Objectives: To evaluate the use of multiple, low-energy, full-face plasma skin regeneration treatments.

Design: Plasma skin regeneration delivers energy to the skin through plasma pulses induced by passing radiofrequency into nitrogen gas. Single-treatment, high-energy, 1-pass treatments have been demonstrated to achieve good results with an excellent safety profile. Eight volunteers underwent full-face treatments every 3 weeks, for a total of 3 treatments, using energy settings of 1.2 to 1.8 J. Before each subsequent treatment, the quality of regenerated epidermis, the degree of downtime, and erythema were recorded. Full-thickness skin biopsy specimens were obtained from 6 patients before treatment and 90 days following the last treatment. Patients were seen for follow-up 4 days after each treatment and 30 and 90 days after the third treatment.

Results: Three months after treatment, investigators found a 37% reduction in facial rhytids and study participants noted a 68% improvement in overall facial appearance. Reepithelialization was complete in 4 days. Patients assessed erythema to persist an average of 6 days after treatment. Epidermal regeneration from the first treatment was longer than from the following treatments (9 vs 4 and 5 days, respectively). One patient developed localized hyperpigmentation after the first treatment, which resolved by follow-up at day 30. No scarring or hypopigmentation occurred. A histologic evaluation 3 months after treatment revealed a band of new collagen at the dermoepidermal junction with less dense elastin in the upper dermis. The mean depth of new collagen was 72.3 µm.

Conclusions: Plasma skin regeneration using the multiple low-energy treatment technique allows significant successful treatment of photodamaged facial skin with minimal downtime. Results are comparable to a single high-energy treatment, but with less healing time.

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Plasma skin regeneration (PSR) technology uses energy delivered from plasma rather than light or radiofrequency. Plasma is a unique state of matter in which electrons are stripped from atoms to form an ionized gas. The plasma is emitted in a millisecond pulse to deliver energy to target tissue upon contact without reliance on skin chromophores. The PSR device (Portrait PSR; Rhytec Inc, Waltham, Mass) is cleared by the US Food and Drug Administration for multiple, single-pass, low-energy treatments and single-treatment, 1-pass, high-energy treatment of facial rhytids and for the treatment of superficial skin lesions.

The technology can be used at varying energy settings for different depths of effect, from superficial epidermal effects similar to microdermabrasion to deeper dermal heating similar to carbon dioxide resurfacing. Preliminary studies examining a single pass of 1 to 4 J over postauricular skin showed that at 1 to 2 J, thermal energy was limited to the epidermis and dermoepidermal junction. At 3 and 4 J, thermal injury reached the papillary dermis (averaging 8.2 and 11.8 µm, respectively). Studies have focused on high-energy single treatments for acne scarring or wrinkle reduction. High-energy treatments are successful but can be limited by postprocedure healing periods of a week or more. This study was conducted to see if equivalent results with less downtime could be achieved with multiple treatments at low energy.
METHODS

PATIENT SELECTION

The study was open to patients of all skin types with significant photoaging. Subjects who had undergone any skin resurfacing procedure within the previous year or any nonablative rejuvenation procedure or adjunctive aesthetic treatment (such as chemical peels or treatment with topical tretinoin, botulinum toxin, or fillers) within the previous 6 months were excluded from the study. Exclusion criteria also included a history of keloid formation, active oral herpesvirus, and a history of collagen vascular disorders.

PSR DEVICE

The PSR device consists of an ultra–high-frequency radiofrequency generator that excites a tuned resonator and imparts energy to a flow of inert nitrogen gas within the handpiece. The activated ionized gas is termed plasma and has an optical emission spectrum with peaks in the visible range (mainly indigo and violet) and near-infrared range. Nitrogen is used for the gaseous source because it is able to purge oxygen from the surface of the skin, minimizing the risk of unpredictable hot spots, charring, and scar formation. On formation, the plasma is directed through a quartz nozzle out of the tip of the handpiece in a 6-mm-diameter spot. As the plasma hits the skin, energy is rapidly transferred to the skin surface, causing instantaneous heating in a controlled uniform manner, without an explosive effect on tissue or epidermal removal.

The depth of thermal effect is determined by the energy setting. The energy can be adjusted from 1 to 4 J per pulse. There is a self-calibration feature within the generator that verifies that the energy delivered matches the preset level. The frequency of pulses can be varied from 1 to 4 Hz.

CLINICAL PROTOCOL

After obtaining institutional review board approval, 8 participants underwent full-face treatments every 3 weeks, for a total of 3 treatments. All patients were educated about the risks, benefits, and potential adverse effects of the procedure, and informed consent (written and oral) was obtained. Energy settings of 1.5 to 1.8 J were used over the forehead, cheeks, chin, and upper lip, while energy settings of 1.2 to 1.4 J were used over the eyelids, nose, and perimeter of the face (Figure 1). A range of energy settings was allowed because, to our knowledge, this was the first low-energy full-face study to be performed and treatment protocol guidelines had not yet been established. Preliminary studies had shown that at energy pulses up to approximately 2 J, thermal injury was limited to the epidermis and the dermoeipidermal junction, but precise levels had not been defined.

Patients arrived an hour before the procedure for the application of topical anesthesia without occlusion or prior skin preparation (LMX-5; Ferndale Laboratories, Inc, Ferndale, Mich). Oral analgesia (1 combination tablet of hydrocodone, 7.5 mg, and acetaminophen, 750 mg; or 1 combination tablet of propoxyphene, 100 mg, and acetaminophen, 650 mg) was administered 30 to 45 minutes before the procedure. Before each subsequent treatment, the degree of overall facial rejuvenation and rhytid improvement was recorded along with any adverse effects, such as scarring, persistent erythema, or edema. Photographs were taken before and 4 days after each treatment, and at the 1- and 3-month posttreatment follow-up visits (FinePix S2 Pro camera; Fujifilm, Tokyo, Japan).

Each subject’s face was divided into aesthetic segments, and the topical anesthesia was removed from each segment with a dry gauze immediately before treatment of that facial zone (Figure 1). Plasma regeneration was performed 1 segment at a time until the entire face was completed in an attempt to have a constant delay time between anesthetic removal and operative start time.

The tip of the handpiece was held 5 mm from the skin’s surface to allow a 6-mm area of contact between the plasma pulse and the skin. Pulses were delivered in a paintbrush fashion without overlap across the treatment area (Figure 2). Wet gauze was used to protect the hairline, eyebrows, and eyelashes. En-
ergy settings used for each treatment zone can be found in Figure 1. To avoid lines of demarcation, the edges of the face bordering the hairline and neck were feathered by increasing the distance of the nozzle from the surface of the skin to about 1 cm. This reduces the amount of plasma in contact with the skin and, thus, decreases the heat energy delivered. After treatment, patients were instructed to avoid sun exposure and apply a bland ointment to the face at least 3 times daily while the skin was healing.

**CLINICAL ANALYSIS**

Subjects were seen for digital photographs and examination on the fourth day following each procedure and at 1 and 3 months postprocedure. Investigators (M.A.B. and others) were asked to rate the degree of reepithelialization, erythema, and hyperpigmentation or hypopigmentation and the presence of any scarring. Investigators also ranked patients on a 9-point facial rhytid scale. This was done by comparing live subjects with 9 stock photographs of individuals with increasingly severe rhytids and solar elastosis. Investigators were blinded to the patient’s baseline photograph, so improvement was measured solely by movement toward 0 on the facial rhytid scale.

Patients were asked to evaluate skin smoothness, satisfaction with the procedure, and percentage improvement in overall facial rejuvenation. Patients did not have access to the photographic facial rhytid scale used by the investigator.

**HISTOPATHOLOGIC ASSESSMENT**

Full-thickness skin biopsy specimens (2-mm punch biopsy specimens of the upper cutaneous lip) were obtained before treatment and 90 days following the last treatment from 6 of the 8 patients participating in the study. Two patients did not consent to the biopsy procedure.

Histologic samples were prepared and analyzed at Northwick Park Institute for Medical Research, London, England. Complete samples were processed by routine automated procedures. Sections were cut at 5-µm thickness for staining with hematoxylin-eosin, the Hart modification of Miller elastin, and picrosirius red 34B.

Sections were examined for epidermal thickness, thickness of the collagen band at the dermoepidermal junction, thickness of the zone of collagen change, and the presence of neocollagenesis. Five direct measurements of each of the thicknesses were taken, and the mean of those was calculated for each feature for each patient for pretreatment and posttreatment samples.

**RESULTS**

**IMMEDIATE TREATMENT EFFECTS**

The procedure was well tolerated, with minimal discomfort after the use of topical anesthesia and adjunctive oral analgesia. Postoperative discomfort was rated as 2.3 on a scale of 1 (no discomfort) to 10 (extreme discomfort). Each treatment session took approximately 15 to 20 minutes to complete.

The degree of epidermal destruction and reepithelialization varied within the treatment series, with the first treatment having greater epidermal destruction and a longer healing time than subsequent treatments. Reepithelialization was judged by the investigator to be between 25% and 50% of normal 4 days after the first treatment, approxi-
mately 80% of normal 4 days after the second treatment, and completely reepithelialized 4 days after the third and final treatment. In terms of healing time, patients self-assessed an average of 9 days of downtime (peeling and posttreatment erythema) after the first treatment, 4 days after the second treatment, and 5 days after the third treatment. The nonviable epidermis remained intact on all patients until reepithelialization was complete underneath, and was gradually shed by mild desquamation. No patients had exposed denuded dermis at any point in the treatment series. All subjects experienced complete reepithelialization when they returned for the next treatment, performed at 3-week intervals.

The average investigator-assessed erythema rating 4 days after treatment was 1.6 on a 5-point scale (0 indicates none; 1, minimal; 2, mild; 3, moderate; and 4, severe). By 3 weeks, erythema decreased to 0.8.

One patient developed localized hyperpigmentation after the first treatment. Subsequent treatments were performed as scheduled, and the hyperpigmentation decreased slightly after each treatment and was resolved 1 month after the end of the treatment series without the use of bleaching agents. No instances of hypopigmentation or scarring were noted.

POSTTREATMENT FOLLOW-UP

One month after treatment, 1 subject had minimal remaining facial erythema and 7 subjects had no erythema. There were no instances of hyperpigmentation, hypopigmentation, or scarring at the 1- or 3-month follow-up visit.

Investigators rated the patients to have a 23% improvement in facial rhytids at the 1-month follow-up and a 37% improvement in facial rhytids at the 3-month follow-up (Figures 3, 4, and 5). Two patients (25%) had considerable facial tightening when comparing poststudy photographs with those at baseline. Participants rated themselves to have an average 35% improvement in overall facial rejuvenation after 1 treatment, 40% improvement after 2 treatments, 58% improvement 1 month after 3 treatments, and 68% improvement 3 months after 3 treatments. All 8 subjects stated that they would recommend the treatment to others at the final 3-month follow-up.

HISTOLOGIC FEATURES

Pretreatment histologic samples revealed solar elastosis with a narrow well-marked collagen band at the dermo-epidermal junction. Posttreatment samples revealed an increase in the thickness of the band of collagen at the dermoepidermal junction and consistently more dermal collagen (Figure 6). In the pretreatment samples, the zone of collagen change showed a dense accumulation of elastin, but in the posttreatment samples, this zone contained less dense elastin with significant interdigitation of new collagen. The mean depth of new collagen was 72.3 µm. Epidermal thickness was not changed by the treatment.
Previous research has shown that the PSR device using ablative energy settings (3-4 J) can induce significant skin tightening and textural improvement similar to single-pass carbon dioxide laser resurfacing. In a pilot study evaluating the use of a single full-facial treatment at high energy (3-4 J), Kilmer et al demonstrated a mean improvement in overall facial rejuvenation of 50% by 1 month. Potter et al used silicone molding to demonstrate a 39% decrease in fine line depth 6 months after 1 high-energy, full-face, ablative treatment.

The present study examined a series of 3 full-face treatments using energy settings of 1.2 to 1.8 J. We found a 37% improvement in facial rhytids 3 months after 3 low-energy treatments, comparable to the 39% improvement seen 6 months after 1 high-energy single-pass treatment in the study by Potter et al. Study participants rated themselves as having a 68% improvement at 3 months' follow-up. The discrepancy between the investigator and subject evaluations could have been because of the participants focusing more on improvements in dyspigmentation rather than facial rhytids because they were asked to evaluate overall improvement in skin rejuvenation. The investigators subjectively noted that the greatest improvement after PSR seemed to be in dyspigmentation, although this end point was not formally evaluated in the current protocol. Further studies are needed to determine whether results at long-term follow-up from low-energy multiple treatment protocols remain comparable to that of single-pass high-energy treatments.

The healing time in our study averaged approximately 5 days per treatment; however, this was a patient-assessed number that included days it took for any residual redness and peeling to completely resolve. The average erythema rating as assessed by the physician at 4 days' follow-up was only minimal (1.6 on a 4-point scale). Less than 20% of the face still had superficial peeling 4 days after the second treatment, and there was no residual peeling 4 days after the third treatment. While nearly a week of healing time may not seem to be an improvement over other minimally invasive resurfacing procedures and micropeels, the intensity of the healing process is quite minor, which makes it an attractive option for many patients.

Study participants had a longer healing time after the first treatment (9 days) than after the second and third treatments (4-5 days). During the healing time, patients had symptoms of erythema and superficial epidermal desquamation. The reason for the longer healing time after the first treatment is not clear; however, it may be that the first treatment removes much of the photodamaged skin and primes the skin for further treatments. It could also be that the newly regenerated skin has a greater hydration content and absorbs less of the plasma energy, or that the newly regenerated skin has up-regulation of certain growth factors used in the wound healing process. In the future, it may be useful to perform the first treatment in the series at slightly lower-energy settings.

Figure 5. Facial appearance before (A) and 3 months after (B) plasma skin regeneration, with improvement in brown mottled pigmentation and overall skin texture. Investigator-rated improvement on the 9-point facial rhytid scale changed from 3 (before regeneration) to 2 (after regeneration); patient-rated improvement in overall skin rejuvenation was 65%.
and to increase progressively as tolerated. This would likely avoid the extended length of recovery time from the first treatment, but further studies would have to be done to determine whether the end result would be affected.

In the high-energy study by Kilmer et al, patients had progressive improvement in the quality of their skin at the 9-month follow-up. While our study was performed with repeated low-energy treatments, longer follow-up (6-12 months) may or may not show more improvement. In addition, the lack of hypopigmentation is encouraging, but there may still be a possibility of delayed hypopigmentation at long-term (9-12 month) follow-up, as seen after other resurfacing procedures; to our knowledge, there have been no known reports thus far.

Compared with other minimally invasive resurfacing procedures, patients with mild to moderate wrinkling have had about a 50% improvement in rhytids after erbium: YAG laser resurfacing, with an average 3 to 4 days of crusting. The low-energy plasma regeneration treatments offer a lower percentage of improvement; however, the recovery time is less intense, with no crusting or denudation. Fractional photothermolysis, like PSR technology, is a relatively new technique and few studies have been published evaluating its results on rhytids. Preliminary studies on fractional photothermolysis for the treatment of periorbital rhytids revealed mild improvement in 12% of patients, noticeable improvement in 30% of patients, and moderate to significant improvement in 54% of patients 1 month after 4 treatments. The study is
difficult to compare with our current one, however, because no precise variables for the terms mild, noticeable, and moderate are defined.

In conclusion, repeated low-energy PSR treatment is an effective modality for improving dyspigmentation, smoothness, and skin laxity associated with photoaging. Histologic analysis of posttreatment skin confirms the production of new collagen and remodeling of dermal architecture. Posttreatment changes consist of erythema and superficial epidermal desquamation without denudation, generally complete by 4 to 5 days.

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