

ORIGINAL ARTICLE

## Evaluation of pulsed light and radiofrequency combined for the treatment of acne vulgaris with histologic analysis of facial skin biopsies

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### Abstract

**Background.** Light and radiofrequency (RF) devices have recently been used to treat acne in selected patients.

**Objective.** To investigate the safety and efficacy of a combination of pulsed light and RF energy for the treatment of acne.

**Materials and methods.** Thirty-two patients with moderate acne were treated twice weekly for four weeks with the Aurora AC<sup>®</sup> (Syneron Medical Ltd, Yokneam, Israel), a combination of pulsed light and RF energy. Twenty-five patients completed the study. In four patients, the number of hair follicles showing perifolliculitis, the diameters of hair follicles, the diameters of sebaceous glands, and expressions of heat shock protein 70 and procollagen-1 were evaluated before and after treatment.

**Results.** The mean lesion count was reduced by 47% ( $p < 0.05$ ) after eight treatments. Adverse effects—erythema, tingling, and burning—were mild and temporary. The percentage of follicles with perifolliculitis decreased from 58% to 33%, sebaceous gland areas decreased from 0.092 mm<sup>2</sup> to 0.07 mm<sup>2</sup>, and heat shock protein 70 and procollagen-1 expressions did not change.

**Conclusion.** The combination of optical and RF energies may be an alternative nonablative modality for the treatment of moderate acne. Clinical improvement may be partly due to reductions in both perifollicular inflammation and sebaceous gland areas.

**Key words:** Acne, ELOS, laser, pulsed light, RF

### Introduction

Acne vulgaris remains a significant problem for adolescents and adults. In the United States, 85% of persons aged 24 years and younger, and 11% of persons aged 25–44 years, have acne (1,2). Acne commonly starts in adolescence when hormonal changes trigger enlargement of the sebaceous glands and increase sebum production. The pathogenesis is believed to involve sebaceous hyperplasia, follicular hyperkeratinization, proliferation of *Propionibacterium acnes*, inflammation, and immune reactions (3).

While many therapies are available for acne, patients may experience side effects, particularly with combination therapies, or may not respond to any treatment. Bacterial resistance to antibiotics is also a concern. Current topical treatments of acne include antibiotics, benzoyl peroxide, retinoids, sulfur, and (alpha and beta) hydroxy acid derivatives. Systemic (oral) therapies—antibiotics and

isotretinoin—may be prescribed when topical treatments are not effective. Systemic treatments are most often used for severe nodulocystic acne and have been associated with toxicity.

Recently noninvasive light and laser devices have been shown to reduce acne lesion counts with fewer side effects, particularly in patients not responding to commonly prescribed methods (4–12). By an unknown mechanism, these light devices may decrease the size of the sebaceous glands, decrease pilosebaceous inflammation, and diminish populations of *Demodex* and *Propionibacterium* species (4–6,8,13–30).

We report our clinical experience with a new nonablative combination of pulsed light and radiofrequency (RF) energies that relies on electro-optical synergy (ELOS<sup>TM</sup>) to treat moderate acne. We also report our histologic and immunohistochemical findings associated with the use of this technology.

Table I. Average inflammatory lesion counts at baseline and follow-up.

<i>n</i> =25	Average inflammatory lesion count	Average reduction in lesion count (%)	Patients with mild ( $\leq 10$ lesions) papulopustular acne (%)	Patients with moderate papulopustular acne (%)
Baseline	31 ( $\pm 14$ )	0%	0%	100%
Follow-up	16 ( $\pm 10$ )	47%	36%	64%

## Materials and methods

Thirty-two patients (23 females, Fitzpatrick skin types I–VI, aged 16 years and older) with moderate papulopustular acne (31) were enrolled. Patients received no medications during the treatment and follow-up periods and had received no acne-related medication (topical or systemic) for five weeks, or systemic isotretinoin for six months before enrollment. Persons who were pregnant, breast-feeding, photosensitive, had diabetes (Type I or II), or were taking oral medication known to induce photosensitivity were excluded. All research documents were approved by the Essex Institutional Review Board. Informed consent forms were obtained from each patient before enrollment.

Patients were treated twice weekly for four weeks on the face with the Aurora AC<sup>®</sup> (Syneron Medical Ltd, Yokneam, Israel), a combination of pulsed light (400–980 nm) and conducted RF. Responses were evaluated two to four weeks after the final treatment. Optical fluences varied according to Fitzpatrick skin type. After an initial treatment with 6 J/cm<sup>2</sup>, optical fluences were increased gradually with successive treatments to a maximum of 10 J/cm<sup>2</sup> (8–10 J/cm<sup>2</sup>) for skin types I–IV and a maximum of 8 J/cm<sup>2</sup> for skin types V and VI (6–8 J/cm<sup>2</sup>), according to recommendations from the manufacturer. All patients were treated with 15–20 J/cm<sup>3</sup> RF energy. Skin was hydrated with a water-based gel before treatment.

Patients recorded potential adverse effects (hyperpigmentation, erythema, edema, blisters, crusting, pain) for 14 days after the initial treatment. Adverse effects were verified and assessed for severity at each treatment session. Patients rated their individual overall improvements according to the following scale: 1=mild or none, 2=good, 3=very good, and 4=excellent.

To evaluate the histologic and immunohistochemical effects of treatment, 4 of the 32 patients with at least 20 inflamed, non-comedonal acne lesions (papules, pustules, nodules, cysts) were selected for biopsy. Three 2-mm punch biopsies were taken from the temple region in each patient—one specimen before the initial treatment, the second specimen one week later, and the third specimen one month later. Biopsy specimens were fixed in buffered formalin and embedded in paraffin. Five-micron sections were stained with hematoxylin, eosin, von Gieson (for visualizing elastic tissue), reticulin (for visualizing reticulin fibers), and Trichrome Masson (for

visualizing collagen fibers). Each specimen was evaluated for the number of hair follicles showing perifolliculitis, the diameter of hair follicles, and the diameter of sebaceous glands.

Expressions of heat shock protein (hsp-70) and procollagen-1 (pc-1) were measured by immunohistochemistry using standard technique (32). Slides were deparaffinized and treated for antigen retrieval by incubation in citrate buffer. Treated slides were heated in a microwave device for 1 minute at full power and for 14 minutes at 30% power. Slides were then incubated overnight at 4 °C with a monoclonal antibody (Santa Cruz, Santa Cruz, CA) at 1:100 dilution. After incubation with the ABC complex, slides were lightly counterstained with hematoxylin and examined.

## Results

Among the 25 patients completing the 8-treatment protocol, the average overall reduction in lesion count was 47% ( $p < 0.05$ , Table I). Lesion counts did not change in two patients. Twenty-two patients were available for follow-up surveys to evaluate patient-reported improvement. Fifty-nine percent of patients rated their overall improvement as “good,” 32% as “very good,” 4.5% as “excellent,” and 4.5% as “none to mild”. Improvement in the forehead of one patient is shown in Figure 1.

Mild erythema occurred in 84% of patients (i) after the initial treatment and (ii) after treatment sessions in which optical light and RF fluences were increased. A mild heating sensation during treatment was noted in 31% of patients, especially when light and RF fluences were increased. First-degree facial burns occurred in three patients, and all resolved within one week without permanent sequelae.

Seven patients did not complete the study due to: unexpected pregnancy ( $n=1$ ), work schedule conflict ( $n=3$ ), noncompliance ( $n=2$ ), and personal reasons ( $n=1$ ).

Histologic examination of biopsy specimens showed a decrease in sebaceous gland areas and no morphologic damage to epidermal or dermal structures. Routine hematoxylin and eosin sections revealed the presence of perifollicular lymphocytic infiltrate in 7 of 12 follicles (58%), compared to only 2 of 6 (33%) follicles after the final biopsy, suggesting a trend toward lower percentages of follicles with perifolliculitis. A similar trend was

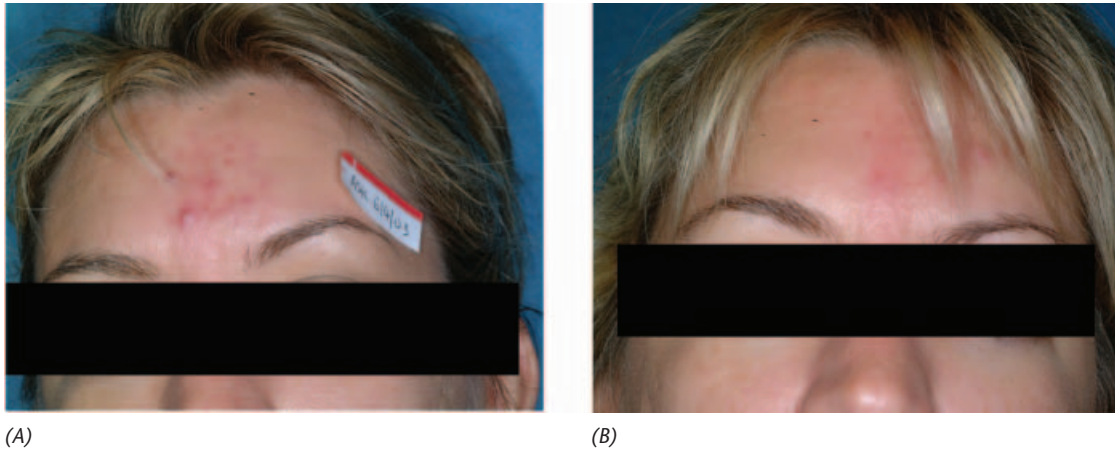


Figure 1. Pre- and post-treatment photographs. (A) Photograph taken at baseline. (B) Photograph taken at 14 days after final treatment.

observed in average areas of sebaceous glands— $0.092 \text{ mm}^2$  initially and  $0.070 \text{ mm}^2$  one month after treatment. Changes in sebaceous glands and inflammatory infiltrates are shown in Figure 2.

Special staining procedures did not reveal differences in the numbers or arrangement of elastic and

collagen fibers, nor damage to epithelial or vascular structures.

Expressions of hsp-70 and pc-1 were similar before and after treatment. Hsp-70 expression was apparent in the epidermal and adnexal keratinocytes (data not shown).

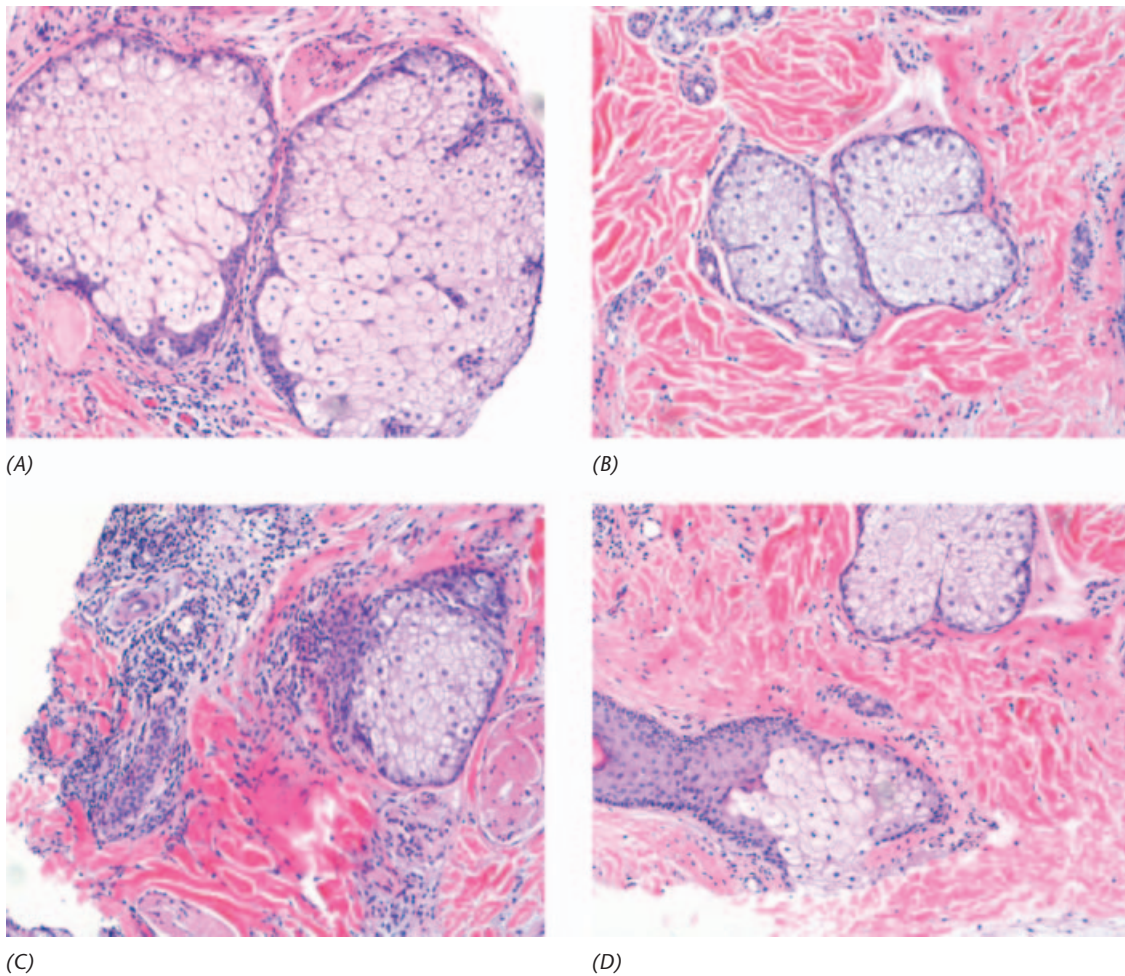


Figure 2. Histologic analysis of facial skin treated with a light and radiofrequency device. Pre-treatment biopsies show large sebaceous glands (A) and perifolliculitis (C). After treatment the size of the glands is reduced (B) and there is minimal inflammatory infiltrate (D). (A and C: pre-treatment biopsies; B and D: last follow-up biopsies. Hematoxylin and eosin, all images  $\times 20$ .)

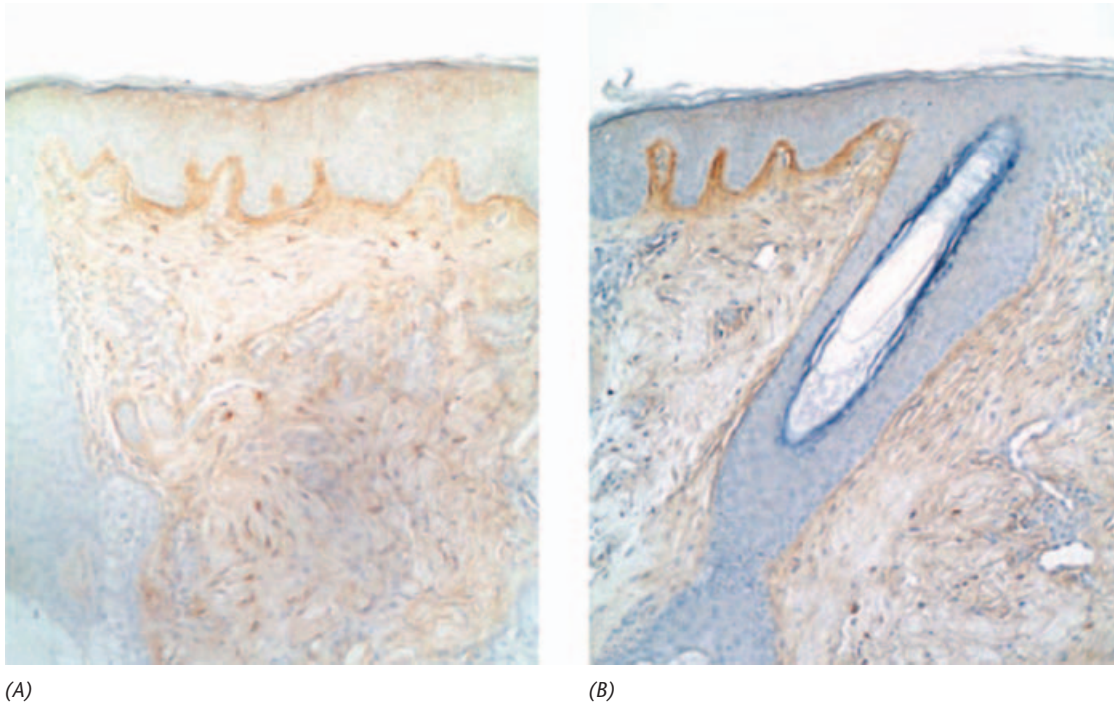


Figure 3. Expression of pro-collagen 1. Notice the expression of this pro-collagen protein mainly in the subepidermal region (A: pre-treatment; B: last follow-up biopsy. Anti-procollagen-1, diaminobencidine and light hematoxylin,  $\times 20$ ).

Expression of pc-1 was mainly seen in the subepidermal and periadnexal regions before and after treatment (Figure 3).

**Discussion**

Noninvasive treatment methods have improved dramatically over the past ten years. Laser and pulsed light technologies provide results with no ablation, down time, or skin injury. Most procedures focus on pigmented lesions, vascular lesions, skin texture, and fine lines, and most have been performed on noninflammatory skin (e.g., acne scars) (25,27). Lasers and light sources for treating inflammatory skin conditions such as acne have been developed recently. In addition, the efficacy of light, laser, RF and photodynamic therapies, as well as the mechanism by which light devices destroy acne, have been reported (4–12).

Released by *P. acnes*, porphyrins absorb light at specific wavelengths to form reactive oxygen species capable of destroying *P. acnes*. Optimum clearing of acne by this reaction depends on porphyrin concentration, photon concentration, photon emission wavelength, and temperature (11). Light devices also resolve acne lesions by selective photothermolysis of sebaceous glands implicated in the pathogenesis of acne (11,23,33). The absorption spectrum of a typical porphyrin, protoporphyrin IX (Figure 4), shows maximal absorption peaks at approximately 410 nm, but absorption bands are at 506, 532, 580, and 630 nm as well (34).

Light devices designed to treat acne include the Clearlight (405–420 nm, Curelight Ltd), iClear (405–420 nm, Curelight Ltd), BLU-U (405–420 nm, Dusa Pharmaceuticals), ClearTouch (pulsed light, visible and infrared; Radiancy, Inc.), and SmoothBeam (1450 nm, Candela, Inc.). Infrared lasers coagulate the sebaceous glands and reduce acne activity via water absorption. Monopolar RF electrical current has also been used to heat sebaceous glands to coagulation temperatures (10). RF energy interacts with tissue to produce heat by electric current rather than by absorption of photons. RF systems are therefore dependent on the electrical conductivity of the target tissues to create selective thermal injury. RF

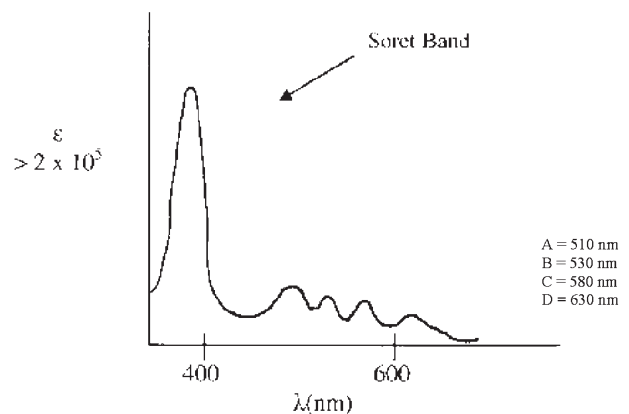


Figure 4. Absorption spectrum of protoporphyrin IX with maximum absorption at 405–420 nm and smaller bands at longer wavelengths.

energy is not scattered by tissue or absorbed by melanin.

The Aurora AC<sup>®</sup> uses a combination of pulsed light (400–980 nm) as its optical energy source and bipolar RF energy ranges from 6–18 J/cm<sup>2</sup> with 200-msec pulse duration. The spot size is 12 mm × 25 mm. The Aurora AC applicator combines visible and infrared light that affects *P. acnes* directly via photochemical activation of porphyrin. Selective photothermolysis of the sebaceous glands is brought about by two types of energy: optical (visible and infrared) and RF. The combination of the two energies allows the use of lower-pulsed optical energy, thus reducing the risk of superficial blisters, burns, pigmentation disorders, scarring, and downtime. The lower optical energy density is compensated for by the addition of RF energy to reach higher energies than that used by other light-based devices, and in a safer manner. As confirmed by histologic examination, our treatment resulted in no damage to epidermal or dermal structures.

Lasers emitting light at 1064, 1319, 1320, and 1450 nm have been shown to reduce inflammatory lesion counts and improve acne scars (4,17–19,24,26,28). Several pulsed light and combined pulsed light RF technologies have also been shown effective in this setting (8,10,14,23,35). These devices may act by decreasing the size of sebaceous glands. Increased collagen remodeling may also temporarily reduce the size of acne scars, decrease pilosebaceous inflammation, and temporarily diminish Demodex or bacterial colonization.

A device that delivers monopolar RF (ThermaCool, Thermage, Heyward, CA) has been also shown to be effective for treatment of cystic acne (10). Although unknown, the mechanism of action is likely that purported for both near infrared/infrared laser technologies.

Our data indicate that the use of a device combining pulsed light and RF does not result in visible morphologic damage to the epidermis or to dermal mesenchymal structures. The treatment appears to reduce both perifollicular lymphocytic infiltration and average areas of sebaceous glands, which may explain the clinical improvement observed in study patients. The absence of change in the expressions of hsp-70 and pc-1 suggests that collagen remodeling does not occur at the settings used in this study.

Few studies have analyzed the morphologic changes induced by laser devices applied to treat acne. The combination of a long-pulse diode laser with the indocyanine green chromophore results in necrosis of the sebaceous glands (35). The 1320 Nd:YAG reportedly induces increased dermal collagen in a number of cases (16). Also, a recent study (24) on both animal tissue (rabbit ear) and *ex vivo* skin reported that the laser-induced damage was mostly selective to the sebaceous glands.

Our results indicate that the Aurora AC<sup>®</sup> provides an alternative modality for the treatment of acne vulgaris. Further studies are in progress to determine the long-term benefits of this device as well as the potential differential effects on acne subtypes and differential treatment protocols for maximum benefit of this novel device.

## Conclusion

The combination of a pulsed light and an RF device (Aurora AC<sup>®</sup>) applied to inflammatory acne lesions results in clinically detectable improvement likely secondary to decrease in size of sebaceous glands and reduced perifollicular lymphocytic infiltrates, without apparent damage to nonsebaceous structures in the skin.

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