Advances in plasma skin regeneration

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Summary

Plasma skin regeneration (PSR) is a novel method of resurfacing that uses plasma energy to create a thermal effect on the skin. PSR is different from lasers, light sources, and ablative lasers in that it is not chromophore dependent and does not vaporize tissue, but leaves a layer of intact, desiccated epidermis that acts as a natural biologic dressing and promotes wound healing and rapid recovery. Histological studies performed on plasma resurfacing patients have confirmed continued collagen production, reduction of elastosis, and progressive skin rejuvenation beyond 1 year after treatment. PSR has received US Food and Drug Administration 510 (k) clearance for treatment of rhytides of the body, superficial skin lesions, actinic keratoses, viral papillomata, and seborrheic keratoses. PSR also has beneficial effects in the treatment of other conditions including dyschromias, photoaging, skin laxity, and acne scars. The safety profile of PSR is excellent, and there have been no reports of demarcation lines in perioral, periorbital, or jawline areas, as can sometimes be observed following CO_2 resurfacing. PSR is effective in improving facial and periorbital rhytides and can be used on nonfacial sites, including the hands, neck, and chest. Numerous treatment protocols with variable energy settings allow for individualized treatments and provide the operator with fine control over the degree of injury and length of subsequent recovery time.

Keywords: facial rejuvenation, plasma resurfacing

Introduction

Laser resurfacing continues to be the most effective treatment for skin rejuvenation. Although numerous nonablative modalities have been developed over the years, none of them is able to deliver results equivalent to ablative devices. The effectiveness of ablative lasers results from their ability to completely vaporize the epidermis, thereby removing unwanted pigment and solar-damaged cells. Deeper penetration and diffusion of thermal energy heats dermal tissues, causes tissue contraction, and stimulates new collagen production. These processes culminate in the elimination of solar elastosis, yielding a brighter and more lustrous skin tone and reduction in wrinkles and laxity.

Plasma skin regeneration (PSR) employs the use of plasma, the fourth state of matter. Plasma is a gas-like state of matter composed of ionized atoms. Ionization occurs when sufficient energy is applied to the gas so that electrons can escape from their atoms leaving the atoms positively charged. When the electron is "recaptured" by a positively charged atom, energy is emitted or stored by vibration and rotation of the gas molecules. Nitrogen plasma releases its energy in the form of heat, and this thermal energy can be channeled onto a target (Fig. 1). The Portrait® PSR system (Rhytec Inc., Waltham, MA, USA) creates a pulse of ultrahigh radiofrequency energy from the device generator (Fig. 2a) that subsequently

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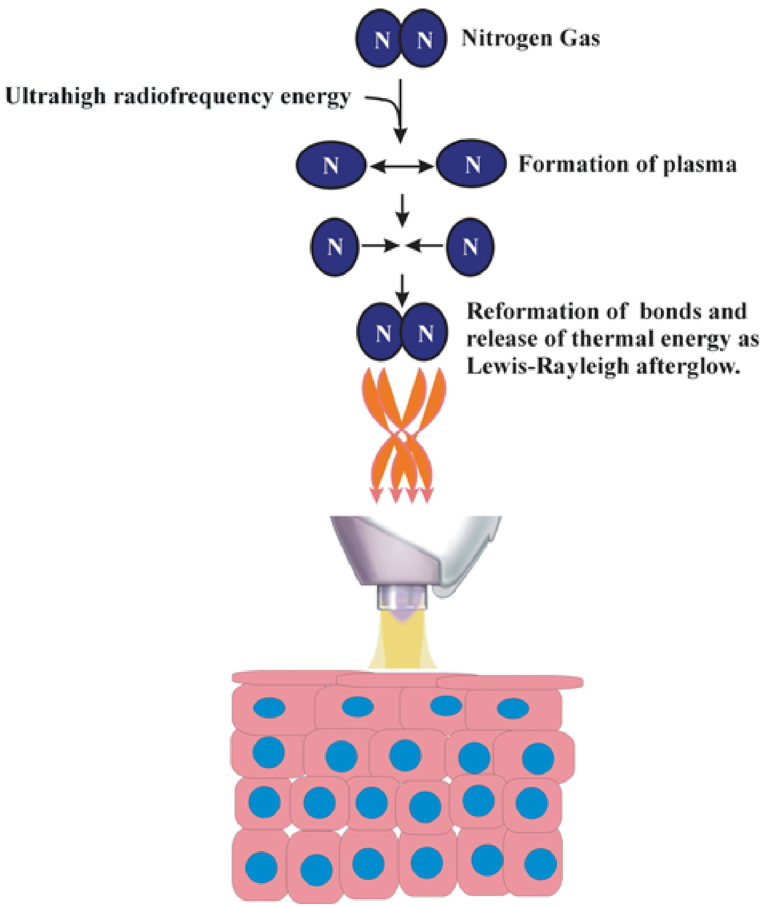

Figure 1 Plasma generation. An ultrahigh frequency radiofrequency generator excites a tuned resonator and imparts energy to nitrogen gas molecules flowing through the handpiece resulting in their ionization. The plasma is directed through a quartz nozzle out of the tip of the handpiece and onto the skin, and appears as a characteristic lilac glow that transitions to a yellowish light called a Lewis–Rayleigh afterglow.

converts nitrogen gas into plasma within the handpiece. Nitrogen is used for the gaseous source because it purges oxygen from the skin surface, thereby minimizing the risk of unpredictable hot spots, charring, and scar formation. The plasma emerges from the distal end of the device handpiece (Fig. 2b), immediately transferring the stored thermal energy to the skin surface. This process exhibits a very low thermal time constant so it is virtually instantaneous. Each pulse of plasma energy is released onto the target in a Gaussian distribution and produces uniform tissue heating. The handpiece does not come in direct contact with the skin, and a blue non-contact illuminated targeting ring enables the user to maintain the plasma pulse at an optimal angle and distance from the skin surface (Fig. 2c). In contrast to ablative lasers, plasma resurfacing leaves a layer of intact, desiccated epidermis that acts as a natural biologic dressing and promotes a more rapid recovery than would be observed with ablative treatments. The desiccated tissue sloughs over the ensuing 4–5 days, leaving a new epidermis formed beneath. PSR is by definition nonablative, not chromophore dependent, and rapid thermal penetration of the skin produces zones of thermal damage and deeper zones of thermal modification with increased fibroblast activity. PSR can be used safely in Fitzpatrick skin types I–IV (no clinical studies to date have been performed for skin types V and VI). PSR has a favorable safety profile, and in contrast to the CO_2 laser, hypopigmentation or demarcation lines in treated perioral, periorbital, or jawline areas are not observed.

Histology and thermal penetration

The deep thermal effects of PSR act in a unique fashion, but with some similarity to that of CO_2 or erbium lasers. First, immediate tissue contraction is accomplished via thermal denaturation of dermal collagen. Second, thermal disruption of solar elastosis and activation of fibroblasts stimulate a wound healing cascade necessary for

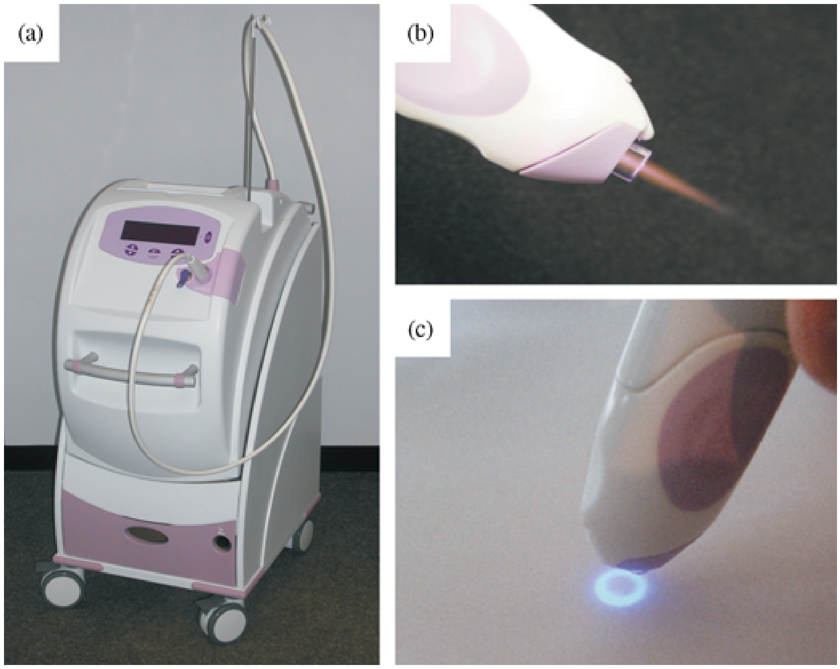

Figure 2 Plasma skin regeneration (PSR) using the Portrait® PSR. The plasma-generating device (a) and handpiece (b) with plasma energy emanating from tip are shown. Appearance of blue non-contact illuminated targeting ring used for gauging appropriate incident angle and distance from skin surface (c). (Modified and reproduced with permission from Rhytec, Inc.)

neocollagenesis and reduction of solar elastosis. With plasma, the effects do not produce explosive vaporization and are more uniform than with ablative lasers because plasma does not depend on interaction with a chromophore. Histologically, immediately after a high-energy (3.5 J) treatment, an intact and nonablated epidermis with vacuolation of the basal cell layer is visible (Fig. 3a). Four days after treatment, a line of cleavage can be noted, which demarcates shedding epidermal and dermal remnants from newly formed stratum corneum and regenerated epidermis and upper dermis (Fig. 3b). The overlying epidermal and dermal remnants serve as a biologic dressing. Ten days after treatment with 3.5 J, a fully regenerated epidermis is noted without basal cell layer vacuolation, and the zone of thermal modification, typified by an intense fibroplasia within the papillary and upper reticular dermis, can be appreciated (Fig. 3c). Continued collagen production is observed for up to 1 year after treatment (Fig. 3d–f). Histological studies have also demonstrated that the depth of cleavage is directly related to the pulse energy of the treatment (Fig. 4). Clinically visible improvements following PSR are a function of thermal penetration and dermal collagen denaturation, a process that requires temperatures of ≥ 60 °C.[1] Through finite element analysis, pulse energies of 4.0 J have been shown to result in thermal penetration well into the reticular dermis, such that temperatures of 60 °C reach a depth of 600 μm in normally hydrated skin (Fig. 5).

Treatment protocols

Several treatment protocols are available to treat the full range of patient conditions, and these can be categorized based on severity of rhytides, outcome expectations, and recovery times (Table 1). The very low energy (VLE) protocol is a minimal recovery time procedure with 0.5 J pulse energy that is roughly equivalent to other "lunchtime" procedures for facial skin rejuvenation. PSR NF (low energy) uses pulse energies ranging up to 1.8 J and 2.5 J for dorsal and ventral surfaces, respectively, and improvements in chest, neck, and dorsal hand skin have been recently demonstrated (Moy and Fincher, unpublished; Alster and Konda[2]). PSR3 (high energy) utilizes 3.0–4.0 J pulse energies and can be used as a more aggressive treatment for facial skin resurfacing that produces a degree of injury similar to single-pass CO_2 resurfacing laser, but is histologically different from CO_2 resurfacing in that the epidermis is not ablated and remains intact following treatment. Other protocols (e.g., PSR1, PSR2, PSR2/3) can be used to treat the full face or regional areas and are further detailed in Table 1.

Other clinical applications of plasma

The Portrait® PSR system is currently the only commercially available gas plasma resurfacing system to date. In some surgical systems, plasma acts as a conduit for delivering energy or is a by-product. A previous technology, coblation,

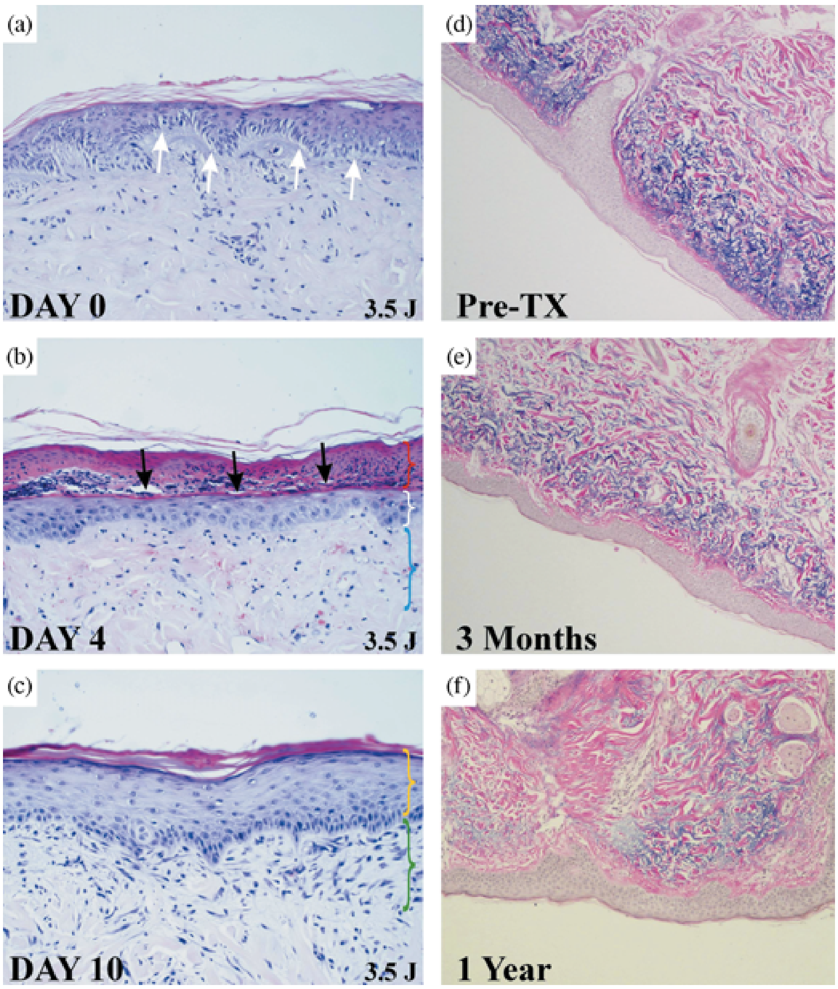

Figure 3 Histological changes following treatment with high-energy plasma skin regeneration (PSR). Immediately after treatment, vacuolation of basal cell layer (white arrows) is noted at the dermoepidermal junction (a). Four days after treatment with 3.5 J, a developing line of cleavage (black arrows) between zones of thermal damage and thermal modification are noted. The zone of thermal damage (red bracket) containing epidermal and dermal remnants is being shed above the developing line of cleavage. Regenerated epidermis (white bracket) and the evolving zone of thermal modification in dermis (blue bracket) are also visible (b). Ten days after treatment with 3.5 J, a regenerated normal appearing epidermis is noted (yellow bracket). The zone of thermal modification (green bracket) is typified by an intense fibroplasia in the papillary and upper reticular dermis (c). Solar elastosis with narrow well-demarcated collagen band at the flattened dermoepidermal junction (d). A 30% reduction of the depth of elastosis is noted, with a widening of the collagen band at the dermoepidermal junction as new collagen is laid down (e). Continued reduction in density of elastosis with in-growth of regenerated reticular collagen is noted (f). (Modified and reproduced with permission from Rhytec Inc.)

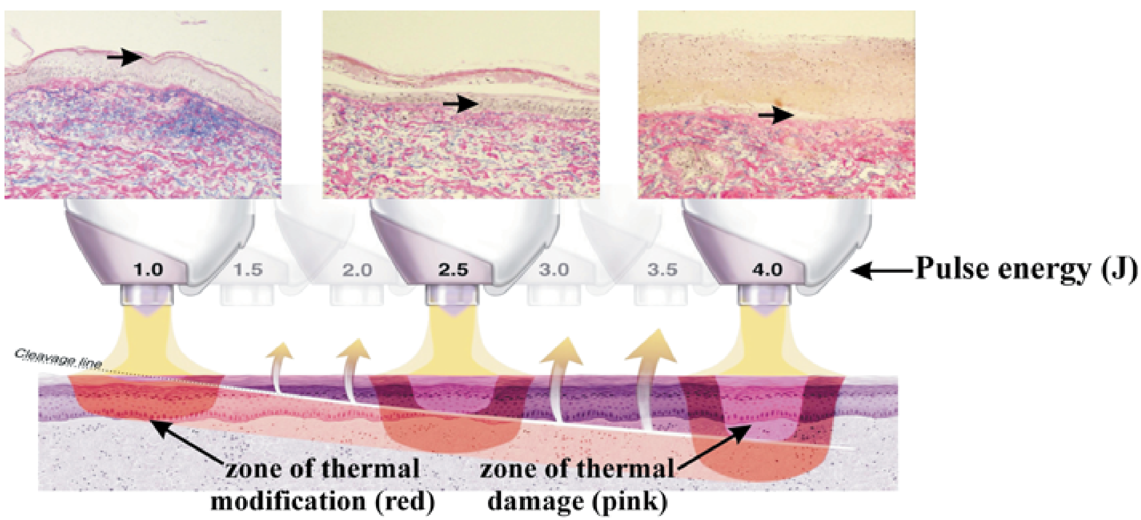

Figure 4 The effects of pulse energy on depth of cleavage. Pulse energies of 1.0 J (left) result in a very superficial cleavage line (arrow) just beneath the stratum corneum. The cleavage line (arrow) resulting from pulse energies of 2.5 J (middle) is localized within the basal cell layer. Pulse energies of 4.0 J (right) result in a cleavage line (arrow) within the papillary dermis. (Modified and reproduced with permission from Rhytec Inc.)

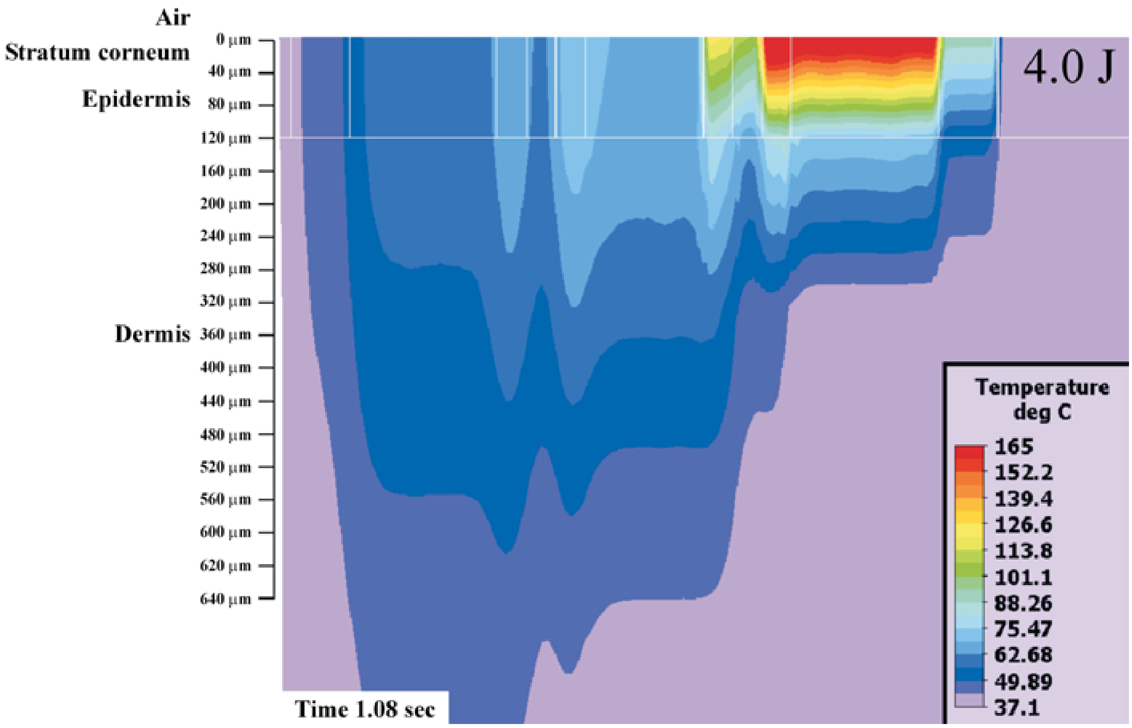

Figure 5 Finite element analysis demonstrating the depth of thermal penetration resulting from three sequential 4.0-J pulses delivered over 1.08 s to adjacent areas of normally hydrated skin. (Modified and reproduced with permission from Rhytec Inc.)

Table 1 Characteristics of Portrait PSR® treatment protocols

Protocol	Energy (J/pulse)	Number of treatments/passes required	Treated areas	Reference
VLE* (very low energy)	0.5	3–6/single	Full face ("no downtime" procedure)	3, 4
PSR NF (low energy)	1.0–1.8	1/single	Chest, hands, neck, nonfacial sites	2
3-pass LE	1.5–1.8	1/triple pass	Full face or regional areas, periorbital skin-single treatment	5
PSR1 (low energy)	1.0–1.8	3/single	Full face or regional areas	6, 7
PSR2 (high energy)	3.0–4.0	1/single	Full face or regional areas	6, 7
PSR2/3 (high energy)	3.0–4.0	1/single pass for full face or regional areas with double pass on deep rhytides	Full face or regional areas	8
PSR3 (high energy)	3.0–4.0	1/double pass	Full face or regional areas	7, 8, 9

*Pending US Food and Drug Administration clearance.

generates a localized plasma as a by-product of delivering low-frequency radiofrequency energy on a tissue surface through a thin layer of saline media. Coblation remains in use as a therapeutic alternative for tonsillectomy, for the treatment of benign polyps or vocal chord nodules, and for sleep-related breathing disorders.[10] Coblation produces immediate tissue vaporization and low energy heating. It failed as a modality for skin resurfacing due to the limited depth of energy penetration. Unlike coblation devices, the Portrait® PSR system offers noncontact gas plasma energy that provides higher energies, uniform and deep thermal penetration, and leaves the treated skin completely intact.

Improvement vs. recovery time

Patient demands for skin rejuvenating treatments have been and continue to be affected by three major variables: the potential for improvement, risk of the procedure, and amount of recovery time. Historically, the potential for

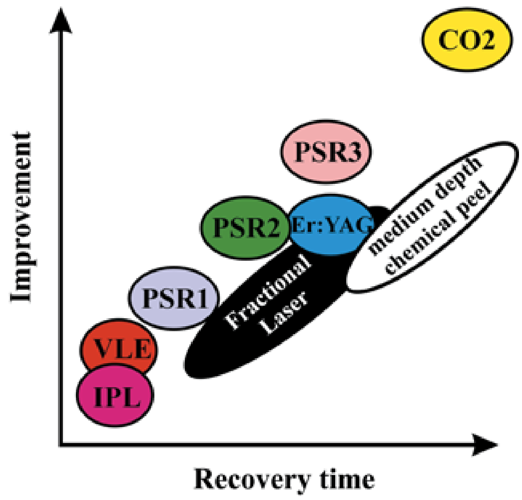

Figure 6 Relative downtime vs. improvement of different resurfacing modalities. IPL, intense pulsed light; VLE, very low energy plasma resurfacing with PSR; PSR1, single-pass plasma resurfacing with PSR at low energy (1.0–1.8 J); PSR2, single plasma resurfacing with PSR at high energy (3.0–4.0 J); PSR3, double-pass plasma resurfacing with PSR at high energy (3.0–4.0 J); Er:YAG, erbium yttrium–aluminum–garnet laser; CO_2, carbon dioxide laser.

improvement has counterbalanced the risks and "downtime," and patient concerns regarding the long recovery times associated with ablative procedures have been the driving force behind the development of nonablative fractional lasers with reduced downtimes and more modest improvements. Generally, with regard to laser resurfacing, efficacy is inversely related to safety. More aggressive treatments, such as CO_2 laser resurfacing, have more risk and potential return than treatments with intense pulsed light or VLE. The Portrait® PSR system offers a broad range of treatments with varying degrees of improvement and recovery times (Fig. 6). Treatment with high-energy PSR3, likened by some to single-pass CO_2 laser resurfacing without wiping, results in shorter recovery times and a more modest degree of improvement than would be seen with double-pass CO_2 laser resurfacing. In contrast, low-energy PSR1 treatments result in recovery times and improvement that approximate those of fractional lasers.

Review of the literature

Plasma skin regeneration is a relatively new technology with 6 years of clinical studies and follow-up including published reports documenting its efficacy in the treatment of facial and nonfacial sites. In a pilot study evaluating the use of a single full-face treatment at high energy (3.0–4.0 J), Kilmer *et al.* demonstrated a mean overall improvement of 50% by 1 month.[10] Potter *et al.* used silicone molding to demonstrate a 39% decrease in fine line depth 6 months after a single high-energy full-face treatment.[11]

Plasma skin regeneration has also been evaluated in the treatment of nonfacial skin including the neck, chest, and hand dorsa.[2] The authors used three energy settings (1.0 J, 1.5 J, and 1.8 J) and clinical evaluations of skin texture, pigmentation, wrinkle severity, and side effects were conducted immediately and at 4, 7, 14, 30, and 90 days after treatment. Mean clinical improvements of 57%, 48%, and 41% were observed in chest, hands, and neck sites, respectively, and significant reductions in wrinkle severity, hyperpigmentation, and increased skin smoothness were achieved. Higher energy settings were found to be of greater benefit but also had prolonged healing times. We performed a similar study using a series of three low-energy (1.0–2.0 J) PSR treatments on the neck and observed an overall improvement in skin tone, dyschromia, and texture (Moy and Fincher, unpublished). Analysis of the degree of skin tightening showed patient-dependent results that ranged from minimal to excellent, and some patients had a 70–80% reduction in skin lines that was noted at 3-month follow-up visits. The benefit of higher pulse energies was minimal in our study and resulted in a more prolonged healing time.

A number of ongoing studies for PSR were recently discussed at the 2007 American Society for Dermatologic Surgery Hot Topic Session in Chicago, Illinois, entitled "Portrait Plasma Skin Rejuvenation Update: Treatment Protocols and Aesthetic Outcomes," and several of these will be mentioned below. VLE settings with pulse energies of 0.5 J have been used to provide "lunchhour" treatments to the face with very minimal recovery times. The PSR device had not originally been designed to deliver such low energies, but this low pulse energy could be approximated by increasing the distance of the handpiece to the skin surface from the normal distance of 5 mm to approximately 20–25 mm with a larger treatment area. Subsequent efforts by the manufacturer have culminated in production of a standardized spacer that can be used clinically for this purpose. In pilot and multicenter studies assessing the efficacy of the VLE protocol, all subjects underwent three to six treatments separated by 3 weeks. Modest improvements in wrinkle severity and pigmentation were noted with minimal side effects.[3]

The effects of PSR on eyelid laxity and periorbital rhytides have also been evaluated.[12] Compared with a 91% improvement with blepharoplasty, treatment of upper eyelid skin with single- or double-pass high energy (3.0 J) resulted in a mean 22% and 35% improvement in upper eyelid tightening and periorbital wrinkles. With the high energies delivered in this protocol, double-pass treatments resulted in mean 13.1-day recovery times, and mean 11.5-day recovery times were noted following single-pass treatments. Prolonged healing times were correlated with increased pulse count/density, high aggregate energies, and posttreatment care. In the second phase of this trial, energy and pulse density were subsequently decreased to 1.5 J double or triple pass with 25–30 pulses per pass. Peeling was noted between days 2 and 4, and no patient developed postoperative erythema. Results with low energy settings approximated those of high-energy treatments, but were better tolerated with reduced healing times.

The effects of PSR on acne scars are also under investigation.[13] A recent multicenter trial included 30 patients who received one double-pass, high-energy (3.0–4.0 J) treatment with follow-up that extended to 180 days after treatment. Topical anesthetic cream under occlusion for 60 min was used before treatments. Posttreatment care consisted of cool compresses and application of petrolatum, and photography and silicon molds of treatment areas were used to assess improvement. Mean improvement in acne scarring on the cheeks was 32% and 25% on the mouth and chin, respectively, and 13% on the forehead. Mean patient-rated improvement was 37% at 3 months and 35% at 6 months after treatment, and mean physician-rated improvement was 29%. Mean recovery time was 4.6 days, and no hyper- or hypopigmentation was noted.

Indications and contraindications

As of September 2006, PSR is currently US Food and Drug Administration 510(k) approved for the treatment of rhytides of the body, superficial skin lesions, actinic keratoses, viral papillomata, seborrheic keratoses, and benign skin lesions of the body. PSR has beneficial effects in the treatment of dyschromias and photoaged skin and has been used anecdotally for the treatment of acne scars, eyelid laxity, Hailey-Hailey disease, and linear porokeratosis. Contraindications to PSR include pregnancy, nursing mothers, predisposition to developing keloids, use of isotretinoin in the past 6 months, darker skin types (Fitzpatrick types V and VI), patients with skin barrier defects, inflammatory skin conditions, and active infections.[8]

Preoperative management

While there are no consensus recommendations regarding preoperative management for plasma resurfacing patients, most surgeons adhere to the same precautions used for ablative laser resurfacing when considering high-energy plasma treatments. Bacterial prophylaxis should have *Staphylococcus* coverage, and we generally prescribe cephalexin 500 mg twice daily for 5 days, although levofloxacin 500 mg once a day for 7 days has also been advocated by some surgeons.[14] Antiviral (valacyclovir 500 mg thrice daily for 7 days) and antifungal (optional) prophylaxis should also be considered. Topical anesthetic creams (lidocaine 2.5%/prilocaine 2.5%), specially compounded anesthetic creams (23% lidocaine/7% tetracaine), or nerve blocks are also useful to minimize discomfort, and oral anxiolytics (diazepam, alprazolam, lorazepam), opiate pain relievers (meperidine, hydrocodone/acetaminophen), and antihistamines (hydroxyzine) may also be useful in certain patients, especially with high-energy treatments. Intramuscular dexamethasone may be helpful to minimize peri- and postoperative edema. Preoperative management should also include educating patients regarding posttreatment care, including vinegar soaks and application of aquaphor or petrolatum. For VLE treatments, hydrating cream may be beneficial, and no prophylactic medications are required.

Safety requirements for the procedure include eye protection for patients. Liberal application of petrolatum to eyelashes, eyebrows, and the hairline reduces the chance of singeing. The surgeon should be aware of any flammable items (e.g., paper table coverings, oxygen, anesthetic inhalants), and when possible, these should be removed from the operative suite or covered with moist towel. A fire extinguisher should be present for emergencies.

Technical considerations

Before beginning treatment, one must ensure that the skin surface is wiped clean of any residual anesthetic cream. After automatic calibration of the plasma generator is complete, the pulse energy (1.0–4.0 J) and repetition rate (1–2.5 Hz) are selected. Novice practitioners will have better control with pulse repetition settings of 1 Hz, but those with more experience may prefer higher repetition rates, up to 2.5 Hz. The handpiece is held 5 mm from the skin at a 90° angle such that the blue non-contact illuminated target ring is focused sharply around the area to be treated. Although the presence of the target ring implies that all the thermal energy remains within the confines of the ring, some heat diffuses onto adjacent areas of skin that are outside of it. Single-pass procedures are generally performed with spot overlap, but double-pass procedures do not require overlap. In contrast to CO_2 resurfacing, there is no wiping between the first and second passes. One drawback with the plasma system is lack of scanning technologies that define the exact size and shape of the treatment spot, a feature of most CO_2

Figure 7 Time course for healing following high-energy treatment with PSR2/3 for moderate to severe photodamage. (Modified and reproduced with permission from Rhytec Inc. and J. David Holcomb, MD.)

Figure 8 Time course for healing following low-energy PSR1 treatments for mild to moderate photodamage. (Modified and reproduced with permission from Rhytec Inc. and Richard Fitzpatrick, MD.)

lasers. For this reason, the operator must be exact with pulse placement to avoid skip areas or unintended pulse stacking.

Postoperative management

Following each treatment at 1.5–2.0 J on the face, there is typically 4 days of erythema and some superficial exfoliation on days 2–4. The higher-energy treatments at 3.0–4.0 J are performed as single treatments with an anticipated healing time of 7 days. The typical course following a high-energy (4.0 J), double-pass treatment is bronzing by day 2 followed by epidermal sloughing on days 4 and 5 and resolution of erythema between days 7 and 10 (Fig. 7). In contrast, low-energy treatments have a much more rapid healing time with milder desquamation and full resolution of erythema by posttreatment day 4 (Fig. 8). Expected improvements in periorbital wrinkles and laxity following high-energy treatments are shown in Figures 9–11. Similar improvements are noted following high-energy treatment of the cheeks, full face, jowls, and perioral regions (Figs 12 and 13).

Postoperative care consists of an open dressing with petrolatum-based ointment with repeat applications

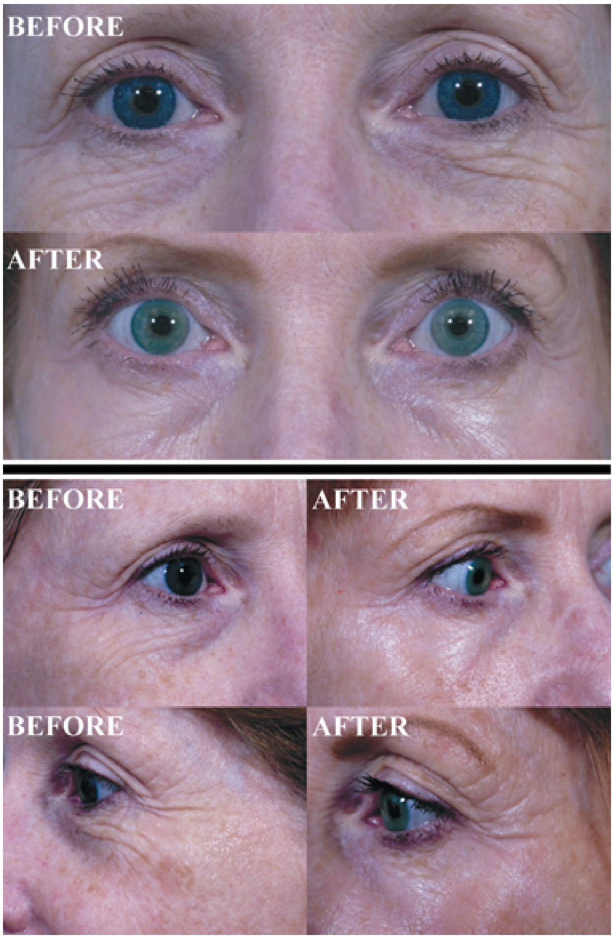

Figure 9 Before and after (30 days) photos showing improvement in periorbital rhytides following treatment with high-energy PSR3. The patient is wearing green contact lenses in after photos.

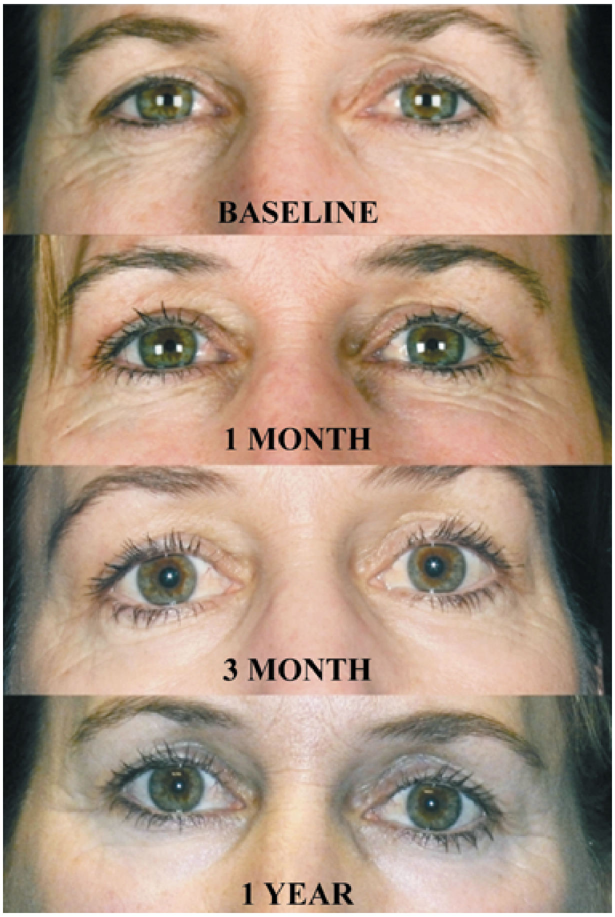

Figure 11 Continued improvement in periorbital rhytides seen up to 1 year after high-energy treatment. (Modified and reproduced with permission from Rhytec Inc. and Richard Fitzpatrick, MD.)

Figure 10 Before and after (1 year) photos showing improvement in periorbital rhytides following treatment with high-energy PSR3. (Modified and reproduced with permission from Rhytec Inc. and S. Bentkover, MD.)

three to four times daily along with gentle cleansing with a non-detergent-based cleanser. Sunscreens and makeup are generally safe to use following desquamation, by postoperative day 7 following high-energy treatment or by postoperative day 1 after VLE. Strict sun avoidance is mandatory during the pre- and postoperative periods as this can worsen erythema. Patients will notice an immediate improvement once any edema has resolved and re-epithelialization is complete; however, maximal benefits are probably not observed until 6 months postoperatively.

Side effects and complications

Side effects and complications following PSR have been recently reviewed in a study by Fitzpatrick and Rothaus that included 120 patients treated with PSR.[14] In their retrospective review, no permanent hyper- or hypopigmentation was noted following PSR, although transient

Figure 12 Before and after (30 days) photos demonstrating degree of improvement in cheek (above) and full face with tightening of the jowls (below) following a single high-energy treatment. (Bottom plate modified and reproduced with permission from Rhytec Inc. and Richard Fitzpatrick, MD.)

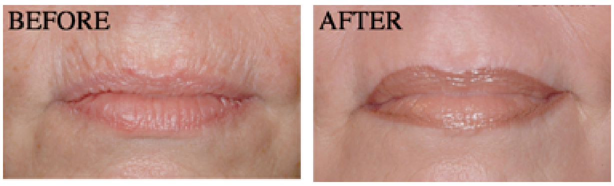

Figure 13 Before and after (30 days) photos demonstrating the degree of improvement following a single high-energy treatment of perioral skin. (Modified and reproduced with permission from Rhytec Inc. and V. Cirillo-Hyland, MD.)

hyperpigmentation was noted in 4% of patients. Only a single patient who was noncompliant with prophylactic measures developed herpes simplex virus reactivation following treatment, and bacterial infection was noted in three to four patients. A focal area of scarring was noted in one patient who had manipulated the treatment area. No patient developed hypopigmentation, a complication that is generally observed in 8–20% of CO_2 resurfacing patients. Prolonged erythema and demarcation lines were not observed.

Transient hyperpigmentation should be treated with hydroquinone creams or combination creams containing a mild topical corticosteroid, retinoid, and hydroquinone. The proper prophylactic measures are generally sufficient to prevent infectious complications. However, in the event that an infection is suspected, culture and sensitivity should be used to guide treatment. Patients should be counseled extensively about proper posttreatment care and the consequences of manipulation of the treatment area. Picking, scratching, or rubbing to accelerate the removal of peeling skin is not allowed due to the risk of scarring.

Conclusion

Plasma skin regeneration is a unique form of nonablative resurfacing that is not chromophore dependent and does not result in vaporization of the epidermis, but leaves a layer of intact desiccated epidermis that acts as a natural biologic dressing and promotes rapid healing. PSR improves fine lines and moderate to deep rhytides and the texture and tone of photoaged skin. The broad range of energy settings enables the operator to individualize treatments and control the degree of injury and length of subsequent recovery time. PSR treatments have an excellent safety profile. Permanent hypopigmentation and demarcation lines have not been observed, and prolonged erythema and scarring are rare. These characteristics have validated PSR as an excellent and versatile modality that offers a wide range of treatment options, and as such, it will undoubtedly command continued interest in the field of skin rejuvenation.

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