Photodynamic Therapy: Practical Cosmetic Applications

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Abstract
Photodynamic therapy (PDT) has been used in the treatment of a variety of benign and malignant cutaneous conditions. More recently, it has been used to enhance the results of skin rejuvenation procedures. The purpose of this article is to review the current practical applications of PDT in a cosmetic practice.

Introduction
The versatility of photodynamic therapy (PDT) has rendered it an indispensable treatment modality in the dermatology practice. While long used to treat cancerous and precancerous cutaneous lesions, the development of short-acting photosensitizing solutions that can be applied to the skin prior to their activation by laser or light has revolutionized the outpatient treatment of a wide variety of common cosmetic dermatologic concerns, including acne vulgaris, rosacea, sebaceous hyperplasia, photodamage (dyspigmentation/poikiloderma), and actinic cheilitis.

The photodynamic therapeutic process involves the topical application of 5-aminolevulinic acid (5-ALA), which is the precursor molecule in the heme biosynthesis pathway from which protoporphyrin IX (PpIX) is formed after several enzymatic reactions. In the US, exogenous 5-ALA is available as Levulan Kerastick® (DUSA Pharmaceuticals, Wilmington, MA). Topical application of 5-ALA penetrates the epidermis and is then converted to PpIX, a photosensitizing molecule with preferential formation and accumulation in tissues known to have a high cellular turnover, such as tumor or photodamaged cells. When PpIX is photoactivated by an appropriate laser or light source, reactive oxygen species (ROS) are produced which are toxic to epidermal cells, causing cell lysis. Clinically, erythema and desquamation ensue with the eventual appearance of smoother skin.

The absorption spectrum of PpIX allows for a wide range of electromagnetic radiation options within the visible spectrum. Thus, many different light sources can be effectively used to activate the product, including those that emit blue (410 nm), yellow (595 nm), or red (630 nm) light, each of which corresponds to different PpIX absorption peaks.

Initial topical 5-ALA treatment protocols required 2 separate office appointments to accommodate overnight incubation of the product (chemotherapeutic models have indicated maximum penetration of the sensitizing agent and production of PpIX at 18 hours). Subsequent trials using shorter incubation times (1 to 3 hours) demonstrated equivalent clinical efficacy as longer incubations in the treatment of a variety of photoinduced conditions. As such, current treatment protocols involve a single therapeutic appointment to accommodate product application and its light activation.

Cosmetic Applications
Acne Vulgaris
The inflammatory papules and pustules seen in acne vulgaris result from a combination of keratin, sebum, and Propionibacterium acnes that leads to the release of proinflammatory mediators and the accumulation of lymphocytes and foreign body giant cells. Endogenous (P. acnes-derived coproporphyrins and protoporphyrins) and exogenous photosensitizers can be targeted by continuous wave (CW) and pulsed light systems and lasers. The preferential accumulation of 5-ALA in the pilosebaceous unit, particularly the sebaceous gland, makes treatment of acne with PDT a natural. Reduction of acneiform lesions have been shown after both short and long 5-ALA incubation. While improved acne reduction is observed with relatively long (>3 hours) 5-ALA application, the risk of edema, crusting, and dyspigmentation is higher. In practice, the use of short incubation times (1 hour) and multiple treatment sessions optimize patient compliance and clinical efficacy.

For those patients whose acne has been recalcitrant to various topical and oral therapies, including antibiotics and retinoids, or for those who are noncompliant with at-home regimens, in-office short-contact PDT offers a viable treatment alternative. In addition, the side effect profile of oral isotretinoin, as well as the challenges associated with its successful administration, render PDT a more practical choice.

Several published reports and studies have demonstrated the efficacy of PDT for acne vulgaris. Treatment regimens have varied in incubation times, treatment intervals, and laser/light sources used. Three different approaches are generally advocated:

1. Short-contact (1 hour) 5-ALA with 410-nm blue light (5 to 10 J/cm²) at weekly time intervals.
2. Short-contact 5-ALA with 595-nm pulsed-dye laser (PDL) irradiation (10-mm spot, 7 to 7.5 J/cm²) at monthly time intervals.
3. Short-contact 5-ALA with intense pulsed light (IPL, 550-nm filter) every 2 to 4 weeks (24 to 32 J/cm², double-pulse 2.4 ms/4.0 ms, 10-s to 20-s delay).

Clinical results using any of these treatment regimens are similar, although no comparative studies have been performed. Side effects are generally limited to transient erythema and edema and, less frequently, hyperpigmentation and vesiculation. Multiple treatments tend to be necessary for more complete and prolonged acne clearance.

Rosacea
PDT is also an effective treatment for rosacea in patients who have demonstrated resistance to topical and oral therapies.
Short-contact (15-minute) 5-ALA application with 595-nm PDL irradiation at fluences averaging 6 J/cm² and pulse durations of 40 ms at biweekly time intervals has been shown to reduce the clinical signs and symptoms of acne rosacea without evidence of recurrence. In addition to its known effects on acneiform papules and pustules as described above for acne vulgaris, the use of vascular-specific laser and light systems (PDL or IPL) for ALA activation has an additional benefit in that selective occlusion of abnormal dermal capillaries seen in rosacea is effected.

**Sebaceous Gland Hyperplasia**

Sebaceous gland hyperplasia is common in persons with a history of chronic sun exposure and is clinically significant when the benign proliferation of sebaceous glands (manifested as 2-mm to 4-mm diameter yellowish papules) collect in large numbers on the face (the predominant location). Treatment of sebaceous gland hyperplasia with topical retinoids has proven to be ineffective in the long run, while the use of cryotherapy, excision, electrodessication, and isotretinoin has been associated with recurrence and less desirable cosmesis. Recently, interest has been shown in the use of PDT as an effective form of therapy for sebaceous gland hyperplasia. This is not surprising since topical 5-ALA converts to PpIX in sebaceous glands. Additionally, PDL treatment of sebaceous hyperplasia has been individually championed as a therapeutic option. Thus, it would be expected that sebaceous gland lesions would be highly sensitive to treatment with PDL-assisted PDT.

**Figure 1a-b.** Antibiotic and topical retinoid recalcitrant acne vulgaris before (Figure 1a-b) and after 3 PDT treatments (20% 5-ALA incubation x 1 hour, IPL 28 J/cm², 550-nm filter, double-pulse 2.4 ms/4.0 ms, 20-s delay). No recurrence was noted 6 months after treatment (no concomitant topical treatment).

**Figure 2a-b.** Acne rosacea in a 52-year-old woman previously unresponsive to traditional topical and oral therapy. Clinical improvement was evident 3 months after 2 successive monthly PDT treatments (1 hour 5-ALA incubation, 595-nm PDL, 6 J/cm², 10 ms, 10-mm spot).
The successful use of PDT for sebaceous gland hyperplasia has been supported by several clinical studies. In one study, sebaceous lesions received topical 20% 5-ALA incubation for 1 hour, followed by irradiation with a 595-nm PDL at 7.0 J/cm² and 6-ms pulse duration using a double-stacking technique with a 7-mm spot size. Several matched lesions in the study patients were either left untreated or received PDL treatment alone to serve as controls. Repeated treatments were delivered after 6 weeks in those cases of incomplete lesional eradication. Using the short-contact ALA-PDL treatment protocol, most lesions resolved after a single treatment and the remainder resolved after 2 treatments.

In another study, patients with sebaceous gland hyperplasia were randomly selected to receive 4 consecutive monthly treatments using short-contact 5-ALA (30 or 60 minutes), followed by a 15-minute treatment with 405-nm to 420-nm blue light (Clearlight™, Lumenis, Inc) or treatment with 500-nm to 1200-nm IPL source (VascuLight™, Lumenis, Inc) with a 550-nm cut-off filter (32 J/cm² fluence, 3.5-ms pulse duration, 20-ms pulse delay). Follow-up patient evaluations at 4 months showed 50.6% lesional reduction in those treated with blue light and 48.4% lesional reduction in those receiving IPL treatment.

Short-contact PDT has several advantages to traditional treatments for sebaceous gland hyperplasia. It is fast and highly effective with relatively few treatment sessions required to ameliorate the majority of lesions encountered. The ease and relatively painless nature of the treatment permits expeditious treatment of large numbers of lesions. In addition to an improved cosmetic outcome, postoperative recovery is limited to transient erythema and edema.

**Photodamaged Skin**

Various lasers and light sources have been used to reduce the rough texture, dyspigmentation, telangiectasia, and loss of elasticity associated with photodamaged skin. The additional use of topical ALA has recently been shown in several comparison studies to enhance the effectiveness of laser and light treatment for these conditions.

In the first published study using short-contact (1 to 3 hours) ALA, 18 patients with facial actinic keratoses and mild to moderate diffuse facial photodamage were treated with 10 J/cm² of blue light. Randomly assigned facial halves were also pretreated with 40% urea cream daily for 1 week prior to PDT treatment. All patients showed reduction in the actinic keratoses as well as significant improvement of several photodamage parameters. Different ALA incubation times and urea cream application had no significant effect on the clinical results.

In a split-face study involving 10 patients with mild to moderate cutaneous photodamage, facial halves were randomly assigned treatment with combined ALA-IPL (1-hour incubation) or IPL alone (mean fluence 30 J/cm², double pulse 2.4 ms/4.0 ms, 10-ms delay). Two treatments were delivered at 4-week time intervals and patients were followed for 6 months. Higher clinical improvement scores were noted in the combination ALA-IPL treated areas.

Two similar studies were conducted using a series of 3 split-face treatments at 3- to 4-week intervals in which facial halves were pretreated with 5-ALA (30- to 60-minute application) followed by IPL and the contralateral halves were treated with IPL alone. The combination ALA-IPL treated facial halves showed greater improvement in mottled pigmentation and fine lines than those treated with IPL alone, once again confirming the usefulness of ALA-PDT in photorejuvenation.

**Actinic Cheilitis**

Actinic cheilitis affects 5% of individuals over the age of 40 and is of concern because of its propensity to undergo malignant transformation with an 11% to 13% metastastic...
risk. Patients often seek treatment because of its associated fissuring, bleeding, crusting, and erosions. While several treatments, including cryotherapy, carbon dioxide laser vaporization, surgical excision, various topical retinoids, 5-fluorouracil, and immunomodulators have been used to effectively treat actinic cheilitis, each has also produced long recovery times and poor immediate posttreatment cosmesis. Most recently, PDT has been proffered as a more reasonable and effective treatment alternative for this condition.

In one published report, PDT was used to treat 3 patients with recalcitrant actinic cheilitis. The patients had each been treated previously with cryotherapy, carbon dioxide laser, various topical treatments (including 5-fluorouracil and retinoids), and excision. Topical 20% 5-ALA was applied to the lips under occlusion for 3 hours, followed by 30-minute exposure to a common slide projector light (55 J/cm², 80,000 lux). The treatment was repeated 3 times at 1-month intervals. Patients experienced burning for 2 to 4 days, followed by peeling which lasted for one to several months. Total resolution of the condition was noted in all patients without recurrence at 6 to 12 months follow-up.

Another study involved the use of 5-ALA (2- to 3-hour incubation) with PDL (595-nm, 7.5 J/cm², 10-ms pulse, 10-mm spot) to treat 19 patients with actinic cheilitis.

Figure 4a-b. Photodamaged facial skin showing mottled pigmentation and fine rhytides before and 6 months after 3 successive monthly PDT treatments (5-ALA incubation x 1 hour, IPL 30 J/cm², double pulse 2.4 ms/4.0 ms, 10-ms delay) showing marked global aesthetic improvement.

Figure 5a-b. Immunosuppressed patient with actinic cheilitis recalcitrant to carbon dioxide laser vaporization, cryotherapy, excision, and topical retinoids. Twelve months after one PDT treatment (3-hour ALA incubation, 595-nm PDL, 7.5 J/cm², 10-ms pulse, 10-mm spot, double-pass), no lesional recurrence was observed.
refractive to prior therapies.\textsuperscript{20} Patients received 1 to 3 treatments at monthly intervals with regular follow-up for 12 months. Complete lesional clearance was achieved in 13 of the 19 patients, while 2 patients achieved partial clearing, 1 patient experienced recurrence, and 3 were lost to follow-up. Posttreatment side effects included transient localized erythema in all patients and impetiginization in 3 patients with ulcerative cheilitis which resolved after a course oral antibiotics.

**Summary**

PDT has become an important cornerstone of dermatologic treatment. Dermatologists have embraced and furthered the technology, including identifying a variety of clinical conditions in which PDT has high efficacy and distinct advantages to traditional therapies. One of the most significant advancements of PDT has been the development of short-contact 5-ALA protocols and the identification of specific laser/light systems that enhance the photochemical-photothermal effect. Given its ease of delivery, applicability to a wide array of dermatologic concerns, and high safety profile, the popularity of PDT is rising. In a cosmetic dermatology practice, the treatment of acne vulgaris, rosacea, sebaceous gland hyperplasia, cutaneous photodamage, and actinic cheilitis with PDT is particularly useful. Since many dermatologists have access to at least one laser or light source, the addition of PDT as a therapeutic modality can reasonably be incorporated into practice.

**References**


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