A SUPPLEMENT TO

JOURNAL OF DRUGS IN DERMATOLOGY

JDD

DRUGS • DEVICES • METHODS

Aesthetic Laser and Light Source Treatments: Skin Rejuvenation and Repair

This supplement to the *Journal of Drugs in Dermatology* is supported by Alma Lasers, Candela Corporation, Cynosure, and Syneron.

ISSN: 1545 9616

November 2009 • Volume 8 • Issue 11 (Supplement)

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JOURNAL OF DRUGS IN DERMATOLOGY

NOVEMBER 2009 VOLUME 8 ISSUE 11 (SUPPLEMENT)

Journal of Drugs in Dermatology
is published monthly by
The Journal of Drugs in Dermatology
377 Park Avenue South, 6th Fl.,
New York, NY 10016
telephone: 212-213-5434
fax: 212-213-5435
www.JDDonline.com

November 2009 s4 Volume 8 • Issue 11 (Supplement)

ORIGINAL ARTICLES Journal of Drugs in Dermatology

Clinical Evaluation of the SmartSkin™ Fractional Laser for the Treatment of Photodamage and Acne Scars

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ABSTRACT

Background and Objective: Fractional photothermolysis with a CO_2 laser shows promise in the treatment of photodamaged skin. The purpose of this study was to evaluate a fractional CO_2 laser device (SmartSkin™, Cynosure, Westford, MA) for the treatment of facial photodamage.
Methods: Twelve subjects seeking treatment of facial hyperpigmentation, skin laxity, wrinkles and fine lines, enlarged pores and acne scars enrolled in the study. Each subject was treated twice with the SmartSkin device at three- to five-week intervals. Results were evaluated at one week, one month and three months after the final treatment.
Results: All 12 subjects completed the study. Physician and subject assessments both indicated that clinical improvements in all photodamage parameters were apparent at one month and persisted at least three months. Improvements in acne scars were noted but not graded. Eleven subjects would recommend the treatment to family and friends. The median pain scores during the initial and final treatments were 2.00 and 2.00, respectively, on a scale of 0–5. Only one adverse effect, facial edema, was judged "probably related to treatment."
Conclusion: The SmartSkin fractional laser device improves photodamaged skin for at least three months. The treatment was well tolerated and adverse effects were limited to transient facial edema.

INTRODUCTION

The traditional CO_2 laser is considered the gold standard device for ablative resurfacing. The ablative effects are due to the heat produced when epidermal water absorbs the 10,600 nm wavelength energy produced by the device. A key advantage to the technique is that the thermal damage does not extend beyond the laser wound.[1] Disadvantages include long recovery time, hyperpigmentation, thermal damage, prolonged erythema, acne flares, milia formation and dermatitis,[2,3] and that high-quality results depend on the skill of the operator.[4,5] Although the 2940 nm Er:YAG laser device absorbs water well and offers more superficial ablation and shorter healing time, clinical improvement is less than what is achieved with the ablative CO_2 laser device.[6]

The drawbacks of these ablative procedures stimulated the development of non-ablative techniques with epidermal cooling. Although these procedures have less downtime and fewer adverse effects, efficacy is limited, clinical improvement is gradual, multiple treatments are required, and many patients fail to respond.[7]

To achieve greater efficacy and reduce adverse effects, Manstein and colleagues[8] introduced fractional photothermolysis (FT) with a 1550 nm Er: glass laser device. Rather than produce a layer of damaged tissue, the beam produces a pattern of microscopic thermal wounds that penetrate to the dermis. The depth of each column of damaged tissue depends on the pulse energy, which is controlled by the operator. Since each tiny wound is surrounded by undamaged tissue, healing can occur quickly, and without neovascularization. Treated areas vary from 10–40% of the skin surface area.[4]

Encouraged by the success of the FP technology with 1550 nm laser energy, manufacturers applied the same technology to CO_2 lasers, whose energy is sufficient to both vaporize tissue and heat nearby dermal collagen. The collateral heating alters the helical structure of collagen, resulting in tissue tightening as in traditional CO_2 laser treatment.[4,9] Additional tightening occurs as the tiny vaporized columns collapse during the following three to six months.[4,10] These fractional CO_2 laser devices were subsequently evaluated (Christiansen 2008, Tan 2008, Groff 2008, Gotkin 2009, Clementoni 2007),[4,7,11–13] as they became available.

The purpose of this study was to evaluate a 10,600 nm fractional CO_2 laser device (SmartSkin™, Cynosure, Westford, MA) equipped with a scanner, for the treatment of facial photodamage, including hyperpigmentation, skin laxity, wrinkles and fine lines and enlarged pores, and acne scars. The SmartSkin device was cleared by the FDA for ablation and vaporization in medical specialties that include aesthetic dermatology and plastic surgery.

PATIENTS AND METHODS

Twelve healthy subjects (11 women, one man, 48.3 + 12.9 years of age, Fitzpatrick skin types II–IV, 11 Caucasian and one Hispanic) with facial photodamage enrolled in the study. Subjects were seeking treatment of hyperpigmentation (n=10), skin laxity (n=4), wrinkles and fine lines (n=10), enlarged pores (n=10), and acne scars (n=2). One subject had only acne scars and another had both photodamage and acne scars. Exclusion criteria were pregnancy, breast feeding, planned pregnancy within the study period; hypersensitivity to light; active local or systemic infection; light-sensitive medication; history of squamous cell carcinoma, melanoma or immunodeficiency disorder; use of botulinum toxin A, dermal fillers in areas to be treated within the previous four or six months, respectively; facelift, use of isotretinoin, or treatment with an ablative laser to target areas within the past 12 months; treatment with chemical peels or dermabrasion within the past three months; treatment of the target areas with laser or other device within the past three months; bleeding disorder or use of anticoagulant for which a 10-day washout is not allowed before study treatment; and the use of immunosuppressive medications.

Each subject was treated twice with the SmartSkin at three- to five-week intervals. Treatment duration was 10–12 minutes. All treatments were administered by the same physician (M.H.G). An anesthetic cream of benzocaine (20%), lidocaine (60%), and tetracaine (5%) was applied to the target areas one hour before each treatment and removed before treatment. Subjects with a history of herpes simplex virus were given valacyclovir for four days before each treatment. All subjects provided signed informed consent to participation and the study protocol was approved by the Independent Investigational Review Board in Plantation, FL.

The initial treatment was preceded by a test spot to determine the optimum treatment parameters. The entire face received two passes as the scanner delivered multiple tiny wounds to the epidermis and dermis. Pulses were delivered in linear fashion with a maximum of 10% overlap. Selectable treatment parameters included the energy per pulse and the distance between each pulse within the scan pattern. A rectangular pattern and 350-micron spot size were used in all treatments. Power settings were 20–24 watts for the initial treatments and 18–26 watts for the second treatments. Dot pitch (the distance between each laser dot or spot) was 750 μm, dwell time (the pulse width or laser exposure to tissue) was 700 ms, and the Zimmer forced-air cooling setting was three for all treatments. Treated areas were covered with a water-based gel (Aquaphor) immediately after treatment. Subjects were instructed to apply gel to the face three times daily for three days. Subjects were also told to apply sunblock daily throughout the study.

Each subject returned one week, one month, and three months after the final treatment for clinical evaluation and photography. Outcomes were evaluated by photographs obtained before and after treatment and questionnaires completed by subjects and the treating physician one and three months after the final treatment. All photographs were obtained with an Omnia system (Canfield Scientific) under standardized conditions of background, lighting, exposure, position and facial expression.

At one week. subjects recorded the durations of postreatment redness, bleeding, crusting, scab formation; and changes in skin color of the treated areas. They also noted the number of days (1) for skin to return to normal color, (2) before make-up could be worn, and (3) before they could return to normal daily activities.

At one and three months, subjects rated improvement in photodamage, wrinkles and fine lines, pigmentation, enlarged pores, and overall appearance on the following scale: 0=none; 1=mild; 2=moderate; 3=excellent. They graded postreatment discomfort, redness, and bleeding, all on the scale of 0=none; 1=mild; 2=moderate; 3=severe. Subjects were also asked if they would recommend the procedure to family and friends. The treating physician rated improvement in photodamage, wrinkles and fine lines, pigmentation, pore size, skin laxity, and overall appearance on the following scale: 0=none; 1=1–<25%; 2=26–50%; 3=51–75%; 4=76–100%. Acne scars, if present, were noted but not graded. Adverse effects were also noted.

To document the recovery and healing process, two subjects kept a diary for four days after the final treatment. The treated areas were photographed under standardized conditions on each of the four days. Pain during treatment was assessed by subjects on a scale of 0–5.

Since most of the data were not normally distributed and linearity could not be assumed for grading scales, non-parametric statistics were used in the analyses. The Wilcoxon signed rank test was used to test for significant differences, using $P<0.05$ at the cutoff level.

RESULTS

All 12 subjects completed the study. Improvements in photodamage parameters at one month and three months are shown in Table 1. Median improvement scores were similar at both follow-up visits. At three months, the median physician scores were 3.0 (51–75% improvement) for all parameters, with the most variation in photodamage (IQR=2.6) and the least variation in skin laxity and overall appearance (IQR=1.0). The median scores for each parameter at one month did not differ significantly from the median scores at three months for both the physician and subjects. A clinical example is shown in Figure 1.

Since subject evaluations were graded on a 4-point scale and physician evaluations were graded on a 5-point scale, agreement between the two groups is difficult to assess. In general, however, physician and subject evaluations agreed in approximately half of subjects. Physician and subject assessments both indicated that improvements persisted at least three months.

Eleven subjects would recommend the treatment to family and friends. The remaining subject experienced pain during treatment because she had not complied with instructions to avoid sun exposure for at least one month before the initial treatment. Although acne scars were visually improved as noted by the investigator, the improvement was not graded because the protocol was designed for the treatment of photodamage rather than acne scars.

Only one of 15 adverse effects, facial edema, was judged "probably related to treatment." Seven other adverse effects (acne or acne bumps) were judged "possibly related to treatment." The remaining adverse effects were not related to treatment.

Posttreatment discomfort, redness, bleeding, crusting and scab formation at each follow-up visit are shown in Table 2. At one week, redness persisted in more subjects (n=7) and for the longer period (four days) than any of the other posttreatment effects. Only one subject reported prolonged bleeding, which resolved in two days. Five subjects reported crusting which resolved in one to six days (mean three days). Three subjects reported scab formation that resolved in three days. Crusting and scab formation were not observed at one month and three months. Eight subjects reported normal skin (at day 7), one subject reported red skin, and three subjects reported dusty-colored skin that had not resolved by day 7. One subject noted mild discomfort one week after the final treatment. Posttreatment postinflammatory hyperpigmentation, hypopigmentation, scarring, or infections were not observed.

The median pain scores during the initial and final treatments were 2.00 (IQR=1.38) and 2.00 (IQR=0.58), respectively, on a scale of 0–5. The median pain values of the first and second treatments did not differ significantly from each other.

Female subjects applied makeup a median of five days (interquartile range [IQR]=2.7) after the final treatment. Subjects resumed normal activities a median of two days (IQR=2.0) after the final treatment.

To document the recovery and healing process, two subjects (05 and 06) recorded the following observations on the day of each treatment (day 0) and for the following four days (1–4). Neither subject experienced pain. Subject 05 reported red skin

FIGURE 1. A 65-year-old man before the first of two treatments (left) and one month after the same treatment (right). Improvement is apparent in facial wrinkles, particularly below the eyes, and in pigmentation spots on both sides of the face and upper forehead.

TABLE 1.
Improvement Scores (Median [IQR]) in Photodamage Parameters at One-Month and Three-Month Follow-Up Visits

Parameter	One Month		Three Months	
	Physician[1]	Subject[2]	Physician[1]	Subject[2]
Photodamage	2.0 (2.0) (26–50%)	2.0 (0.6) Moderate	3.0 (2.2) (51–75%)	2.0 (1.2) Moderate
Wrinkles, fine lines	2.5 (2.0) (51–75%)	1.5 (1.0) Mild to Moderate	3.0 (1.6) (51–75%)	1.5 (1.0) Mild to moderate
Pigmentation	2.5 (1.6) (51–75%)	2.0 (2.0) Moderate	3.0 (1.6) (51–75%)	2.0 (1.6) Moderate
Pore size	3.0 (2.6) (51–75%)	1.5 (1.6) Mild to moderate	3.0 (1.6) (51–75%)	1.5 (1.0) Mild to moderate
Skin laxity	3.0 (1.0) (51–75%)	—	3.0 (1.0) (51–75%)	—
Acne scars	—	—	—	—
Overall appearance	3.0 (1.0) (51–75%)	2.0 (1.6) Moderate	3.0 (1.0) (51–75%)	2.0 (1.6) Moderate

[1]Scale: 0=none; 1=1–<25%; 2=26–50%; 3=51–75%; 4=76–100%.
[2]Scale: 0=none; 1=mild; 2=moderate; 3=excellent.
IQR=interquartile range, the difference between the 75th and 25th percentiles, a measure of dispersion.

TABLE 2.
Number of Subjects Who Reported Post-Treatment Effects at One Week, One Month and Three Months After the Final Treatment

Symptom	One Week (Mean Duration)	One Month (Severity)*	Three Months (Severity)*
Redness	7 (4 days)	6 (1)	4 (1)
Bleeding	1 (2 days)	—	—
Crusting	5 (3 days)	—	—
Scab formation	3 (3 days)	—	—
Discomfort	—	1 (1)	1 (1)

*Scale: 0=none; 1=mild; 2=moderate; 3=severe.

on days 0–3 and pink skin on day 4, while subject 06 reported brown (days 0–2) and faint red-brown skin (days 3, 4). Bleeding and scab formation were not observed in either subject. Subject 05 reported mild crusting on days 0 and 2 and subject 06 experienced mild crusting on day 1. Subject 05 reported skin flaking off the entire face on days 1 and 2. Both subjects were able to keep their faces moist and free of crusting during the entire four days, except for subject 05 on days 1 and 3. Subject 05 washed her face two to four times daily and subject 06 washed her face two to five times daily. Neither subject applied makeup on days 0–4. Both subjects performed their normal activities on days 0–4.

DISCUSSION

The results show that with the treatment settings used in the present study, two double-pass treatments with the SmartSkin are well tolerated and provide predominantly moderate improvement in wrinkles and fine lines, pigmentation, pore size, skin laxity and overall appearance in subjects with facial photodamaged skin. The improvement is apparent one month (or earlier) and persists at least three months after the final treatment. The 51–75% physician-assessed improvement in skin laxity suggests that the laser energy penetrates to the dermis and promotes collagen shrinkage and remodeling. Adverse effects are minimal and healing appears to be rapid and uneventful. The two subjects who kept diaries returned to their normal activities on the day of treatment.

The results of the present study are in general agreement with those of Gotkin and colleagues (2009), who recently reported the safety and efficacy of a device similar to the SmartSkin. After a single treatment, significant clinical improvement was noted in wrinkles, scars, striae, lentigines, and skin texture and color associated with solar elastosis. Improvement data were supported by histological evidence of neocollagenesis. As in the present study, treatment was associated with transient posttreatment erythema, edema, crusting, skin color changes and hyperpigmentation.

Studies with other fractional CO_2 devices have recently been reported. Clementoni and colleagues[7] treated 55 photodamaged patients with a “single-session, single-pass, full-face ablative fractional treatment” protocol, using a non-sequential fractional ultrapulsed CO_2 laser. The authors noted significant subjective improvement from baseline in global score, fine lines, mottled pigmentation, sallow complexion, tactile roughness, and coarse wrinkles. Downtime and adverse effects were minimal.

Christiansen and Bjerring (2008)[11] recently reported their use of single-pass, low-spot density treatment with a nonablative fractional CO_2 device to rejuvenate the perioral areas of 12 patients. Patients were given three treatments at one-month intervals. Subjective improvements in wrinkles, skin texture and mottled pigmentation were achieved in 80% of patients, and ultrasonigraphically determined improvement in dermal density was achieved in 72.7% of patients. Results were supported by histological studies. Temporary posttreatment redness, skin color changes and crusting were also noted. Downtime ranged from two to 10 days after the first treatment and from one to six days after the second and third treatment.

Groff and colleagues (2008)[4] recently summarized their experience with ablative fractional CO_2 resurfacing, using two different devices. They reported success in the treatment of photodamage, scars, dyschromia and vascular ectasia. Improvements are apparent after a single treatment but are cumulative after multiple treatments. The authors have safely treated the face, chest, neck and isolated areas in these locations. Treatment parameters are selected on the basis of the number and depth of wrinkles and the degrees of textural irregularity, dyschromia, capillary telangiectasia and tissue laxity.

At first glance, the physician improvement ratings appear to be higher than the patient ratings. This is due, at least in part, to differences in rating scales and this may be considered a limitation of our study. Clementoni and colleagues[7] also used a five-point scale for physician ratings and a four-point scale for patient ratings, but did not compare clinical and patient ratings, number for number, as the authors did in Table 1 of the present study. Christiansen and Bjerring[11] assessed clinical improvement by ultrasonography and by blinded evaluation of analog photographs by a dermatologist experienced in cosmetic dermatosurgery. The scale for the blinded evaluation was not reported, and volunteers (patients) graded improvement on a five-point scale. Gotkin and colleagues[13] used a five-point scale for both physician and patient ratings and reported good agreement between the two ratings in most cases. In this study, a comparison between physician and patient ratings is valid because the rating scales are the same. This was not the case, however, in this study.

The present study shows confirms the safety and efficacy of the SmartSkin fractional laser device in the treatment of photodamage. Studies with more subjects with severe photodamage and different treatment settings may even further improve treatment outcomes.

CONCLUSION

The SmartSkin fractional laser device improves photodamaged skin for at least three months. The treatment was well tolerated and adverse effects were limited to transient facial edema.

DISCLOSURES

Dr. Gold speaks and performs research on behalf of Cynosure. Ms. Heath and Ms. Biron have no relevant conflicts of interest to disclose.

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November 2009 s9 Volume 8 • Issue 11 (Supplement)
 ORIGINAL ARTICLES Journal of Drugs in Dermatology

Sublative Rejuvenation: Experience With a New Fractional Radiofrequency System for Skin Rejuvenation and Repair

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ABSTRACT

Several laser-based ablative resurfacing and nonablative rejuvenation technologies offer non-surgical options for improving the appearance of the skin. Although efficacy and good safety profiles have been demonstrated, limitations do exist with these systems.

A more recent technology has been developed that employs fractionated bipolar radiofrequency (RF) energy. Referred to as "sublative rejuvenation," the treatment improves skin appearance while addressing some of the limitations of both ablative resurfacing and nonablative skin rejuvenation.

This article describes the technology and reports on the authors' experience with it in clinical practice. Unlike fractional ablative laser treatments, which can disrupt 10–70% of the epidermis and most of the effect is in the epidermis, the sublative rejuvenation technique impacts only up to 5% of the epidermis and most of the effect is in the dermis. As a result, healing is rapid and downtime is minimal. The treatment is appropriate for all skin types and is an effective alternative for patients with darker skin who may be at risk for hyperpigmentation from laser treatments.

INTRODUCTION

For patients seeking non-surgical options for improving the appearance of their skin, several laser-based ablative resurfacing and nonablative rejuvenation technologies are available.1 The principle behind these treatments is similar: creating controlled thermal damage in the dermis stimulates a wound healing response that leads to collagen remodeling.

Although these systems have proven efficacy with good safety profiles, limitations exist. Nonablative systems protect the epidermis with cooling while enabling some thermal injury or direct stimulation in the dermis to initiate neocollagenesis. Although mild-to-moderate improvement in tone and texture, as well as fine lines, has been demonstrated, multiple treatments are needed to reach this goal. Ablative systems yield greater efficacy, but require prolonged downtime and have greater potential for complications.[2] For instance, the epidermal injury poses a risk of post-inflammatory hyperpigmentation (PIH) for patients with darker skin. Fractionated ablative systems help address some of these issues because they generate thermal injury in a noncontiguous pattern, leaving a portion of the surrounding epidermal tissue intact to promote fastidious healing.[3–5] However, these systems typically ablate 10–70% of the epidermal surface, proportional to factors such as the energy delivered, density overlap, spot size and coverage ratio, and downtime can still be significant. The energy impact is widest at the epidermal surface and narrower deeper in the dermis, and the epidermal injury in fractionated systems can still result in PIH for patients with darker skin.

More recent technology, fractionated bipolar radiofrequency (RF) energy, addresses some of the limitations of both ablative resurfacing and nonablative skin rejuvenation. Referred to as "Sublative Rejuvenation™" the treatment is delivered via a handheld applicator with the eMatrix™ system (Syneron Medical Inc., Irvine, CA). This treatment is used for patients with mild-to-moderate tone or texture irregularities such as wrinkles, rhytids, acne scars and other tone or texture irregularities.

Sublative rejuvenation causes limited epidermal disruption—less than 5% of the surface is treated with one pass—which translates to minimal downtime for patients and makes it an optimal choice for darker skin. The bulk of the effect is coagulative and occurs mainly in the mid-dermis, where it has the most effect on wrinkles and scars.

Mechanism of Action

RF-based technologies are capable of producing higher volumetric heating via tissue impedance with subsequent heat diffusion to deeper tissue compared to laser-based technologies. The radiofrequency modality in the bipolar electrode scheme applies the configured energy in a "pyramid" shape, which creates a predetermined controlled wound with a small epidermal component and larger volume in deeper tissue. Ablative technology commonly forms a conical or columnar injury zone. The term "sublative" is a derivative of "sub-ablative," referring to the ability to generate heat energy well beneath the ablated zone below the epidermal surface and where the effect is largely caused by a large volume of heated tissue.

FIGURE 1. The radiofrequency energy produces a pyramid-shaped thermal injury zone, which results in minimal epidermal disruption. The white area represents superficial epidermal heating, and the red zone represents the deeper coagulation. A substantial amount of the heat-derived coagulative damage occurs deeper in the dermis.

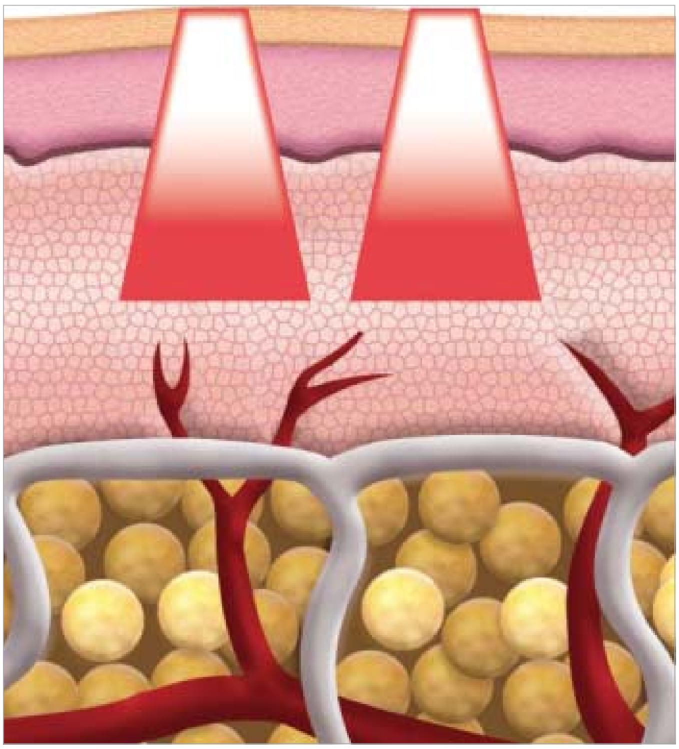
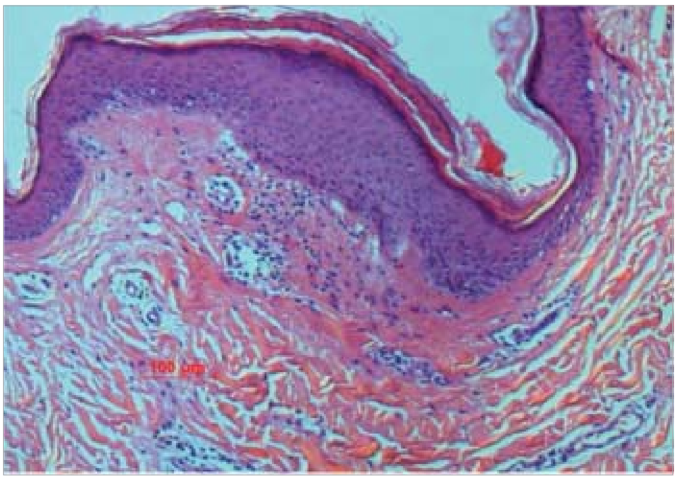


FIGURE 2. Significant leucocytes inflammation and immediate contracture occurs in the dermis as part of dermal remodeling.



The tip of the sublative rejuvenation applicator contains an array of 64 electrode pins, each 200 microns wide, which directly contact the dry stratum corneum of the epidermis. The radiofrequency energy flows between the positively and negatively charged electrode pins to form a closed circuit of bipolar RF current within the tissue that passes through the epidermis deeper into the dermis, delivering 1 MHz of conducted RF current to the tissue. The electric field produces a pyramid-shaped thermal injury zone, with the tip of the pyramid at the epidermal surface branching out to a wider area deeper into the dermis (Figure 1). The RF energy penetrates the dermis with a visible coagulative effect up to 450 μ depth, with only a 200 μ epidermal width of effect.

The variable energy of radiofrequency current can create different spatial and depth impacts with a larger relative area and volume of dermal tissue affected than epidermal tissue. The greatest temperature rise occurs where the electrodes contact the dry skin, causing a visible ablative injury that manifests as a pattern of small pixilated dots on the surface of the skin. These surface wounds and their effect on the dermis promote neocollagenesis, providing rhytid reduction and minimizing dermal atrophic scarring as well as smoothing the skin surface, although much of the effect of the treatment is due to the nonablative heating of the dermis.

In general, applying thermal energy to the skin activates a cascade of physiological healing responses to promote reepithelialization and remodeling of the extra cellular matrix (ECM). With the sublative rejuvenation modality, the major impact occurs with the ECM, while epidermal response is minimized.

The initiating event—in both sublative rejuvenation and ablative skin resurfacing—is local inflammation.[6] However, in ablative skin resurfacing, a massive destruction of the epidermis results in a healing process that largely involves keratinocyte proliferation and migration and relatively less dermal matrix remodeling. In sublative rejuvenation, a more widely diffused and volumetric impact is formed inside the dermis with minimal involvement of the epidermis in the healing. This is reflected by a healing process that is focused primarily on fibroblast stimulation and ECM dermal remodeling (Figure 2).

Three programs built into the eMatrix system enable the user to adjust the depth and intensity of the dermal heating to achieve desired effects and meet specific patient downtime requirements. Each program has a different RF setting and therefore different heating profile reflected in changes in depth and nature of impact, ranging from ablation to provide a shallow impact, a mid-level impact and the deepest and highest-volume impact. The epidermal ablation takes place within the first 10 ms of the pulse, and up to another 100 ms of controlled RF current travels between the electrode array to further heat the dermal tissue for optimal remodeling of both collagen and elastin. The three energy settings are: program A (2–8 J), program B (8–16 J), or program C (16–25 J).

The treatment impacts a relatively large volume of dermal tissue while leaving the epidermis minimally affected. Unlike fractional ablative laser treatments, which can disrupt 10–70% of the epidermis, the sublative rejuvenation technique always impacts only up to 5% of the epidermis. As a result, healing is rapid with minimal downtime.

RESULTS

Hruza et al. evaluated the sublative rejuvenation treatment in a study involving 35 subjects, ages 52 ± 8 years with Fitzpatrick skin types II–IV.[7] Each subject received three treatments on facial areas at one-month intervals. The average treatment energy was 8–20 joules (J) at a 5% density. Histologic examination revealed that the surface lesions where the electrodes contacted dry skin had completely healed within less than 48 hours. No post-inflammatory hyperpigmentation was reported.

The investigators' assessment at one month following the last treatment was that 90% of subjects showed improvement in smoothness/wrinkling, 87% in skin tightness, and 83% in skin brightness (Figures 3a and 3b). Improvement of 40% or greater in all of these categories was seen in over half of the subjects. The authors also observed the overall appearance of tighter and smoother skin. The greatest improvement was observed in the periorbital areas and the least change was seen in the perioral areas.

FIGURE 3. a) Before treatment; **b)** After treatment. Photos courtesy of George Hruza MD.

The subjects' evaluation correlated closely with the investigator assessment. In total, 80% of the subjects were satisfied with the treatment: 40% were somewhat satisfied, 17% were satisfied, and 23% were very or extremely satisfied.

Practice Considerations

Pain Level

In the Hruza study most (87%) of the subjects reported only minimal pain and discomfort during the treatment. This is consistent with the experience in using this treatment in practice, based on patient feedback. The authors usually apply a topical anesthetic prior to the procedure, but in some cases have performed the treatment without an anesthetic.

Downtime

A key advantage of the treatment is the minimal downtime. Patients will usually exhibit some erythema and edema for a few to several hours immediately following the procedure. The superficial ablation points, mirroring the electrode pattern, heal within the first one to three days. Patients may experience some roughness as the tiny scabs develop, but they can usually wear makeup within a day of the procedure. No special post-procedure care is required. As with all patients, the use of sunscreen is recommended.

Safety

The authors' patients have not experienced any complications that may occur with more ablative resurfacing, such as hyperpigmentation, acne flares, infection, prolonged erythema or scarring.

Treatment Course

The manufacturer suggests a course of three treatments, four to six weeks apart, but the authors adjust the number of treatments based on the severity of the skin condition and the patient's objectives. The authors find that an effective treatment protocol for moderate to severe wrinkles or acne scars involves five to six monthly treatments. The treatments can typically be completed in 15–20 minutes. With the minimal downtime and short procedure duration, the course of treatment is relatively convenient for patients to comply with.

Results/Patient Satisfaction

The treatment is not appropriate for superficial pigment changes, since very little surface ablation occurs. The authors can see noticeable improvement in deep and/or dynamic wrinkles and scars, and many patients are commenting on the overall smoothing effect the treatment produces. The vast majority of patients are extremely, very or somewhat satisfied with the results.

Darker Skin

The ability to treat all skin types, including darker skin, is a significant advantage. Optical energy from laser or other light-based technologies tends to be absorbed by the melanocytes in darker skin types, causing hyper- and/or hypopigmentation. Also, the wider impact of optical energies at the skin's surface presents a risk for darker-skinned people. However, the minimal impact at the skin's surface as well as the fact that RF energy does not target a chromophore makes the treatment appropriate for all Fitzpatrick skin types. RF wounding creates a different biologic response with no prolonged erythema, which is associated with hyperpigmentation in darker skin.

The Authors' Experiences/Techniques

Lori Brightman, MD

For acne scarring that is more superficial, rolling scars, Dr. Brightman uses program C, 18–25 J. On average, these patients will require three to five treatments once monthly, depending on severity of scarring. One unique feature Dr. Brightman has noted is the treatment concomitantly diminishes telangiectasia. Many acne scarring patients have scattered fine telangiectasia from long-term topical retinoid use, prior corrective procedures for their scarring or natural wound healing response to the scars themselves. Sublative rejuvenation has been effective for my patients in treating both issues. This treatment regimen has been used on Fitzpatrick skin types I–IV without any noted cases of post-inflammatory hyperpigmentation.

For facial rejuvenation, including tone, texture and rhytids, Dr. Brightman chooses a regimen based on the degree of improvement needed and the patient's personal goals. For example, she will treat a patient with mild photodamage using program A or B, with perhaps two to three treatments needed. For a patient with more moderate sequelae from UV exposure, she will use program C, and likely perform two to four treatments once monthly.

Dr. Brightman has also used fractional RF to help improve the appearance of striae. She has treated abdominal striae on program C, 25 J, treatments one month apart. The number of treatments is dependent on the width and degree of atrophy of striae. Results show decreased atrophic appearance and improvement in the cigarette paper-like appearance of the striae. Again, she also notes improvement in the telangiectasia within the striae rubra.

On average, a patient treated with program A or B can be makeup-ready in one to two days. The rough texture of the healing pinpoint spots can still be appreciated, but it is coverable with makeup nonetheless. A patient treated on program C is usually makeup-ready by day two to three. Again, the healing pinpoint scabs may be appreciated, but a more opaque foundation can cover the areas. Regardless of treatment regimen, for all of her patients, Dr. Brightman suggests washing twice daily with a nonabrasive noncomedogenic cleanser such as Cetaphil Daily Cleanser and using TNS Ceramide or Control Tactics for the recovery period along with sunscreen use.

Mitchel Goldman, MD

Dr. Goldman has found the majority of acne scar patients have improved with the combination Matrix IR/sublative RF treatment. Patients have four to five treatments, spaced one month apart. The treatment begins with the IR head used at maximum settings of 70 J/cm2 and 100 J/cm2 RF energy. Two passes to each depressed acne scar is completed—this results in mild erythema and slight edema of the treated areas, which resolves over the next 30–90 minutes. Patients find the IR head more uncomfortable, so Dr. Goldman has used a 20/6/4% BLT topical numbing cream prior to treatment.

Next, the nonablative RF resurfacing is used to field treat the entire acne scarred area. In most cases (skin types I–III, sometimes IV), Dr. Goldman will start at maximum settings of program C and 25 J/cm^2. If patients are skin type IV/V, he starts at 21 J, and then treats at 25 J for the second treatment on. He has not noted a disappearance in erythema/telangiectasia, even after specifically treating these lesions. However, three patients of Mexican descent have commented after the first treatment that their hyperpigmentation has greatly improved. Almost unanimously, by treatment three, most patients report the texture of their skin is smoother and softer to touch. Physicians/PAs also report this finding on physical examination. For higher skin types (IV), the RF woundscabs seem to last longer—appearing the next day and lasting three to five days, as opposed to showing up at day 2 after treatment and disappearing in one to two days. These are camouflaged by makeup in most cases, and no patients, including males, have been concerned enough by the pattern left by the RF head to discontinue treatment.

The IR/RF system seems to be most effective for shallow, rolled acne scars. Some traumatic/surgical scars around the face have also improved in texture/appearance. Usually, this is a well-tolerated procedure. The IR portion is always the more uncomfortable of the two. The RF portion requires frequent cleaning of the tip as well prepping the face prior to treatment.

Amy Taub, MD

Dr. Taub uses sublative rejuvenation for mild to moderate photodamage focused on rhytides and firming, but also uses it in combination with IPL with bipolar radiofrequency. She does not find programs A or B to be as effective as program C so she uses program C. If the patient is skin type I–III and is not tanned, Dr. Taub will typically start immediately with 25 J and 5% for three treatments. For skin types IV–V, she starts at 17–19 J and increases by 2 J per treatment. For acne scarring, she uses the same parameters, but the patients typically require five treatments (Figures 4a and 4b). Dr. Taub has also been using this in combination with a fractional diode laser with bipolar RF and getting good results even with ice pick scars. Dr. Taub believes that, for skin types I–III, a higher energy than 25 J will be necessary to achieve significant improvement in moderate-to-severe acne scarring.

One of the unique features of this modality is the fact that it is not necessary to do the entire face to get a blended look. Just an aesthetic subunit can be done without fearing any demarcation line. Dr. Taub believes that the entire subunit should be treated because some of the benefit seen is from tissue tightening. This is useful for periorbital areas, cheek acne scars, forehead lines of expression, etc. Dr. Taub would like to see a smaller tip to be able to do upper and lower eyelids; she thinks this would be an excellent modality for the fine wrinkling that is often seen there and is so hard to treat. Postoperatively, she prefers a bland zinc oxide-based sunscreen for all skin types. She usually recommends growth factors, either TNS Recovery Complex or Neocutis Biorestorative Gel BID during, after and between all the treatments to enhance collagen production. Dr. Taub has not treated any skin type VI but sees no reason not to do so with the same parameters used for skin type IV–V.

CONCLUSION

Sublative rejuvenation strikes a balance between downtime and noticeable improvement that many patients are seeking. It results in low epidermal disruption with high dermal remodeling. The bulk impact of coagulation and residual heating occurring deep within the dermis generates significant collagen contracture and remodeling, leading to the appearance of smoother, more luminous skin. Moreover, the treatment is appropriate for all skin types, and offers an effective alternative for patients with darker skin who may be at risk for hyperpigmentation from laser treatments.

Future developments with this technology may bring even greater results for a broad base of patients. For example, the ability to measure skin impedance and adjust energy levels accordingly may allow higher energy levels to be used on patients who are deemed appropriate.

FIGURE 4. a) Before treatment; **b)** After treatment. Photos courtesy of Amy Forman Taub MD.

DISCLOSURES

Dr. Brightman has received honoraria and travel expenses for lectures and meeting attendance for Syneron Medical Ltd.

Dr. Goldman has received funding and the loan of the Matrix RF system from Syneron to conduct clinical studies.

Dr. Taub has received honoraria as well as travel expenses and equipment in return for being an investigator and speaker for Syneron Medical Ltd.

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Permanent Laser Hair Removal With Low Fluence High Repetition Rate Versus High Fluence Low Repetition Rate 810 nm Diode Laser—A Split Leg Comparison Study

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ABSTRACT

High fluence diode lasers with contact cooling have emerged as the gold standard to remove unwanted hair. However, laser hair removal is associated with pain and side effects, especially when treating dark or tanned skin. A novel diode laser with low level fluence (5–10 J/cm^2) with a high repetition rate at 10 Hz (Soprano XL in SHR mode, Alma Lasers, Chicago, IL) using multiple passes in constant motion technique was compared to traditional one pass high fluence (25–40 J/cm^2) diode laser (LightSheer ET, Lumenis, Santa Clara, CA) in a prospective, randomized split-leg study on 25 patients with Fitzpatrick skin types I–V. Hair counts were done six months following the fifth treatment and were found to be comparable with a 86-91% hair reduction. There was one superficial burn with the high energy diode treatment. The rapid, multiple pass in-motion technique was faster and associated with significantly less pain. Multiple passes of diode laser at low fluences but with high average power results in permanent hair removal with less discomfort and fewer adverse effects, especially on darker skin.

INTRODUCTION

Laser hair removal has enjoyed substantial popularity, and is presently the second most popular non-surgical cosmetic procedure in the U.S. following botulinum toxin injections.[1]

Laser and light-based techniques rely on the process of selective photothermolysis.[2] The selective absorption of red and near-infrared wavelengths by melanin in the hair shaft and follicular epithelium confines thermal damage to the hair follicles and, to a point, limits the untoward diffusion of excess thermal energy to the surrounding tissue. Laser hair removal was first described in 1987 in an experiment to remove rabbit eyelashes with an argon laser.[3] Subsequently, physicians used the Nd:YAG laser[4] and the ruby laser[5] to remove hair. The alexandrite laser[6] and diode followed;[7] all have been thoroughly described and reviewed.[8] All of these laser systems used the highest fluence possible without damaging the tissue surrounding the hair follicle with a single pass.

The approach of using low fluences with repetitive millisecond pulses to achieve heat stacking in the hair bulb and bulge represents a paradigm shift in laser hair removal methodology. This study compares efficacy, safety and treatment speed of a new low fluence rapid pulse with multiple passes 810 nm diode hair removal modality with a traditional high powered single pass 810 nm laser diode system.

This is the first study designed to evaluate the hypothesis that low level fluences done repetitively on a hair follicle will produce permanent hair removal with less discomfort and fewer side effects than a single high fluence pulse.

MATERIALS AND METHODS

This prospective single-center, bilaterally paired, blinded, randomized comparison study was conducted in accordance with recognized Good Clinical Practice (GCP/ICH) guidelines and applicable regulatory requirements. Thirty-three (33) female subjects (skin types I–V) with hair on the legs who in the opinion of the investigator were viable candidates for laser hair removal were enrolled in the study. These patients were offered five complimentary laser hair removal treatments on their legs as an inducement to enroll in the study. Alma lasers partially funded the cost of the study.

Subjects were to be between 25 and 65 years of age, in good general health with no known photosensitivity or use of medication with photosensitivity as a side effect, no obvious skin disease or history of chronic skin disease other than moderate facial acne vulgaris, no history of keloid or hypertrophic scar formation, and no tattooing in the treatment area. Subjects were excluded if they were pregnant, nursing or unwilling to use birth control during the study period if of childbearing age; had waxed the lower legs or undergone therapy with any radiofrequency or light source; used prescription or over-thecounter therapy to the skin of the lower leg within 30 days prior to enrollment; had history of any confounding cancerous or pre-cancerous skin lesions; or had been treated with an investigational drug or device within 30 days prior to and during the study period. Tanning for at least 30 days prior to and during the study period was discouraged. Shaving the legs was permitted; waxing was prohibited.

Using manufacturer-recommended methods and settings, one leg of each patient (randomly determined) was treated with the Soprano XL in SHR mode (Alma Lasers, Chicago, IL) using a technique of maintaining the handpiece in constant motion, fluence up to 10 J/cm^2, 10 Hz, 20 ms pulse duration. With the constant motion technique, an area of about 100 cm^2 was treated with six to ten mulitple passes. The operator never remains stationary in one spot, and is always moving the laser handpiece on the entire 100 cm^2 area, similar to ironing. By using this technique, the skin is never subjected to a single diode laser pulse greater than 10 J/cm^2. Since this is below the threshold of burning, the incidence of adverse effects should be lower, as well as the sensation of discomfort which is directly related to fluence. The purpose of the study was to evaluate the degree of discomfort using this constant motion technique and the amount of hair reduction. With six-month post-treatment hair counts, the efficacy of the low fluence-multiple pass technique could be compared to standard high fluence laser hair removal: the other leg was treated with the LightSheer device (Lumenis, Santa Clara, CA) using a conventional single pass, fluence to tolerance (20–50 J/cm^2), 2 Hz, 30 ms pulse duration. LightSheer parameters were aggressive so that there could be no criticism that the leg treated with the high fluence had inadequate energy. Subjects were treated five times at intervals of six to eight weeks with each device to permit hair regrowth and mimic real-life laser hair removal.[9]

Hair counts were made within a pre-determined square-shaped area (surface area=2.5 cm^2, measured 12 cm above the superior border of the malleolus) on each treated leg before initial treatment and at final follow-up, which occurred six months following the fifth and final laser treatment. Visual baseline hair density and final results were documented by digital photography. Hair counts were done by a university student who was blinded as to which laser was used on the leg and had no interest in the outcome of the study. The digitial photographs were enlarged so that any hair shafts growing within the 2.5 cm^2 grid were easily visible and counted.

Pain during treatment was measured subjectively by patients on a 0–10 visual analogue linear scale (0=no pain, 10=unbearable pain) and recorded by evaluators for each leg after each treatment session. Treatment time (in minutes) was recorded for each treatment session. Subjects were also asked which laser they preferred based on their results following the fifth and final laser session. Adverse events were noted by the investigator.

Data were to be analyzed using appropriate statistical tests based on normality of data distribution.

RESULTS

Twenty-five subjects completed the study. Seven patients were removed from the study for failing to return for scheduled appointments. One patient withdrew from the study due to minor superficial burns on the LightSheer-treated leg. Adverse effects were not observed in any other subject.

Data were analyzed and expressed non-parametrically as medians and interquartile ranges (IQR) because values for final hair count, treatment time, or pain score were not normally distributed. IQR is a measure of dispersion determined by the difference between the 75th and 25th percentiles. Statistical significance was measured by Wilcoxon Signed Rank test. In any case where n=123, this represents 125 total treatment sessions (five sessions x 25 patients) minus two missing data points due to evaluator error.

Based on final hair count values (n=25), overall median hair reduction was 86% with Soprano XL in SHR mode and 91% with LightSheer. According to Wilcoxon signed rank test comparing hair removal percentages between LightSheer and Soprano, differences were not statistically significant (P=0.1564). These results are demonstrated graphically in Figure 1.

Overall study results showed a statistically significant difference (P<0.0001, Wilcoxon Signed Rank test) in median treatment times between Soprano (20 min) and Lightsheer (26 minutes) over the course of five treatments (n=123). This is shown in Figure 2. IQR for each was 4.0 and 6.0, respectively.

FIGURE 1. Graph comparing the overall median hair removal percentages for Soprano XL in SHR mode (86%) and LightSheer (91%).

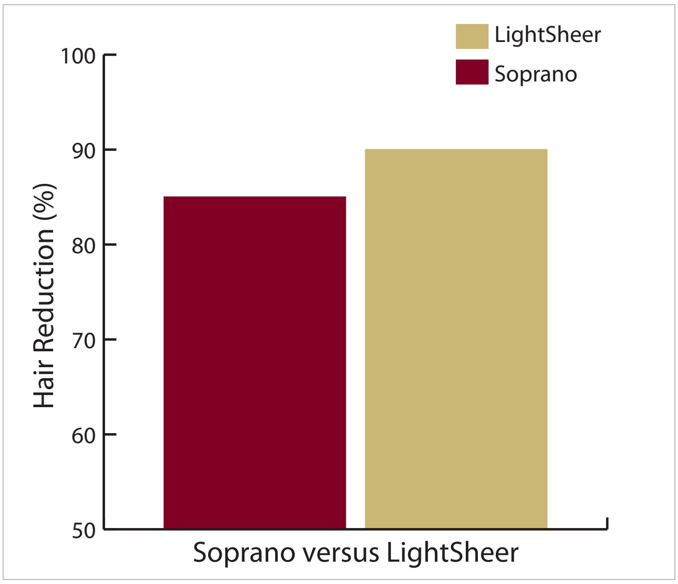


FIGURE 2. Graph comparing the overall median treatment times for Soprano XL in SHR mode (20 minutes) and LightSheer (26 minutes).

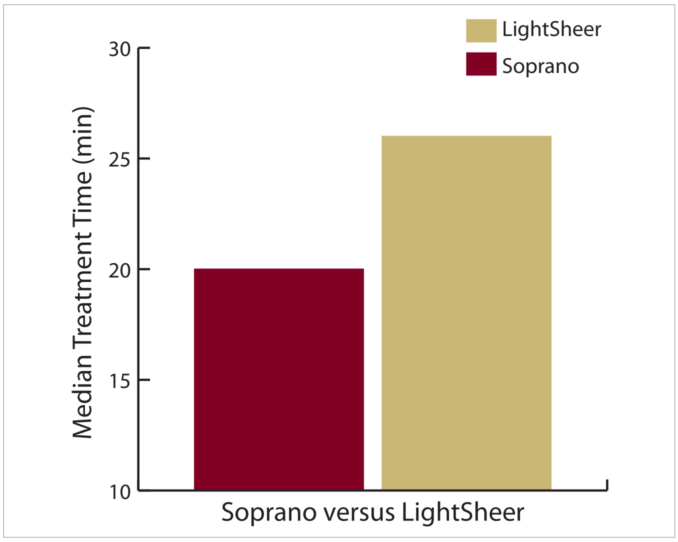
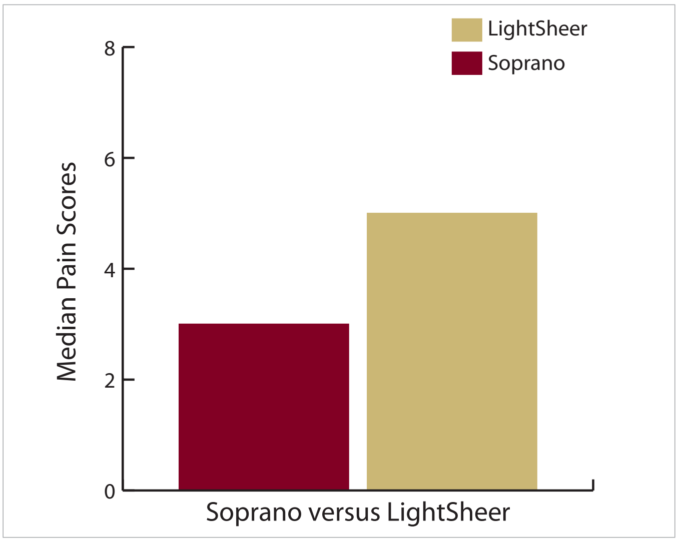


FIGURE 3. Graph comparing the overall median pain score data (0–10 scale) for Soprano XL in SHR mode (3) and LightSheer (5).



Study results showed the median pain scores of Soprano and LightSheer to be three and five, respectively, as measured on a 0–10 scale (0=no pain, 10=unbearable pain) over the five-treatment course (n=123). This result is highlighted graphically in Figure 3. IQR for each was 3.0 and 2.0, respectively. The difference between median overall pain scores for Soprano and LightSheer for treatments overall was 2.0, which is statistically significant (*P*<0.0001, Wilcoxon Signed Rank test).

DISCUSSION

Laser hair removal is painful, and can result in hypopigmentation or post-inflammatory hyperpigmentation, especially in dark skin tones. Lowering the energy should result in less pain and potential side effects, but this could theoretically affect efficacy. This study shows that low energy, high repetition diode laser pulses (ie. high average power) with the Soprano XL in SHR mode results in comparable hair reduction to the traditional high fluence single pass technique using the LightSheer laser. The Soprano XL in SHR mode has several advantages over traditional high fluence treatments, including less pain and a lower chance of adverse effects, especially with dark skin.

There are multiple techniques to reduce pain associated with laser hair removal, including topical anesthetic creams[10], tumescent anesthesia[11], topical non-steroidal anti-inflammatory creams[12], and cooling with cryogen which can also lead to permanent hypo- and hyperpigmentation.[13] Topical creams are expensive, time-consuming, and their injudicious use has resulted in deaths due to lidocaine toxicity.[14] In motion technique using low fluences reduces the pain associated with laser hair removal and has eliminated our need for any of the aforementioned techniques to improve tolerability. The median pain score was 3/10 for the Soprano, verses 5/10 for the LightSheer. This difference was statistically significant. Furthermore, the only high pain scores of 9 or 10/10 occurred during the first session with the LightSheer. Again, the patient with apprehensive anxiety may report a higher pain score on their first treatment session, and may not return for further treatments.

An advantage of the Soprano diode laser is that it can also be used as a high fluence diode laser, up to 120 J/cm^2. The high fluence one pass mode is easier to perform for hair removal near small, awkward areas like ears or upper lips. Repetitive passes would be difficult, if not impossible, to perform on those types of anatomical areas. A previous study by Krauss demonstrated that the Soprano diode laser is efficacious for hair removal in its high fluence mode, similar to other diode lasers.[15]

Due to Drs. Rox Anderson's and Parish's theory of selective photothermolysis, it has generally been assumed that one has to treat the hair follicle with one pulse of high laser energy sufficient to disable the hair follicle but not damage the surrounding tissue.[2] Laser manufacturers have designed their lasers to produce high energy pulses, with one pass at maximum tolerated fluence over the hair bearing skin. Since the laser photons have to cross the epidermal melanin in order to reach the melanin of the hair bulge and bulb, there exists the potential for adverse effects to the epidermis including hypo- and/or hyperpigmentation. Adverse effects increase with darker skin tones and higher fluences as these individuals have more epidermal melanin.[16,17] A recent histological study demonstrated that repetitive low energy diode laser pulses do induce necrosis of the follicular structures. Using the Soprano SHR mode, investigators treated 30 patients with a single Soprano SHR 810 nm diode laser session using the identical parameters used in this study. They examined 5 mm punch biopsies following a single treatment and demonstrated that the physical integrity of hair follicles was altered with inflammatory infiltrate, hair shaft detachment from its sheath, and perifollicular edema, related to incipient necrosis.[18] Although the present study did not include any histology, one can infer that multiple treatments will destroy more follicles than a single treatment.[16,17,18]

The reader may wonder how several smaller bursts of energy can induce necrosis of the hair follicle. The total energy delivered to the tissue with multiple passes exceeds the amount of Joules per cm^2 delivered with the conventional high fluence one pass technique. It is simple to calculate the mean amount of energy delivered to the tissue by multiplying the number of laser pulses by the joules per pulse, and dividing by the area (in cm^2). This figure was frequently in the range of 30-50 J/cm^2 which exceeded the 25–40 J/cm^2 used in the single high energy pass. The amount of energy is limited in the single pass high fluence diode laser technique due to tolerability of the tissue to a single laser pulse. One patient withdrew from the study: a Fitizpatrick type V skin female who sustained minor burns to her leg by the LightSheer. Despite assurances that we could reduce the fluence and treat her again safely with the LightSheer, she refused further treatments.

CONCLUSION

Treatment with the Soprano XL in SHR mode is significantly less painful than with the LightSheer. Both devices produced hair reduction counts in excess of 85% six months following the final treatment, and there were no significant differences in efficacy. Rapid pulse, low fluence constant motion laser hair removal with the 810 nm diode laser represents an advance in safety, efficiency, and tolerability of laser hair removal treatment. This type of laser hair removal represents a paradigm shift from conventional one pass, high fluence procedures. The Soprano XL in SHR mode provides a new level of safety for darker skin tones without compromising efficacy. Further study of this modality with larger populations and testing on different body areas would be beneficial to determine the optimal amount of average energy density required for the best results in various skin types.

DISCLOSURES

Dr. Braun is a consultant for Alma Lasers, Inc., and received a stipend for performing this study.

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November 2009 s18 Volume 8 • Issue 11 (Supplement)

ORIGINAL ARTICLES
Journal of Drugs in Dermatology

Purpura-Free Treatment of Lentigines Using A Long-Pulsed 595 nm Pulsed Dye Laser With Compression Handpiece: A Randomized, Controlled Study

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ABSTRACT

Background: Pulsed dye lasers (PDL) are one of the first, and popular, nonablative lasers for the treatment of rhytids and superficial pigmented lesions. Recent addition of a compression handpiece (CHP) allows treatments with minimal adverse effects.
Objectives: The purpose of this study was to investigate the efficacy and safety of new parameters of 595 nm PDL in the treatment of lentigines and wrinkles in the darker skin phototypes.
Materials and Methods: Ten female subjects with photodamaged skin were enrolled in this study. One side of the face received three monthly treatments with one pass of PDL with the fluence of 6 J/cm^2, 6 msec pulse duration followed by a second pass when lentigines were individually treated with CHP 6 J/cm^2, 6 msec with CHP. The untreated side served as control. Digital photography was used for global evaluation while the numbers of lentigines and wrinkles were analyzed by VISIA.
Results: All 10 subjects, aged 39–55 years, completed the study. The mean changes in numbers of lentigines at the twelfth week on the treated side was -6.1 (decrease), while that of the controlled side was +2.8 (increase) (P=0.075, paired t test). There was also a statistically significant difference in the degree of improvement of lentigines by global assessment (P=0.008, Wilcoxon signed rank test). No statistically significant difference in the degree of improvement of wrinkles analyzed by VISIA (P=0.490) and global assessment (P=0.157, Wilcoxon signed rank test) was observed. Hyperpigmentation was seen in two subjects.
Conclusion: The parameters of 595 nm PDL used in this study are effective and safe in the treatment of facial lentigines. There was no significant improvement in wrinkles in this study. A study limitation may be the relatively small sample size.

INTRODUCTION

A decade ago, Zelickson and colleagues were among the first to show that 450 microsecond, 585 nm pulsed dye laser (PDL) was of benefit in treating photodamaged skin.[1] Following that, several microsecond-domain lasers have been used to treat facial rhytids in a nonablative fashion, and in fact increase in collagen formation have been demonstrated by different techniques, such as suction blister,[2,3] histologic,[1,4–5] and ultrastructural analysis[1,4,6] as well as ultrasonography.[7] These shorter pulse durations are, however, associated with a significant risk of purpuras.[1]

Use of pulse duration longer than 10 msec can theoretically reduce the chance of purpura. In fact, in several studies it was documented that pulse durations longer than 6 msec are much less purpura-producing when compared with shorter ones, such as 0.5, 1.5 or 3.0 msec.[8–10] and evidently more so with the microsecond-domain pulse widths 1 and Q-switched lasers.

Treatment with long-pulsed dye lasers (LPDL), such as 595 nm PDL, also removes epidermal pigmented lesions, but is still associated with similar adverse effects, which results from the competing chromophore, the hemoglobin absorbing the laser fluences, resulting in extravasation. To overcome that, Kono et al. reported that addition of flat-glass compression hand piece (CHP) to the PDL treatment effectively improves epidermal pigmented lesions with no purpuras.[11,12] They then later reported that convex CHP together with the new pulsed dye laser, V-Beam Perfecta with the innovative train of eight micropulses, further improved the therapeutic outcome while reducing the adverse effects with better and more convenient compression of blood.[13]

Kono et al. proposed that to treat epidermal pigmented lesions, especially lentigines, the duration of laser pulses should match the thermal relaxation time of the epidermal basal layer,[11,13] approximately 1.6–2.8 milliseconds (for the 20-microns thick basal layer).[14,15] and thus, proposed that 1.5 milliseconds is the suitable pulse duration.[11] However, the authors feel that the laser pulses should target the entire epidermal layer, and not just the basal layer. Moreover, lentigines often display "lentiginous hyperplasia" resulting in even longer thermal relaxation time. Secondly, in the authors' experience the very same pulse duration (i.e., 1.5 msec), even at lower fluences used by Kono et al. and in other studies, often results in post-inflammatory hyper- and hypopigmentation in darker skin types of the Thai subjects.

The authors thus sought to investigate whether the use of longer pulse widths, above the purpuric threshold, will result in clinical improvement of rhytids and lentigines.

MATERIALS AND METHODS

The study protocol was approved by the ethics committee of Faculty of Medicine, Chulalongkorn University/King Chulalongkorn Memorial Hospital, Bangkok, Thailand. Written informed consent was obtained from each participant after enrollment.

Subjects

Female subjects, aged between 35 and 55 years, with moderate-to-severe photodamage (Fitzpatrick wrinkle severity scores between 4 and 9) were eligible for this study. Participants were recruited from the outpatient dermatology clinic at King Chulalongkorn Memorial Hospital.

Subjects with any dermatoses affecting the treatment areas, photosensitivity of any kind, keloidal tendencies, as well as those who were pregnant or lactating, were excluded. Patients who had had prior laser treatment, chemical peeling, dermabrasion or microdermabrasion, hormone replacement therapy or retinoid as well as alpha hydroxy acid within the past 12 months prior to enrollment were excluded. Subjects with grossly asymmetric facial structures, or those with more than a 20% difference in the number of lentigines, as documented by VISIA (Canfield Scientific, Fairfield, NJ), were also excluded.

Details regarding occupation, daily and cumulative sun exposures, photoprotection, smoking, medical history, prior cosmetic/procedural treatments were obtained at baseline visits.

Randomization

Patients were randomized to receive laser treatment to one cheek while the other cheek served as the control. Randomization was done by the treatment provider who simply drew one of the 10 cards, five of which read "right" and the other five read "left."

Laser Treatment

All laser treatments were performed by a single operator (PA). The 595 nm pulsed dye laser (V-Beam, Candela Corporation, Wayland, MA) was delivered in two successive passes, the first of which was delivered all over the cheek with minimal overlaps using the following parameters: 6 msec, 6 J/cm^2 with a 10-mm handpiece and DCD on time of 30 msec with a 20 msec delay. After a brief pause, this was then followed by a second pass, which was specifically delivered only to the lentigines with the following parameters: 6 msec, 6 J/cm^2 with a 7-mm compression handpiece without the cryogen. The authors' compression handpiece was made by simply attaching a clear, flat plastic plate to the handpiece provided by the company. No anesthesia was used for any pass. Laser treatments, using the very same settings were repeated every four weeks for a total of three treatments.

Subjects were observed for 30 minutes following each treatment, specifically for purpura or any other immediate adverse events. Visual analog scale (0–10) was used to evaluate pain during the treatment. After each treatment, sunscreen (Anthelios XL SPF 50, La Roche Posay) was dispensed and sun avoidance advised. Prior to each successive treatment, patients were questioned about satisfaction, adverse events and history of sun exposures during the treatment intervals.

Evaluation

At baseline and all successive visits thereafter, evaluation including VISIA digital photography and VISIA analyses of UV spots and wrinkles were carried out by an evaluator (SP) who was blinded as to the treatment allocation. Three board-certified dermatologists who were unaware of the treatment assignments graded the changes in clinical appearance of rhytids and lentigines, separately, from digital images, which were in random (and not always in the before-and-after) sequences by assigning scores ranging from -4 to +4. The grading system, used for both rhytids and lentigines, was as follows: 0=no improvement; 1=1–25% improvement; 2=26–50% improvement; 3=51–75% improvement; 4=76–100% improvement; -1=1–25% worsening; -2=26–50% worsening; -3=51–75% worsening; and -4=76–100% worsening.

Each participant also graded the overall satisfaction, using numerical scores of 0–4 as follows: 0=not satisfied, 1=minimally satisfied, 2=moderately satisfied, 3=markedly satisfied, and 4=most satisfied. Upon completion of the study, the subjects were asked if they wish to receive treatment on the other cheek. They were also asked specifically whether such treatment would be recommended to other people.

Statistical Analysis

Sample size calculation was based on pooled results from study by Tanghetti and co-workers.[8] Results are presented as mean ± SD. Student's t test and Wilcoxon signed-rank tests were used where appropriate. In all instances, $P<0.05$ was considered statistically significant. Statistical analysis was carried out with SPSS for Windows version 11.5 (SPSS Inc., Chicago, IL).

RESULTS

Of the 20 female subjects screened, 10 with skin types III and IV, mean age of 50.4 ± 5.66 (range 39–55), were enrolled and completed the study. The demographic data are summarized in Table 1. The subjects recruited were somewhat "naïve" to any aesthetic treatment. Specifically, only two had received ablative or nonablative laser treatment (more than 10 years prior to enrollment). No botulinum toxin, filler injections nor even topical retinoids or antioxidants were reported by these participants.

From VISIA analysis of UV spots, it was shown that the number of lesions on the laser-treated cheek decreased by 6.1 ± 0 lesions, while the number of lentigines on the control side did increase by 2.8 ± 6.8 lesions (P=0.075, paired + test) (Table 2).

These changes were reflected in the global assessment, which showed gradual and continuous improvement in the overall appearance of lentigines, as graded by dermatologists at each time point (Table 2). At four weeks, the average overall assessment scores were 0.6±0.84 and 0±0 for the laser-treated and control sides, respectively (P=0.063, Wilcoxon signed rank test). At 8 weeks, the average overall assessment scores were 0.7 ± 0.82 and 0 ± 0 for the laser-treated and control sides, respectively (P=0.038, Wilcoxon signed rank test). This difference was highly significant at 12 weeks where the average overall assessment scores were 0.9 ± 0.74 and -0.1 ± 0.32 for the laser-treated and control sides, respectively (P=0.008, Wilcoxon signed rank test) (Figures 1 and 2).

VISIA analysis of wrinkles did not show any changes whatsoever on either side of the face, while global assessment showed only modest improvement with the score of 0.2±0.42 on the laser-treated side and 0±0 on the control side (P=0.157, Wilcoxon signed rank test).

Adverse events developed in eight subjects. These included minimal erythema, lasting not more than 24 hours in six subjects and hyperpigmentation in two subjects. The hyperpigmentation developed within two weeks after the initial laser treatment in one subject and 10 days after the final treatment in the other. These brown spots gradually faded upon use of 4% hydroquinone cream within the following months. Average pain by visual analog scale was 2.44 ± 0.79 (range 1.2–3.7). Of note is the fact that no purpuras were seen in any subjects.

TABLE 1.

Demographic Data of Participants (n=10)	
Character	
Sex (female/male)	10/0
Age	
31–40	1
41–50	2
51–60	7
Skin Phototypes	
III	5
IV	5
Smoker/Non-Smoker	0/10
Daily Sun Exposures	
Less than two hours	7
Two to three hours	2
More than three hours	1
Use of Sunscreening Agent	
Never	
Occasionally	2
Regularly	7

Seven subjects were markedly satisfied with the results, while three stated that they were moderately satisfied. Even the two subjects who developed post-inflammatory hyperpigmentation were pleased with the outcome. Nine subjects decided to receive treatment to the other cheek and would recommend it to their friends.

DISCUSSION

This study demonstrates that the use of pulse duration above the purpuric threshold can safely improve lentigines. Specifically no purpuras were seen. This is a significant finding as pointed out above that using 1.5 msec pulse duration, even at lower fluences and compression handpiece, often results in hyper- and hypopigmentation in the darker skin types, especially when treatments are delivered in the sunny climates. An interesting observation by Tanghetti et al.[8] and Galeckas et al.,[16] which is similar to the authors' is that subjects with more dyspigmentation had greater benefits from the laser treatment (Tables 2 and 3).

Treating superficial pigmented lesions with Q-switched lasers, such as QS-ruby,[17,18] Nd:YAG,[17,19] frequency-doubled Nd:YAG[19] and alexandrite lasers, which were popular in the 1990s, is associated with significant pain,[19] even when used in conjunction with topical anesthesia,[17] purpura,[17] as well as crusting.[18] This is significantly lessened with the use of nonablative laser

FIGURE 1. Patient at baseline.

FIGURE 2. Patient after two laser treatments.

systems with pulse durations in the micro- and millisecond domains. This could be due to the fact that long-pulsed lasers produce only photothermal and not photo-acoustic effect.[11] Indeed, when compared with Q-switched ruby laser [11] and intense pulsed light[12] pulsed dye laser with CHP produces significantly superior results, with much fewer adverse events.[11] Another "advantage" of the newer systems is that each "macropulse" contains 8 micropulses allowing for better and more uniform energy delivery resulting in higher purpura threshold. Although this system is a more conventional system with 4 micropulses,

TABLE 2.

Changes in the Number of Lentigines and Global Assessment

Subject #	Treatment Assignment	Lentigines (VISIA analysis)			Global Assessment
		Baseline	12 Weeks	Change at 12 Weeks From Baseline	Change at 12 Weeks from Baseline
1	Laser	53	53	0	0
	Control	50	52	2	-1
2	Laser	98	94	-4	1
	Control	90	92	2	0
3	Laser	74	74	0	1
	Control	87	88	1	0
4	Laser	39	47	8	0
	Control	40	43	3	0
5	Laser	69	71	2	1
	Control	68	66	-2	0
6	Laser	60	68	8	1
	Control	75	76	1	0
7	Laser	103	91	-12	0
	Control	91	109	18	0
8	Laser	91	65	-26	2
	Control	78	80	2	0
9	Laser	105	92	-13	2
	Control	120	129	9	0
10	Laser	116	92	-24	1
	Control	95	87	-8	0
Mean ± S.D.	Laser	80.8 ± 25.51	74.7 ± 17.09	-6.1 ± 0	0.9 ± 0.74
	Control	79.4 ± 23.01	82.2 ± 25.42	+2.8 ± 6.8	-0.1 ± 0.32

Global assessment scores: 0=no improvement; 1=1–25% improvement; 2=26–50% improvement; 3=51–75% improvement; 4=76–100% improvement; -1=1–25% worsening; -2=26–50% worsening; -3=51–75% worsening; and -4=76–100% worsening.

the authors obtained similar results to other reports (Table 3).

This study demonstrated that statistically significant improvement in clinical appearance of lentigines can be achieved with pulsed dye laser as evident from global assessment by dermatologists. This was similarly reflected in the VISIA analysis of the UV spots, although this latter outcome did not quite reach statistical significant levels. This probably resulted from the fact that most improvement was in the quality of lentigines and really not the number. Whether increasing the number of sessions will result in further improvement remains to be seen.

One advantage of pulsed dye laser is that different features of photoaging (e.g., dyschromias, telangiectasias and rhytids) can be treated at the same time, similar to IPL treatment.[16,20] By investigating the treatment of wrinkles with nonablative lasers, several groups have reported similar results with the pulsed dye laser. Using the same parameters as the authors' first pass, Rostan et al. showed that 66% of subjects with moderate facial wrinkles and virtually all with severe wrinkles had significant improvement after receiving four monthly treatments, which was clearly superior to the results obtained from coolant.[21] Mild erythema immediately after treatment is extremely commonly observed[10] and this also took place on the coolant-only side.[21] Other settings such as 10 msec pulse duration, fluence of 7 J/cm^2, reported by Tay et al. have also been used with resultant mild to moderate improvement and minimal adverse effects.[22] Similarly, Bernstein used 10 mm spot size, 10 msec pulse duration, and fluences ranging from 8–10 J/cm^2 [10] and finally Kono and co-workers used 7 mm spot size, 20 msec pulse duration, and fluences of 10–12 J/cm^2.[12] Purpura is extremely rare with these settings.[10] Moreover, hyper- and

TABLE 3.

Results of Long-Pulse Pulsed Dye Laser in the Treatment of Epidermal Pigmented Lesions

	Subjects	Number of Tx	Spot Size (mm)	Pulse Duration (msec)	Fluence (J/cm2)	Results	Adverse Events
Kono et al.[11] 2006 n=18	Japanese skin types III–IV	One	7 CHP (flat glass)	1.5	10–13	83.3±12.9 % improvement*	Mild erythema, no purpura or dyspigmentation
Kauvar et al.[9] 2006 n=21	Skin types I–III	Three every four weeks	7 CHP	1.5-3	9	Significant improvement	Minimal pain, no purpura
Bernstein et al.[10] 2007 n=11	Skin types I–II	Three every four weeks	10 CHP	10	7.5–8.0	Variable degree of improvement	Purpura in 1/33 sessions
Kono et al.[12] 2007 n=10	Japanese skin types III–IV	Three every four weeks	7 CHP (flat glass)	1.5	9–12	81.1% lightening*	None
Kono et al.[13] 2007 n=54	Japanese skin types III–IV	One	7 CHP (convex)	1.5	9–13 (mean 10.8)	84.4 % lightening*	Hyperpigmentation in 1/54, no purpura or scar
Galeckas et al.[16] 2008 n=20	Skin types I–III	Three every three to four weeks	10 CHP (convex)	1.5	6.5–8.0	-84.75% improvement for "dark" lentigines -62.75% improvement for "light" lentigines	Minimal pain and infra-orbital edema, purpura not directly mentioned
Galeckas et al.[20] 2008 n=10	Skin types I–III	Three every three to four weeks	10 CHP (convex)	1.5	6.5–8.0 (mean 7.2)	-86.5% improvement for "dark" lentigines -65% improvement for "light" lentigines	-Minimal pain and infra-orbital edema -Purpuras in 10% of treatments
Present Study n=10	Thai skin types II–V	Three every four weeks	7 CHP (flat)	6.0	6.0	Significant improvement	Hyperpigmentation in 2/10, no purpura

CHP: Compression handpiece
*Assessed by reflectance spectrometer

hypopigmentation are not commonly seen.[10] Most importantly, scarring has never been reported.[10]

Interestingly, there are variable responses in the different regions of the face. Notably, the peri-orbital area tends to respond best to the various nonablative laser rejuvenation systems.[23,24] Tay et al. theorized that this could be due to the thinness of the skin in that particular region.[22] The laser treatment used by the authors was performed mostly in the cheek area and in fact, the peri-orbital areas were not treated. This could have resulted in the fact that modest results were obtained with regards to rhytids.

The longer pulse duration used in this study reduces the chance of adverse events. No purpura was seen in any subjects. Pain was minimal and compares relative well with that seen in other studies.[9]

Transient hypopigmentation has been observed in some subjects who underwent the treatment while having suntans.[9] This was not observed in this study. On the other hand, the authors saw hyperpigmentation lasting a few months, which developed in two subjects. Upon detailed history, they admitted spending hours in the afternoon sun while commuting home, despite the fact that strict sun avoidance was advised. The authors believe this is the result of laser treatment over tanned skin and not cryogen burn.

CONCLUSION

The authors have demonstrated that 595 nm PDL at longer pulse duration can be used to effectively and safely treat lentigines. Further modifications will certainly improve the therapeutic outcome of this long-pulsed dye laser. Limitations in this study are small sample size and relatively short-term follow-up, especially with regard to treatment of wrinkles

DISCLOSURES

The authors disclose no conflicts of interest.

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This supplement to the *Journal of Drugs in Dermatology* is supported by
Alma Lasers, Candela Corporation, Cynosure, and Syneron.

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