup>Three of 15 patients withdrew; 2 (dark-skinned) due to postinflammatory hyperpigmentation with both modalities and 1 due to pain during treatment with both modalities.

patients, this treatment has largely fallen out of modern dermatologic practice.

### **Microdermabrasion**

Microdermabrasion is a procedure that is designed to physically exfoliate the stratum corneum with suction and aluminum oxide crystals. Initially used as a treatment for acne scarring,<sup>19</sup> it has become a popular treatment for aging and pigmentation abnormalities. The mechanism of action appears to be removal of the stratum corneum, which when accomplished repeatedly, leads to stimulation of dermal fibroblasts and epidermal renewal.<sup>20</sup> Newer

methods use vibration, cavitated water,<sup>21</sup> or other noncrystal modalities. Duration of improvement of microdermabrasion, however, may be shorter, and cost to the physician is higher than that of chemical peels.<sup>22</sup>

Despite this procedure's popularity, scientific data on its efficacy and safety are limited.<sup>22</sup> With regard to acne, efficacy has been studied for oily skin, dilated pores, and fine wrinkling<sup>23</sup> as well as acne.<sup>24</sup>

*Randomized Controlled Trial* The use of microdermabrasion to enhance the efficacy of the 1,450-nm diode laser in the treatment of

inflammatory facial acne appears to provide no additional benefit, as shown in a study of 20 patients.<sup>25</sup>

**Case Series Study** In a pilot study,<sup>24</sup> 25 patients with Grades II to III acne were treated eight times with microdermabrasion. One patient withdrew to begin isotretinoin therapy. Patients were permitted to continue acne medications during the study. Results were excellent in 38%, good in 34%, fair in 17%, and poor in 12%. The procedure was well tolerated and all but 1 patient (96%) would recommend the procedure to others. One author questioned the value of the information given the lack of controls, however, and the fact that medications were allowed to be changed during the course of the study.<sup>26</sup>

As a superficial peeling agent, microdermabrasion may be considered a temporary superficial adjunctive procedure, although the literature neither supports nor refutes a role for the treatment of active acne. Microdermabrasion may also enhance absorption of topically applied medications,<sup>27</sup> as pretreatment for PDT<sup>28</sup> or to increase the penetration of light into the epidermis.<sup>29</sup>

## Chemical Peeling

### Glycolic Acid

An  $\alpha$ -hydroxy acid, glycolic acid is used in cutaneous conditions associated with abnormal keratinization.<sup>30</sup>

**Randomized, Controlled, Evaluator-Blinded Trial** A 26-patient study<sup>31</sup> comparing glycolic acid (70%) with Jessner's solution for the treatment of facial acne showed that improvements were similar in both treatments but exfoliation was significantly greater in patients treated with Jessner's solution.

**Controlled Trial** Glycolic acid peels, which tend to be used in a higher strength than that for daily home care (e.g., 30%–70% vs. 6%–15%), have resulted in significant resolution of facial comedones, papules, and pustules with improvement in skin texture of 40 Asian patients with moderate to moderately severe acne.<sup>32</sup> Patients (aged 16–51 years) received four treatments (35 or 50% glycolic acid, depending

on oiliness of skin) at 3-week intervals while using 15% glycolic acid regularly in their homes. Side effects included postinflammatory hyperpigmentation ( $n = 3$ ), mild local herpes simplex infection ( $n = 3$ ), and mild skin irritation ( $n = 3$ ), all transient.

**Case Series Study** Atzori and colleagues<sup>33</sup> treated 80 women (aged 13–40 years) with 70% glycolic acid and found that comedonal acne improved more rapidly than papulopustular acne (6 treatments) and nodulocystic acne (8–10 treatments). Glycolic peels appear to be a useful adjunctive method for treatment of acne. They appear to reduce both comedonal and inflammatory acne as well as improve postinflammatory changes<sup>34</sup> that could be expected to benefit due to dermal changes.<sup>35</sup>

### Salicylic Acid

An excellent keratolytic agent, salicylic acid is useful against comedones due to its strong lipophilicity and ability to penetrate the pore. Salicylic acid has anti-inflammatory effects and is effective against both inflammatory and anti-inflammatory lesions.<sup>36</sup>

**Controlled Trial, Double Blinded** Low concentrations (0.5%–3%) speed up resolution of inflammatory lesions and decrease the formation of microcomedones. Shalita<sup>37</sup> showed in a study of 49 patients. Low concentrations are frequently tolerated by patients who cannot tolerate benzoyl peroxide.

**Case Series Study, Evaluator Blinded** Lee and Kim<sup>36</sup> treated 35 Korean patients with salicylic acid (30%) biweekly for 12 weeks. The longer the duration of treatment, the greater the reduction in lesion counts for inflammatory and noninflammatory lesions. Side effects were tolerated well. Side effects included erythema, dryness, burning, and crusting, all temporary.

**Case Series Study** Grimes<sup>38</sup> used salicylic acid in darker-skinned type patients ( $n = 25$ , 9 with acne). The treatment cleared acne in 8 of 9 patients.

Although they do not replace topical or systemic medications, superficial glycolic and salicylic acid-based chemical peels are very effective adjunctive

methods to enhance and speed resolution of acne, both inflammatory and comedonal. They also may be used safely in skin of color as well as to help resolve postinflammatory hyperpigmentation.<sup>34</sup>

Chemical peels require maintenance treatments to sustain their effect. On the basis of the limited literature, these appear to be more useful or better appreciated by patients<sup>39</sup> than microdermabrasion for active acne.

### **Trichloroacetic Acid**

To the author's knowledge, studies of the use of trichloroacetic acid peels for the treatment of acne vulgaris have not been published.

## **Newer Methods Utilizing Light, Laser, PDT, and Radiofrequency**

### **Blue Light and Blue/Red Light Combinations**

Therapy with visible light takes advantage of the photosensitivity of porphyrins produced by *Propionibacterium acnes*,<sup>40</sup> the skin bacterium associated with acne. Activation of protoporphyrin IX (PpIX) in the presence of oxygen produces singlet oxygen, a metastable intermediate that destroys cells (in this case, *P. acnes*).<sup>41,42</sup> PpIX absorption peaks occur at 410 (maximum), 505, 540, 580, and 630 nm,<sup>43</sup> all wavelengths in the visible light spectrum. Although absorption of light is greatest at 410 nm (blue light), penetration into skin at this wavelength is considerably less than at longer wavelengths.<sup>44,45</sup> As a result, practitioners must sacrifice absorption efficiency for penetration depth and vice versa. A recent study of keratinocyte cell lines,<sup>46</sup> however, suggests that narrowband blue light reduces the cytokine-induced production in keratinocytes of interleukin-1 $\alpha$  and intercellular adhesion molecule-1, two markers of inflammation, suggesting that blue light may have anti-inflammatory effects as well. Studies of light-based therapies are shown in Table 2.

*Randomized Controlled Trials* Sigurdsson and coworkers reported in 1997<sup>47</sup> that visible light (full

spectrum, violet, green) was moderately effective in improving acne. (This study was randomized and evaluator-blinded, but not controlled.) Several years later, Papageorgiou and colleagues<sup>48</sup> reported a study in which 107 patients with acne were randomized into four treatment groups: blue light, mixed blue and red light, cool white light, and benzoyl peroxide cream (5%).<sup>48</sup> Treatment was given daily (15 min) for 12 weeks. Results of light therapies were evaluated by blinded observers. Mean improvement was greatest (76%) for mixed blue and red light, with follow-up of 12 weeks.

Other studies reported the safety and efficacy of commercial devices cleared by the US Food and Drug Administration (FDA). Elman and colleagues<sup>49</sup> studied a blue light (405–420 nm) device (ClearLight manufactured by CureLight Ltd, Gladstone, NJ; marketed at the time of the study by Lumenis Corp., Santa Clara, CA) for the treatment of acne in 46 patients. Efficacy ranged from 59 to 67%, a 64.7% reduction. Tzung and colleagues<sup>50</sup> reported efficacy with the blue light (F-36 W.Blue V, Waldmann, Villingen-Schwenningen, Germany) in 31 Taiwanese patients with mild to moderately severe acne. In a 25-patient evaluation of a blue light source (BLU-U, DUSA Pharmaceuticals, Wilmington, MA), Gold and colleagues<sup>51</sup> reported greater inflammatory lesion count reduction with blue light therapy than with clindamycin therapy. Results were supported by photographs but claims of significance were not supported by probability values.

*Case Series Studies* Two groups<sup>52,53</sup> reported success in the treatment of inflammatory acne in studies of 30 patients<sup>52</sup> and 45 patients<sup>53</sup> with a light-emitting diode blue light device (Omnilux Blue, Photo Therapeutics, Inc., Lake Forest, CA). Mild or no adverse effects were reported. Kawada and colleagues<sup>54</sup> and Omi and colleagues<sup>55</sup> studied the ClearLight in 30 patients<sup>54</sup> and 28 patients, respectively.<sup>55</sup> Efficacies were consistent (64 and 64.7% reduction or improvement, respectively) and adverse effects were limited to dryness.<sup>54</sup> In a 19-patient study evaluating a pulsed light and heat energy technology

TABLE 2. Light-Based Therapies for the Treatment of Acne

Reference (number of patients)	Acne type (location)	Light source(s) (number of treatments)	Efficacy	Adverse effects	Strengths	Limitations	Significance of study
<i>Randomized controlled trial, double-blinded</i>							
Elman et al. <sup>49</sup> (46)	Papulopustular (face)	Blue light (high-intensity, narrow-band (405– 420 nm))* (8)	59%–67% reduction of inflammatory lesion in 80% of patients; maintained for 8 weeks after final treatment	None reported	Three studies: split-face dose response (n = 10), full-face open trial (n = 13), split-face double- blinded, self-controlled (n = 23); supported by numerous photographs	Only 8-week follow-up; severities of acne in all studies not reported; comorbidities not stated; patient evaluation not reported; dropouts not discussed	First split-face, double- blinded, controlled study to show efficacy and safety of high-intensity, narrow- band blue light in papulopustular acne
<i>Randomized controlled trial, investigator-blinded</i>							
Gold et al. <sup>51</sup> (25)	Mild to moderate (face)	Blue light† (8)	34% reduction in inflammatory lesions, 14% reduction by clindamycin	None reported	Blinded analysis of lesion counts, global severity scores, overall improvement score; compared with standard antibiotic; included non-responders in overall improvement calculations; results supported by clinical photographs; two-center trial	Probabilities for statistically significant differences not reported; distribution of data appears to be skewed in some cases; limited follow-up; improvement scores mentioned but not reported; patient characteristics, comorbidities not reported	First study to compare blue light with a well-known topical antibacterial agent
<i>Randomized controlled trial, evaluator-blinded</i>							
Papageorgiou et al. <sup>48</sup> (107)	Mild to moderate (anatomic location of acne not reported)	Blue (415 nm), red (660 nm) + blue light (60; daily for 12 weeks)	76% improvement in inflammatory acne with mixed blue-red light; 58% improvement in comedones	Acne flare-up, dryness/itch, facial rash, headache	Randomized into four treatment groups; controls; assessments for light treatment made by blinded observer; large number of patients; patients stated as healthy; includes inflamed and non-inflamed lesions; assessments by patients too; patients well screened	No follow-up; UV content was 7% of mixed light and 9% of blue light and not filtered out	Suggested mixed blue- red light had antibacterial action from blue light and anti-inflammatory action from red light; suggested phototherapy with mixed red-blue light was better than blue light alone



TABLE 2. Continued

Reference (number of patients)	Acne type (location)	Light source(s) (number of treatments)	Efficacy	Adverse effects	Strengths	Limitations	Significance of study
Sigurdsson et al. <sup>47</sup> ¶ (30)	Mild to moderate (face, chest, back)	Full spectrum, violet, green (20)	30, 22, and 14% re- duction in acne score with violet, green, full-spec- trum light; most effective on pus- tules and infil- trates	None reported	Three anatomical areas treat- ed, acne score calculated for all types of acne le- sions; patients received no medications during study	No controls; limited to cystic acne; no follow- up; comorbidities not stated; no discussion of potential confound- ing variables	First study to evaluate visible light in treatment of acne and indirectly ex- clude UV light for treatment of acne; suggested that therapeutic effect might be due to photodynamic de- struction of bacteria because porphyrins were also reduced
<i>Randomized controlled trials</i>							
Tzung et al. <sup>50</sup> (31)	Mild to moderately severe (face)	Blue light (400– 440 nm) (8)	52% mean improve- ment; exacerba- tion of acne in 14.3% of patients (all had severe acne)	None reported	Shows individual improve- ments in comedone, pap- ulopustular, and nodulocystic lesions as well as overall improve- ment compared with con- trol; assessments performed by two blinded dermatologists; randomly selected sides of face treated with blue light; ac- ne symmetrical on faces	Short follow-up time (1 month); no photographs to sup- port results; comorbid- ities not stated	Shown efficacy and safety of blue light in Asian patients and that blue light was most effective in patients without nodulocystic le- sions
<i>Case series studies</i>							
Kawada et al. <sup>54</sup> (30)	Mild to moderate (face, back, chest)	Blue light (high- intensity, nar- rowband, 405–420 nm)* (10)	Comedones + pa- pules + pustules reduced by 64%; reduction in comedones, pa- pules, pustules	Dryness in 2 patients	Supported by reduced in vi- tro activity of <i>P. acnes</i> isolates exposed to light source. Patients well char- acterized; clear criteria for inclusion, grading acne; two methods of assess- ment; photos show dra- matic improvement	1-month follow-up; im- provement assessed only by non-blinded investigator; no con- trols or randomization; no mention of comor- bidities	Shown that high-in- tensity, narrow- band blue light alone was effective against comed- ones, papules, pus- tules

TABLE 2. Continued

Reference (number of patients)	Acne type (location)	Light source(s) (number of treatments)	Efficacy	Adverse effects	Strengths	Limitations	Significance of study
Elman and Lask <sup>56</sup> (19)	Mild to moderate (location not stat- ed)	430–1100 nm; pulsed light <sup>†</sup> (8)	Clearance: 63% (noninflammato- ry) and 50% (in- flammatory) at end of treatment; 79 and 74% 1 month; 85 and 87% 2 months	None reported	2-month follow-up results re- ported; studied inflamma- tory and noninflammatory lesions; acne severity graded by known scale	Photographs taken but not presented; no con- trols; raw data not presented; location of acne not reported; comorbidities not men- tioned; results not evaluated by blinded assessor	First study to evaluate combination of pulsed light and heat energy in a broader spectrum for acne treatment
Omi et al. <sup>55</sup> (28)	Grades 0 to 5 (Bur- ton) (face)	Blue light (high- intensity, nar- rowband (405–420 nm)* (8)	Overall, 64.7% im- provement in ac- ne lesions	None reported	Acne severity graded by Bur- ton scale; all grades of ac- ne counted before and after treatment; 2- to 3- month follow-up. Sup- ported by studies of changes in dermal moist- ure, P. acnes on skin, pH, sebum levels, and blood flow	All results evaluated by investigators; comor- bidities not stated; no controls; no patient evaluations; new sta- tistical methods used to evaluate data	First attempt to study mechanism of ac- tion of high-intensi- ty, narrow-band blue light
Morton et al. <sup>52</sup> (30)	Mild to moderate (face)	Blue light LED <sup>§</sup> (409– 419 nm) (8)	25, 53, 60, and 64% reduction in pa- pules, pustules at 1, 4, 8, and 16 weeks posttreat- ment; no reduc- tion in noninflamed le- sions; 75% of subjects would use treatment again	Slight redness, dryness, pruritis	Compared 10- and 20-minute treatment; 4-month fol- low-up; included subject evaluation	Assessment not blinded; comorbidities not mentioned; no con- trols	First study to show ef- ficacy and safety of blue light LED for the treatment of in- flammatory acne with intermediate- term follow-up



Tremblay et al. <sup>53</sup> (45)	Mild to moderate (nodulocystic excluded)	Blue light (high-intensity, LED, 415 nm) <sup>§</sup> (8–16)	Mean improvement scores 3.14 (4 weeks) and 2.90 (8 weeks); 9 patients completely cleared at 8 weeks; 50% of patients highly satisfied	None reported	2-month follow-up; patient assessments included; results supported by photographs showing dramatic improvement; three centers	SD of mean improvement scores not reported; no discussion of nonresponders (10%); comorbidities not mentioned; treatment protocol sketchy; no controls; no blinded evaluation; not randomized	Confirmed efficacy and safety of blue light LED for the treatment of inflammatory acne
Goldberg and Russell <sup>29</sup> (24)	Mild to severe (face)	Blue light (415 nm), red light (LED), 633 nm, (8)	Mean lesion count reduction 46% (4 weeks), 81% (12 weeks)	Minimal, transitory	3-month follow-up, patient assessments included, well-matched patients	No blinded evaluation, no controls; not randomized	Confirmed efficacy and safety of blue, red light combination

\*ClearLight (CureLight Ltd, Gladstone, NJ).

<sup>†</sup>BLU-U (DUSA Pharmaceuticals, Inc., Wilmington, MA).

<sup>‡</sup>ClearTouch (Radiance, Inc., Orangeburg, NY).

<sup>§</sup>Omnilux Blue (Photo Therapeutics, Inc., Lake Forest, CA). LED, light-emitting diode; UV, ultraviolet.

\*Study randomized and evaluator-blinded, but not controlled.

(ClearTouch, Radiance Inc., Orangeburg, NY), Elman and Lask<sup>56</sup> reported greater clearance of noninflammatory than inflammatory lesions (63% vs. 50%, respectively) at the end of eight treatments. Two months later the clearance rates both increased and became essentially equal (Table 2). More recently a study utilizing biweekly alternating treatments with blue and red light in 24 patients with mild to severe acne showed a significant reduction in lesion counts at 4 and 12 weeks, with more improvement in severe acne than mild acne.<sup>29</sup>

Although all studies showed efficacy supported by photos and minimal adverse effects in the treatment of acne, none addressed duration of clinical benefit beyond 2 to 4 months and none indicated the presence or absence of other skin diseases that might have influenced outcomes. Many were not controlled and outcomes were not blindly assessed.

Even with this abundant literature demonstrating not only good but consistent results, questions remain in the author's practice about the reproducibility, practicality, and duration of benefit of blue light. Of the first 10 patients that this author treated with a high-intensity blue light source with a similar protocol as the articles cited above,<sup>49,54,55</sup> only 1 was satisfied with the outcome (unpublished observations). In addition, there was a rapid exacerbation for this 1 patient. Perhaps the combination of blue and red light will yield better improvements, due in part to the potential deeper penetration of red light and ability to reach the sebaceous gland. The idea of having a painless nonpharmacologic treatment for teenage acne is extremely attractive. Barriers to acceptance of this therapy are high cost and the fact that it is very time-consuming to provide, especially if frequent maintenance therapy will be required. Because blue light therapy for acne is not covered by insurance companies, the cost to the patient is also a drawback of this modality.

## Lasers

### Randomized Controlled Trials

**Pulsed Dye Laser** The efficacy and safety of the pulsed dye laser (PDL) has been studied by Seaton

and colleagues<sup>57</sup> and by Orringer and colleagues.<sup>58</sup> In their 41-patient study, Seaton and colleagues reported a reduction in acne severity and lesion count compared to controls while Orringer and colleagues, in a study of 40 patients, reported no clinical benefit with PDL treatment.

The reasons for the discrepancy of results are not clear. The study of Seaton and colleagues included a treated and control group, whereas Orringer and colleagues chose a split-face study design. The study by Seaton and colleagues was conducted during the winter months to minimize sun exposure as a confounding variable, whereas the study by Orringer and colleagues was conducted between August 2002 and September 2003, which included summer months.

*Potassium Titanyl Phosphate (KTP) Laser* The 532-nm KTP laser has been evaluated for the treatment of mild to moderate acne.<sup>59</sup> The randomized split-face study of 26 patients showed moderate reduction in acne score at 1 week and diminished reduction at 4 weeks posttreatment supported by histologic studies. The study suggests that the KTP laser may have promise in the treatment of acne.

*The 1,450-nm Laser* In 2002, Paithankar and colleagues<sup>60</sup> showed that a mid-infrared (1,450-nm) laser device (Smoothbeam, Candela Corp., Wayland, MA) with cryogen spray cooling could thermally damage the upper dermis (where sebaceous glands are located) without injuring the epidermis in an animal model. In their clinical study of 27 subjects with acne on the bilateral areas of the upper back, the authors showed that lesion counts on the treated sides of the backs were statistically significantly reduced after treatments compared to the control sides and that side effects were minimal and transient.

The 1,450-nm laser has been evaluated by Wang and colleagues,<sup>25</sup> who compared lesion count reductions with the laser alone and the laser plus microdermabrasion in the treatment of inflammatory facial acne. Adverse effects were limited to mild erythema, mild edema, and small papules. The mean reductions in lesion counts after four treatments were 53.5 and

55.6% with and without microdermabrasion, respectively.

Most recently, Jih and associates<sup>61</sup> completed a 20-patient study of the 1,450-nm wavelength and treating patients with skin types II to VI for inflammatory acne. Three split-face treatments were performed at 3- to 4-week intervals at randomly assigned fluences of 14 or 16 J/cm<sup>2</sup>. Mean lesion count reductions were 75.1% for 14 J/cm<sup>2</sup> and 70.6% for 16 J/cm<sup>2</sup>. These improvements were maintained at 12-month follow-up. The treatments were tolerated with minimal side effects and a mean visual analog pain score of 4 to 6.

#### *Case Series Studies*

*The 1,450-nm Laser* The 1,450-nm laser has also been evaluated by Friedman and colleagues.<sup>62</sup> Adverse effects were similar to those of Wang and colleagues. Lesion count reduction was higher at 83%, possibly because the Friedman patients continued to take topical and oral medications during the study.<sup>62</sup> Lasers of both studies were equipped with cooling devices. Treatment parameters were similar (6-mm spot size, 11–14 J/cm<sup>2</sup> fluence, cooling devices set at 30–40 ms), although the Friedman patients received three treatments and the Wang patients received four treatments. One criticism of 1,450-nm laser therapy is that it is too painful for many teenagers to tolerate.

*Pulsed Dye and 1,450-nm Diode Laser Combination* Glaich and colleagues<sup>63</sup> evaluated the dual-treatment protocol in which patients were treated three times with a sequential combination of 585-nm PDL and 1,450-nm diode laser. As in the study of Friedman and colleagues,<sup>62</sup> patients were permitted to continue oral and topical medications during the study period. The authors suggested that PDL reduces *P. acnes* colonization and reduces postinflammatory erythema while the 1,450-nm diode laser, as described by patients, shrinks oil glands and reduces skin oiliness. Patients also noted improvement in acne scarring.

From the available data, the 1,450-nm infrared laser appears to be a significant advance for the treatment of acne. It is unclear whether the PDL component of the new combination laser confers any benefit over the infrared wavelength alone. The results with the KTP laser are limited and preliminary. It is unlikely, however, that any short wavelength that did not have a profound effect on the sebaceous gland could produce a long-term acne remission by itself. The studies are evaluated in Table 3.

### ***PDT with 5-Aminolevulinic Acid***

PDT with either 5-aminolevulinic acid (ALA) or methyl aminolevulinate (MAL) applied topically has shown efficacy in the treatment of acne vulgaris. Although neither photosensitizing agent is FDA-cleared for the treatment of acne by PDT, both (ALA as Levulan Kerastick, DUSA Pharmaceuticals; and MAL cream as Metvix, PhotoCure ASA, Oslo, Norway) are cleared for the photodynamic treatment of nonhyperkeratotic actinic keratosis of the face and scalp. MAL cream is not yet available in the United States.

*Randomized Controlled Trials* The topical use of ALA in PDT was introduced and evaluated by Kennedy and colleagues.<sup>64,65</sup> As ALA penetrates epidermal cells, it enters the heme biosynthetic pathway and is converted to PpIX, a photosensitive compound.<sup>66,67</sup> As ALA-induced PpIX accumulates in the cells, the ALA-treated area is irradiated with light which, in the presence of molecular oxygen, activates PpIX to form singlet oxygen, a metastable intermediate that destroys the cells in which it is produced.<sup>41,42,65,68</sup> For photoactivation to occur, the light used in treatment must include wavelengths absorbed by PpIX.

*Red Light (Broadband)* PpIX also accumulates in pilosebaceous units.<sup>65,69</sup> In their 2000 landmark study, Hongcharu and colleagues<sup>70</sup> took advantage of this property by applying ALA PDT to the treatment of mild to moderate acne (Table 4). This study laid the foundation for the use of ALA PDT in the treatment of acne. The authors reported statistically

significant clearance (1) for 10 weeks after a single treatment and (2) for 20 weeks after four weekly treatments. The authors also suggested a mechanism of ALA PDT by showing that after ALA PDT, sebum excretion was decreased, bacterial fluorescence was decreased, and sebaceous glands were damaged. Adverse effects included transient hyperpigmentation, superficial exfoliation, and crusting. These encouraging results stimulated other investigators to further explore the use of ALA PDT for acne of the face and other locations. Their treatment parameters and results are presented in Table 4.

*Red Light (Laser)* The mechanism of ALA PDT was further explored by Pollock and colleagues<sup>71</sup> in their study of ALA PDT with activation by laser-generated red light. In their study of nine patients with mild to moderate acne, the authors found a reduction in lesion count (only at the ALA PDT site) after the second of three weekly treatments, but no reduction in the population of skin surface *P. acnes* and no reduction in sebum excretion after ALA PDT. The authors attributed the contrasting results to those of Hongcharu and colleagues to the broadband wavelengths used by Hongcharu and colleagues, possibly responsible for the reduced sebum excretion and reduced bacterial fluorescence observed in their study.

### ***Controlled Trials***

*Blue Light* In a controlled study, Goldman and Boyce<sup>72</sup> showed that ALA PDT with blue light was more effective against acne than blue light alone and showed that short-contact ALA (<1 hr) provided efficacy and minimal adverse effects.

*Long-Pulsed PDL* Alexiades-Armenakas<sup>73</sup> showed that ALA PDT with long-pulsed PDL activation was effective against a variety of acne lesion types with minimal adverse effects.

*Intense Pulsed Light (IPL)* In a 15-patient study, Santos and co-workers<sup>74</sup> showed that the formation of new acne lesions could be reduced by ALA PDT with activation by IPL.

TABLE 3. Laser-Based Therapies for the Treatment of Acne

Reference (number of patients)	Acne type or severity (location)	Light source (number of treatments)	Efficacy	Adverse effects	Strengths	Limitations	Significance of study
<i>Randomized controlled trial, evaluator blinded</i>							
Orringer et al. <sup>58</sup> (40)	Not reported (face)	PDL (585 nm) (2)	No significant difference in le- sion counts or graded severity for treated group vs. place- bo	Hyperpigmenta- tion, focal bruis- ing, transient cutaneous cy- anosis, erythema	Randomized, con- trolled, single- blind, split-face trial; intent-to- treat analysis	Did not investigate use of higher fluences; only one to two treat- ments; comor- bidities not mentioned	Concluded that PDL has no benefit for the treatment of acne
<i>Randomized controlled trials</i>							
Jih et al. <sup>61</sup> (20)	Inflammatory (face)	1450-nm diode laser (3)	Mean lesion count reduction 76.1% (14 J/cm <sup>2</sup> ) and 70.5% (16 J/cm <sup>2</sup> ) at 12 months	Transient ery- thema, edema	12-month follow-up; randomized; split- faced; investigator and patient as- sessments	Only two fluences studied; fluences differ only slightly	First dose-response study for 1,450- nm laser with long follow-up
Seaton et al. <sup>57</sup> (41)	Mild to mod- erate (face)	PDL (585 nm) (1)	Acne severity of PDL group re- duced more than control; to- tal lesion counts reduced by 53% in PDL groups vs. 9% in con- trols	Pain during treatment; tran- sient purpura, pruritis, dry skin, dry lips, watery eye	Double-blind, ran- domized con- trolled trial; 3- month follow-up; acne graded; in- tention-to-treat; study conducted in winter and spring to avoid summer sunlight confounding vari- able; 12-week fol- low-up	Possible selection bias in patients; comorbidities not mentioned	First randomized controlled trial to evaluate PDL treatment of acne
Wang et al. <sup>25</sup> (20)	Moderate to severe (face)	1450-nm diode laser (4)	Reduced lesion count by 53.5%, maintained for 3 months	Mild erythema, edema, small papules, postin- flammatory hyperpigmenta- tion, all transient	Split-face study with microdermabra- sion; 3-month fol- low-up; random- ized, controlled; lesion counts by independent observer	No mention of co- morbidity	First study to com- pare 1,450-nm laser to micro- dermabrasion for the treatment of acne

Table 3. Continued

Reference (number of patients)	Acne type or severity (location)	Light source (number of treatments)	Efficacy	Adverse effects	Strengths	Limitations	Significance of study
Baugh and Kucaba <sup>59</sup> (26)	Mild to moderate (face)	KTP (532 nm) (4)	34.9% reduction in acne score at 1 week and 20.7% reduction at 4 weeks posttreatment; greatest lesion count reduction in papules	None reported	Split-face; patient evaluations; treatment sides randomized; results supported by histologic studies showing post-treatment wound-healing response; screened patients with test spot laser treatment	1-month follow-up; no comorbidities mentioned	First study to evaluate efficacy and safety of KTP laser for the treatment of acne
<i>Case series studies</i>							
Friedman et al. <sup>62</sup> (19)	Mild to severe (face)	1,450-nm diode (3)	37% reduction in lesion counts after one treatment, 58% after two treatments; 83% after three treatments; all patients satisfied or highly satisfied	Transient erythema, edema; pain during treatment	Conclusions supported by photographs showing dramatic improvement; includes patient satisfaction data	No controls; patients continued topical and oral medications during study period; no follow-up; no randomization; comorbidities not mentioned	First report of 1,450-nm diode laser for the treatment of inflammatory facial acne
Glaich et al. <sup>63</sup> (15)	Mild to moderate (face)	Combination of 595-nm PDL and 1,450-nm diode laser (3)	Mean lesion counts reduced by 52% (one treatment), 63% (two treatments), and 84% (three treatments); patient satisfaction high	Mild, transient erythema, edema	Patient evaluations included; patients well characterized	Patients continued topical and oral antiacne medications during study; no controls; no mention of comorbidities	Introduced the sequential combination of 595-nm PDL and 1,450-nm diode laser for the treatment of acne

KTP, potassium titanium phosphate; PDL, pulsed dye laser.

### *Case Series Studies*

**PDL** In an early study of ALA PDT, Itoh and colleagues<sup>75</sup> used ALA PDT to treat a single facial lesion of a patient with intractable acne. They allowed ALA to remain in contact with the lesion for 4 hours before irradiation with a 630-nm PDL. The treated lesion was resolved with a single treatment and did not recur for at least 8 months.

**IPL** Gold and colleagues<sup>76</sup> were the first to use IPL for ALA-PDT for acne and demonstrated its effectiveness. In a subsequent randomized study of patients with moderate to severe acne, the author compared IPL, blue light, and electrico-optical synergy (ELOS) devices as activators in ALA PDT.<sup>77</sup> Acne grade and lesion count data showed approximately 70, 50, and 30% improvement associated with activation by IPL, ELOS, and blue light, respectively.

**ELOS** Taub<sup>78</sup> confirmed the efficacy of short-contact ALA for patients with moderate to severe refractory acne and showed that ELOS technology was effective. The results of these studies culminated in a consensus recommendation for the treatment of acne:<sup>28</sup> "American Panel members agreed that ALA PDT provides (1) the best results when used to treat inflammatory and cystic acne and (2) modest clearance when used to treat comedonal acne (although recent data shows that ALA PDT was effective against comedonal acne when the long-pulsed pulsed dye laser is used<sup>73</sup>). They also agreed that (1) acneiform flares may occur after any treatment, including ALA PDT, and (2) although not supported by extensive documentation, PDL activation provides the best results in ALA PDT for acne. One member (Dr. Nestor) stated that only PDL with ALA PDT has maintained clearance of acne lesions for up to two years, even in patients resistant to other treatments." (To the author's knowledge, Dr. Nestor's data have not been published.)

### **PDT with MAL**

*Randomized Controlled Trial, Investigator Blinded*  
In a recent study of MAL PDT in acne treatment,

significant reductions in sebum excretion and bacterial indicators were not associated with clinical efficacy.<sup>79</sup> The data are shown in Table 4. Wiegell and Wulf<sup>79</sup> proposed that the mode of action of PDT may be more complex than that suggested by Hongcharu and colleagues.

### **PDT with Indocyanine Green**

#### *Controlled Trial*

**Diode Laser** The use of indocyanine green (ICG) in combination with an 803- to 810-nm diode laser has been reported by three groups.<sup>80–82</sup> ICG is a photosensitizing dye used to evaluate hepatic function, blood volume, and cardiac output.<sup>81,83</sup> In a complex, multifaceted study, Tuchin and colleagues<sup>82</sup> reported that multiple treatments yielded more favorable results than a single treatment and attributed the efficacy to bacterial suppression.<sup>83</sup>

#### *Case Series Studies*

**Near-Infrared Diode Laser** Lloyd and Mirkov<sup>80</sup> evaluated the effect of long pulse, 810-nm diode laser (Cynosure, Inc., Westford, MA) energy on enlarged sebaceous glands of a single patient preloaded with ICG. After confirming penetration of ICG into the enlarged gland, the authors performed a laser-tissue interaction analysis to determine the appropriate treatment parameters to selectively damage the enlarged ICG-loaded glands. After finding that laser energy of 810 nm, 50-ms pulse duration, 40 J/cm<sup>2</sup>, and 4-mm spot size was required, they applied an ICG microemulsion to 10 sites on the backs of patients with active acne, covered the areas with occlusive dressing for 24 hours, cleansed the areas, and treated them with the laser. Fluorescence microscopy and histologic studies of the treated areas revealed selective necrosis of the targeted glands, whereas clinical observations and serial photographs showed an improvement in acne at the treated area at 3, 6, and 10 months after the treatment. The authors concluded that the diode laser had selectively and safely damaged enlarged sebaceous glands.



TABLE 4. Reports Evaluating the Efficacy and Safety of PDT for Acne Vulgaris

Reference (number of patients)	Acne type (location)	Hours ALA or MAL incubation (number of treatments)	Light source	Efficacy	Adverse effects	Strengths	Limitations	Significance of study
<i>Randomized controlled trial, investigator blinded</i>								
Wiegell et al. <sup>79</sup> (36)	Moderate to se- vere (face)	3 MAL (1-2a)	Red	68% reduction in inflammatory lesion count; no reduction in noninflamma- tory lesion count vs. no changes in control group 12 weeks post- treatment	Moderate to severe pain during treat- ment; severe erythema, pustular eruptions, epithelial ex- foliation	Randomized, blinded assess- ment, controls, patients re- ceived no con- current medica- tions; reported PpIX fluores- cence	No information regarding possible co- morbidities that might have influ- enced out- comes	First blinded, random- ized, controlled study on use of MAL PDT for the treatment of mod- erate to severe acne vulgaris
<i>Randomized controlled trial, evaluator blinded</i>								
Hongcharu et al. <sup>70</sup> (23)	Mild to moder- ate (back)	3 (ALA) (1, 4)	550–700 nm (red)	Statistically signif- icant clearance (1) for 10 weeks after a single treatment and (2) for 20 weeks after four weekly treat- ments	Significant; temporary erythema, edema, itch- ing hyper- pigmenta- tion (up to 20 weeks posttreat- ment), su- perficial ex- foliation, crusting; pain, burn- ing during treatment	Randomized, blinded assess- ment, controls, patients re- ceived no con- current medica- tions; studied effect of ALA PDT on sebum secretion, seba- ceous gland, and <i>P. acnes</i> .	No patient-as- sessed out- comes, no clear state- ment of co- morbidities that might have influ- enced out- comes	First to present clinical, microbiologic and histologic evidence that ALA PDT with red light activation was effective against inflamma- tory acne
<i>Randomized controlled trial</i>								
Pollock et al. <sup>71</sup> (10)	Mild to moder- ate (back)	3 ALA (3)	635 nm (red, laser)	Significant reduc- tion in inflam- matory lesion counts with ALA PDT (3 weeks post- treatment)	Burning during treatment; erythema; mild perifol- licular erup- tion; postin- flammatory pigmenta- tion	Randomized, blinded assess- ment, controls, patients re- ceived no con- current medica- tions	Severity of acne lesions not graded	Suggested that ALA PDT mechanism may be more com- plex than PDT-in- duced injury to sebaceous glands, photodynamic kill- ing of <i>P. acnes</i> , and reduction of follicu- lar obstruction by altered keratinocyte shedding and hyperkeratosis

TABLE 4. Continued

Reference (number of patients)	Acne type or severity (location)	Hours ALA or MAL incubation (number of treatments)	Light source	Efficacy	Adverse effects	Strengths	Limitations	Significance of study
<i>Controlled trials</i>								
Goldman and Boyce <sup>72</sup> (22)	Mild to moderate (face)	0.25 ALA (2)	417 nm (blue)	Improvement in severity and reduction in papule count with ALA PDT (blue light) > blue light alone (2 weeks post- treatment)	None serious; erythema af- ter posttreat- ment sun exposure	Controls included, patients re- ceived no con- current medica- tions	No randomiza- tion or blind- ed assess- ment; short follow-up time	Shown that ALA PDT with blue light is more effective against mild to moderate acne than blue light alone. This was the first study to limit ALA incubation time to 1 hr for the photody- namic treatment of acne
Santos et al. <sup>74</sup> (15)	Various degrees (face)	3 ALA (2)	IPL (560-nm cutoff)	Significant reduc- tion in new le- sion formation in 10/13 pa- tients on ALA PDT (IPL)-treat- ed side of face vs. nonsignifi- cant reduction in IPL-treated side (6 weeks after second treatment)	Stinging, burn- ing during treatment; posttreat- ment ede- matous ery- thema; crusting with exfolia- tion	Split-face study, controls includ- ed, patients re- ceived no concurrent medications	No randomiza- tion or blind- ed assess- ment	Confirmed that IPL was an effective activator of ALA for acne with split-face control
Alexiades- Armen- akas <sup>73</sup> (19)	Mild to se- vere (face)	0.75 ALA (1–6)	LP PDL (595 nm)	Complete clear- ance in all pa- tients (1–13 months post- treatment) with mean of 2.9 treatments	Minimal ery- thema	Comprehensive study with con- trols; results analyzed in de- tail	No randomiza- tion, blinded assessment; patients re- ceived con- current medi- cations	First to use LP PDL for acne, introduced idea LPPDL may be superior light source for ALA PDT for acne

Table 4. Continued

Reference (number of patients)	Acne type (location)	Hours ALA or MAL incubation (number of treatments)	Light source	Efficacy	Adverse effects	Strengths	Limitations	Significance of study
<i>Case series studies</i>								
Itoh et al. <sup>75</sup> (13)	Intractable (face)	4 ALA (1)	600–700 nm (halogen)	reduction of new lesions 1, 3, and 6 months posttreatment	Burning during treatment; edematous erythema, exfoliation, irritation, hypersensitivity to physical stimulation	Patients received no concurrent medications	No randomization, blinded assessment, or controls	Showed efficacy of single ALA PDT treatment, used noncoherent light for activation
Gold et al. <sup>76</sup> (20)	Moderate to severe (face)	1 ALA (4)	IPL + heat	50, 68, and 72% reduction in lesion count at end of final treatment, 4 weeks posttreatment, respectively; no recurrences	None	Patients received no concurrent medications	No randomization, blinded assessment, or controls	Introduced IPL device for ALA PDT activation in treatment of acne
Taub <sup>78</sup> (18)	Moderate to severe (face, chest, back)	0.25–0.5 ALA (2–4)	417–420 nm (blue) or 580–1,000 nm with RF ELOS	1.75 mean improvement (1–4 scale) at 4-month follow-up	Erythema, peeling; impetiginization in one patient	Long follow-up time, data presented in detail, treated acne at multiple locations, patients received no concurrent medications	No randomization, blinded assessment, or controls	First study to use ELOS to activate ALA-induced PpIX for the photodynamic treatment of acne; confirmed efficacy of short-contact ALA PDT in acne

PDT, photodynamic therapy; ALA, 5-aminolevulinic acid; MAL, methyl aminolevulinate; PDL, pulsed dye laser; IPL, intense pulsed light; LP, long-pulsed; RF, radiofrequency; ELOS, electrodynamical optical synergy.

In a similar study, Genina and colleagues<sup>81</sup> reported that the ICG-diode laser protocol provided the best results in patients with moderate to severe acne. The consistent results of these studies support the conclusion that the ICG-diode laser is a valid option for the treatment of moderate to severe acne.

### Summary of PDT

The versatility of PDT and the emergence of short-acting photosensitizing agents that can be applied to skin before activation by light or laser devices has “revolutionized” the treatment of acne vulgaris and other cosmetic dermatologic conditions. The use of short (0.25–1-hr) incubation times and multiple treatment sessions provides optimal clinical efficacy and patient compliance, even in cases of recalcitrant acne. Adverse effects include temporary edema and erythema and occasional vesiculation and hyperpigmentation.<sup>84</sup>

Although the efficacy of PDT in the treatment of acne has been established, the mechanism is not completely understood. Clinical data have been correlated with changes in sebum excretion,<sup>70</sup> damage to sebaceous glands,<sup>70,75</sup> posttreatment recovery of sebaceous glands,<sup>75</sup> *P. acnes* levels,<sup>70</sup> and PpIX fluorescence.<sup>79</sup> Hongcharu and colleagues<sup>70</sup> suggested that topical ALA PDT may (1) inhibit sebum secretion by injuring sebaceous glands, (2) sterilize sebaceous follicles by killing *P. acnes*, and (3) reduce follicular obstruction by altering keratinocyte shedding and hyperkeratosis.

Even with this wealth of studies demonstrating a marked effectiveness of PDT for the treatment of even mild to severe refractory acne, there is still a need for randomized, blinded, placebo-controlled studies leading to an FDA approval of ALA and MAL in the photodynamic treatment of acne to increase the acceptance of PDT as a viable alternative to isotretinoin. Understanding the mode of action of ALA PDT in the treatment of acne may shed light on the role of sebum excretion, *P. acnes*, hair follicles, and other factors in the pathogenesis of acne itself.

### Radiofrequency

Radiofrequency (RF) energy is a relatively new treatment modality in aesthetic medicine. The thermal effects of RF energy depend on the electrical properties of tissue. A high-frequency RF current directed at tissue produces heat which, for a given current density, increases with the impedance of the tissue.<sup>85</sup> RF is currently used in two nonablative devices investigated for the treatment of acne [Thermacool (Thermage, Inc. Hayward, CA), which delivers monopolar RF energy; and Aurora AC (Syneron Medical Ltd, Yokneam, Israel), which uses bipolar RF in addition to blue light].<sup>85,86</sup>

**Case Series Studies** In the first report on the use of RF energy (Thermacool) for the treatment of moderate to severe acne (Table 5),<sup>87</sup> most patients received a single treatment and were followed up to 8 months. Effects due to RF alone are not clear, however, because 9 of the 22 patients received medical therapies for acne during the RF treatment period. The authors obtained encouraging results, however, and suggested that the responses are due to inhibition of sebaceous gland activity by RF-produced heat.

Prieto and colleagues<sup>88</sup> (Table 5) evaluated the efficacy and safety of the Aurora AC (Syneron Medical Ltd), a device that delivers pulsed blue light and RF energies by ELOS, a proprietary technology that purports to cause (1) destruction of bacterial porphyrins by pulsed light and (2) sebaceous gland thermolysis by both light and RF energy.<sup>86,88</sup> An eight-treatment course (twice weekly for 4 weeks) resulted in reductions in (1) lesion count, (2) percentage of follicles with perifolliculitis, and (3) areas of sebaceous glands.

The results of both studies suggest that RF is a promising nonablative alternative for the treatment of acne. Too little information is available to be able to comment on effective protocols, duration of effect, or reproducibility of results. Randomized, placebo-controlled investigations are required to confirm these results.

TABLE 5. Reports (Case Series Studies) Evaluating the Efficacy and Safety of RF Devices for Acne Vulgaris

Reference (number of patients)	Acne type or severity (location)	Device (number of treatments)	Efficacy	Adverse effects	Strengths	Limitations	Significance of study
Ruiz-Esparza and Gomez <sup>87</sup> (22)	Moderate to severe active, cystic, scarring acne (face)	Thermacool TC (1–3) 6 MHz RF energy delivered with current cooling during treatment (Thermage, Inc., Hayward, CA)	≥ 75% reduction in active lesion counts in most patients, high patient satisfaction	None reported	Conclusions based on pre- and post-treatment lesion counts, photographs showing dramatic improvement, and patient satisfaction; treatment end point specified	No clear statement of comorbidities that might have influenced outcomes, no microbiologic or histologic evidence, no randomization, blinded assessment, or controls; 9 patients taking concomitant medical therapy	First to present acne-specific outcomes for RF treatment
Prieto et al. <sup>88</sup> (32)	Moderate papulopustular acne (face)	Aurora AC (8): 400- to 980-nm pulsed light + bipolar RF ELOS (Syneron Medical Ltd., Yokneam, Israel)	47% mean reduction in lesion count	Mild erythema, first degree burns (n = 3) resolved in 1 week	Patients received no antiacne medications; simple numeric grading system for patient evaluations; histologic and immunohistochemical studies of sebaceous glands, epidermal and dermal structures	High dropout rate (25%), no clear statement of comorbidities that might have influenced outcomes; no randomization, blinded assessment, or controls; short follow-up time	First to present acne-specific outcomes for RF-pulsed light with ELOS technology

RF, radiofrequency; ELOS, electro-optical synergy.

## Conclusion

Many procedural treatments for acne are available now for both adjunctive use and as alternatives to pharmacologic therapies. Advances in technology and concern regarding adverse effects from medications are driving these changes. Whereas older procedures such as comedone extraction and intralesional steroids continue to be used in daily practice, superficial chemical peels have become standard adjunctive practice. Both salicylic acid- and glycolic acid-based peels show definite results for inflammatory and comedonal acne and are safe for use in darker skin types. Blue and blue/red light therapies have a significant body of literature showing efficacy but lack long-term follow-up. This treatment may be limited by the need for frequent and time-consuming, albeit painless, maintenance procedures, although longer term studies may clarify this issue. Radiofrequency seems promising but there is a very small body of work to depend on. Laser with 1,450-nm diode, ICG-diode PDT, and MAL- or ALA-assisted PDT with light or laser sources have the most literature to confirm their efficacy as treatments for moderate to severe acne that may produce long-term results. This comprehensive review of these procedures will hopefully provide a starting point for physicians seeking to treat their acne patients utilizing technical innovations that are the safest and most effective methods. This field is very early in its development, although it appears that having a profound effect on the sebaceous gland may be necessary to achieve long-term remission. A better understanding of the evidence thus far may lead to better-designed studies that might elucidate the underlying factors necessary to achieve a long-term result for acne patients.

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