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ORIGINAL CONTRIBUTION

Randomized, single-blinded, crossover study of a novel wound dressing vs current clinical practice after percutaneous collagen induction therapy

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Summary

Introduction: Skin rejuvenation procedures have become common with sophisticated technologies with reduced downtime and related risks. Recently, microneedling has been paired with radiofrequency to create Fractional Radiofrequency Microneedling (FRFM) to induce neocollagenesis. Frequently, topical products are applied immediately after the needling. This procedure is known as percutaneous collagen induction therapy (PCIT). Postoperative topical wound care is critical for prompt rapid and safe healing, with moist wound healing deemed of primary importance for fast and correct scarring process. An ideal dressing enables a moist environment while reducing postprocedural inflammatory responses in the first stages of wound healing.

Objective: To evaluate whether an innovative silicone-based wound dressing is superior than standard of care therapy in decreasing severity and duration of treatment-site acute inflammatory reactions post PCIT.

Materials and Methods: Endymed PRO Intensif Handpiece (Endymed, Israel) was used for the full-face FRFM procedure. Subjects (n = 20) applied treatment (Stratacel®—Stratpharma SG, Switzerland) and control (Aquaphor®—Beiersdorf Inc, USA) immediately after the procedure and daily; they were evaluated immediately postprocedure (baseline assessment), at 2, 3 and 7 days postprocedure. Digital and 3D pictures (Antera 3D Camera for Skin Analysis—Miravex, Ireland) were taken at each assessment.

Results: All patients healed properly without reporting adverse reactions to any of the studied products. Erythema at each study visit was significantly reduced with the use of the novel wound dressing ($P < 0.001$). A statistically significant difference in favor of the innovative wound dressing also emerged with respect to the patient-rated product properties ($P = 0.008$), such as feel on skin, drying time and stickiness.

Conclusions: The novel wound dressing reduced signs of acute inflammation following PCIT when compared to standard of care, without reporting adverse events and resulting in a more favorable outcome from a patient perspective.

KEYWORDS
healing, silicone, wounds

1 | INTRODUCTION

Moist wound healing is deemed of primary importance for a fast and correct scarring process.[1] It has been well-established in the literature that acute wounds heal 40% faster in a moist environment than when air-exposed.[2] Keratinocytes migrate sooner, angiogenesis is more pronounced, postinjury growth factors persist longer on the skin, wound debridement is faster and more efficient, infection rate is less, and healing-promoting superficial electric fields are kept undisturbed in moist wound healing.[3-5]

Various types of wound care products have been developed over the years that attempt to maintain a moist environment during the healing process to reduce the potential for scar formation. Foams, films, hydrocolloids, hydrogels, alginates, hydro-fibers, and silicones have all been used as wound care, with variable degrees of success.[6] Data regarding wound care dressings have demonstrated that there is a positive correlation between the amount of full contact time with the wound and the healing response.[7] Moreover, evidence exists that demonstrates that the time at which a wound is treated has a significant effect on the likelihood of abnormal scar formation.[8,9]

Skin rejuvenation procedures have become popular worldwide due to the advent of more sophisticated technologies with reduced patient downtime and patient-related risks. The skin is carefully injured on the surface and/or at various depths, to induce neocollagenesis and increase elastin production, resulting in dermal rejuvenation.[10]

Needling devices, initially stamps covered with pins, have existed since the 1980s in the United States for skin tightening. The needles poke into the skin, causing superficial injury that stimulates collagen and elastic production to replace the damaged collagen through the body's innate wound-repair mechanisms, resulting in skin tightening.[11] Frequently, topical products are applied immediately after the needling while the channels are still open to allow the product to penetrate deeper into the skin.[12] This procedure is known as percutaneous collagen induction therapy.

Recently, microneedling has been paired with radiofrequency to create a combination therapy also referred as Fractional Radiofrequency Microneedling (FRFM) to induce neocollagenesis from both direct physical injury from the needles and through thermal coagulation zones from the RF. The depth of needle penetration and the frequency of the RF can be manipulated on the devices. This procedure has shown efficacy in improving wrinkles, pigmentation, acne scarring, and skin tone and texture. The most common adverse events for nonpharmacological treatments like FRFM comprise erythema, pain, purpura, edema, and occasionally hyperpigmentation.[13] Downtime resulting from FRFM is commonly around a week, with reported treatment-site responses such as erythema. Reducing the subject's downtime and the severity of the postprocedural responses translates into an enhancement of the subject's experience and satisfaction with FRFM.[12]

The foundations of topical postoperative wound management encompass wound protection, hydration, and enhancement of anti-inflammatory chemical signaling and the maintenance of the wound surface's granulating environment in a way that does not traumatize the wound bed with dressing changes.

Primary dressings are not always capable of achieving full contact with the injured skin surface, leaving some areas irregularly coated, dry, or less moist.Ideally, a primary dressing should be formulated as a transparent, semifluid, viscous, semipermeable, easily to apply topical form, able to gently solidify while keeping full conforming contact with dynamically moving, healing skin. Its external surface should be dry while forming full contact with the wounded tissue to enable a uniform moist environment.[14] Dressing properties should provide this environment while reducing the inflammatory markers well known to prolong wound healing and subsequently increasing the risk of infection and abnormal wound contracture leading to fibrosis.

Physical dressings, including commercially available masks formats, are cumbersome to be applied on a patient's face to ensure full contact on the treated area, as sometime the therapy includes eyelids and vermilion borders. This is the reason why physicians frequently favor the use of ointments. Most often physicians choose petrolatum-based ointments like Aquaphor (Beiersdorf Inc, Wilton, CT, USA) or Vaseline (Unilever Inc, Englewood Cliffs, NJ, USA). This trend was confirmed in a survey published in 2010 by the American Academy of Facial Plastic and Reconstructive Surgery were 60% of the 172 respondents admitted to most regularly using Aquaphor and 34% Vaseline postoperatively in facial rejuvenation.[15] Despite the fact this survey was performed in 2010, the results still apply to our practice as we conventionally have been using Aquaphor postoperatively in facial rejuvenation.

These habit-based prescription patterns need to be challenged, as Aquaphor and other over-the-counter ointments have been associated with erythema and inflammation, possibly as a consequence of contact dermatitis and promotion of the inflammatory environment due to their physical properties. A response of hypersensitivity secondary to contact dermatitis may be revealed postoperatively with symptoms of itchiness, and signs of inflammation, edema, heat, and erythema. Consequently, a severe case of contact dermatitis can lead to the deferral of wound healing. A study by Morales-Burgos et al evaluated postsurgery wound inflammation on two patient groups applying either Aquaphor or white petroleumjelly. The authors assessed a 52% incidence in redness at the wound site when using Aquaphor, with 33% of patients presenting both redness and swelling. The group administering white petroleum jelly showed a 12% incidence of redness, with 9% presenting both redness and swelling ($P < 0.002$). In contrast and due to the dry healing environment, the untreated patients developed more crusting vs Aquaphor; 47% vs 18% ($P < 0.030$).[16] The data around acute erythema have been linked with the ingredients of Aquaphor in previous studies especially in the pediatric population evoking its irritant nature.[17,18] In addition, Aquaphor is a fully occlusive dressing, which when applied immediately postoperatively does not allow heat to escape readily from the wound, thereby prolonging the time with which the detrimental growth factors associated with acute inflammation are in this environment. While

Aquaphor provides a moist wound healing environment, it subsequently prolongs the dampening of the pro-inflammatory markers induced by the procedure.

After facial rejuvenation procedures, the most regular postoperative concerns by physicians are especially sustained erythema, hypo- and hyperpigmentation. At a lower grade physicians are also precautious about dermatitis and scarring.[15] It is very conventional to increase cautiousness in handling patients with darker skin types. These concerns are supported by postprocedure complications especially postinflammatory hyperpigmentation (PIH) due to a continuous erythema that can last up to 6 months. These findings are especially acute in Fitzpatrick skin types greater than III.[19,20] Due to the fact that FRFM does not target melanin as part of its mechanism of action, it can be carefully assumed that patients with darker skin types can be treated for rejuvenation purposes with lower incidence of side effect compared with other energy devices.[21] Ethnic skin has been also studied specifically with FRFM devices, and occurrence of PIH has been reported with various degrees of incidence up to 10%.[22]

The studied film-forming wound dressing was specifically designed to perfectly adapt to irregular and contoured areas, such as those of the face. The gel's formula enables the dressing to be particularly suitable for damaged or compromised skin following fractional procedures, due to its ease of use and spreadability. The gel will dry to form a film and stay on the surface of the compromised skin for several hours, benefitting from the features of the physical dressing but still having a high degree of applicability due to the gel formulation. Most importantly, this wound dressing is semi-occlusive, allowing the exchange of gases to prevent maceration and while enabling the wound's transpiration. Recent studies have demonstrated that its features promote a fast recovery postprocedure, enhancing healing and reducing acute symptoms, overall improving the visible treatment outcome.[14]

2 | METHODS

2.1 | Study design

A randomized, single-blinded (investigator), crossover study was performed to evaluate a novel wound dressing gel compared to standard clinical wound care therapy to improve wound healing and postprocedural responses following FRFM. The patient was serving as its own control as the 2 studied products had to be applied on either the left or the right side from the midline according to the randomization schedule.

2.2 | Patient population and sample size

Twenty subjects (n = 20) underwent FRFM procedure. As the study was a first exploratory trial in post FRFM wound care, a sample size of 20 subjects was considered adequate in order to show a difference between the two products. All patients included in the study were adult females, treated with both products for the whole trial duration on opposite sides of their face.

2.3 | Randomization

The patient's sides of the face was randomly assigned to both treatments maintaining the assessor blinded. Randomization for treatment allocation sides was created utilizing Excel randomization in blocks of 10 subjects each. Only unblinded site staff had access to the randomization scheme.

2.4 | Treatment delivery and planning

Endymed PRO Intensif Handpiece (Endymed, Israel) was used for the full-face FRFM treatment. The FDA approved Intensif Handpiece utilizes a consumable sterile tip containing a matrix of small RF micro-needle (300 micron diameter) electrodes arranged to deliver RF energy. Immediately postprocedure, a petrolatum-based gel (Aquaphor®—Beiersdorf Inc, Wilton, CT, USA) or a film-forming wound dressing (Stratacel®—Stratpharma AG, Basel, Switzerland) were applied to either the right or the left side of the face. Subjects applied both products as per patient information leaflet and were evaluated by the investigator immediately postprocedure (baseline assessment), at 2, 3 and 7 days postprocedure. Digital and 3D pictures (Antera 3D Camera for Skin Analysis—Miravex, Dublin, Ireland) were taken at each assessment.

2.5 | Study endpoints and measurements tools

At each assessment, the investigator-rated erythema. Patients were asked to express an overall perceived outcome for both products. Erythema was measured through the Antera 3D Camera—Hemoglobin average level (expressed in quantitative measurable units generated by Miravex software) at each study visit. The overall patient-perceived outcome was measured at the last visit through four different items: product properties (feel on skin, drying time, stickiness), ease of use, healing time, and outcome of the FRFM procedure. The patient was requested to indicate a preference for one side of the face (left side, right side, both sides were the same).

2.6 | Statistical analysis

SPSS 24 (IBM, Chicago, IL) was used for all statistical analyses. Descriptive analysis was done using standard statistical procedures. To determine statistical significance, $P < 0.05$ and power = 0.80 were used. No patient was excluded from the statistical analysis. Statistical significance of erythema was determined by repeated measurements mixed-effects model: in the model, days postprocedure and product were included as fixed effects, as they were constant across visits, whereas side of the face was factored in as a random effect, in order to control for a possible bias toward either

side. The patient-perceived outcome between the two products was ascertained by means of paired samples *t* test.

3 | RESULTS

All patients healed properly without reporting adverse reactions to any of the studied products.

Demographics of the patient population enrolled in the study are displayed in Table 1.

Erythema was measured via the Antera 3D camera (Hemoglobin average level) at each study visit. Results were measured as improvement (Δ) vs baseline assessment (immediately postprocedure). An overall statistical significance emerged through the repeated measurements mixed-effects model ($P < 0.001$). As shown in Figure 1, post hoc dependent samples *t* tests confirmed a robust advantage in favor of Stratacel at each study visit ($P < 0.001$).

With regard to the overall patient-perceived outcome, product properties (feel on skin, drying time, stickiness), ease of use, healing time, and outcome of procedure (Table 2) were rated by the patient at the last study visit (day 7 postprocedure).

A statistically significant difference ($P = 0.008$) in favor of the innovative wound dressing was measured with respect to the product properties (Figure 2).

No statistically significant difference between the two products was instead found regarding ease of use, healing time, and outcome of procedure (Table 2).

TABLE 1 Demographic data of patients enrolled in the study

Total sample size	N = 20
Gender split (M/F)	F = 20
Average age of the sample	48.45 y (range 35-56)
Skin type split	
Type II	N = 13
Type III	N = 7
Reported history of abnormal scarring	N = 0
Smoking habits	N = 0 (no smokers in the recruited group)
Skin conditions/Chronic diseases	N = 0

4 | DISCUSSION

FRFM is becoming an ever more utilized procedure of skin rejuvenation. Reduced patient downtime associated with the avoidance of patient-related risks is key factors for the obtainment of a fast wound healing with a favorable patient perception. Most of the literature focuses on the procedure but neglects the postoperative wound care, forgetting that patients still have to endure downtime and acute symptoms. The initial purpose of this publication is to focus on the postprocedure care and optimal wound healing as it is as crucial as the intervention itself to achieve a proper clinical outcome. The studied medical device is a transparent, semipermeable

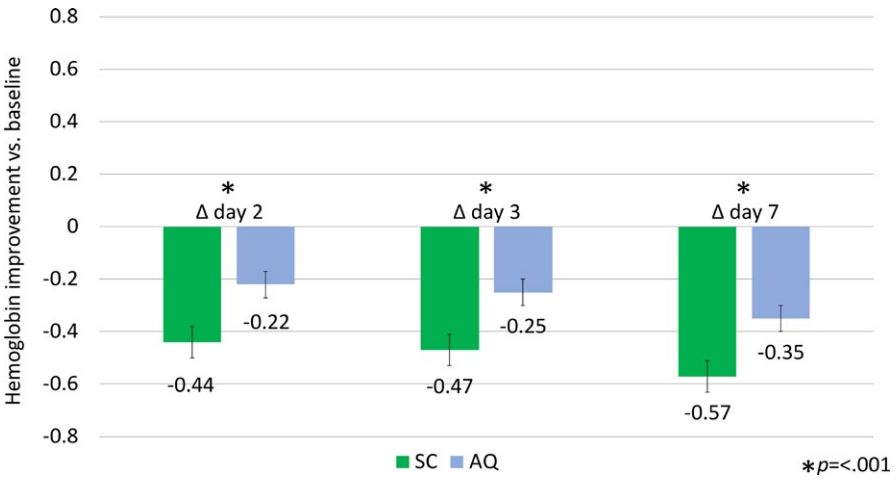

FIGURE 1 Reduction of erythema from baseline assessment at each study visit. Hemoglobin levels are presented as mean values ± standard error mean

TABLE 2 Patient evaluation of the two study products

Patient-rated items	Stratacel (mean ± SD)	Aquaphor (mean ± SD)	*P* value
Product properties (feel on skin, drying time, stickiness)	0.85 ± 0.37	0.25 ± 0.44	0.008
Ease of use	0.80 ± 0.41	0.60 ± 0.50	0.258
Healing time	0.45 ± 0.51	0.75 ± 0.44	0.137
Outcome of procedure	0.55 ± 0.51	0.85 ± 0.37	0.083

wound dressing in the form of a gel that is capable of perfectly conforming to skin irregularities, avoiding skin maceration and creating a moist wound healing environment and is ideal for use in wound care immediately after such procedure. Our intention was to compare its effectiveness vs commonly used over-the-counter products based on petrolatum.

In the current study, acute post-inflammatory reactions and wound healing was measured through erythema of the skin. The redness was significantly reduced with the use of the innovative film-forming wound dressing starting to see a clear difference as early as 2 days postprocedure (Figure 3). Statistical analysis confirmed a significant advantage in favor of the use of the studied dressing when compared to standard of care therapy.

Reduction of erythema from early posttreatment is a reflection of a quicker transition to a remodeling wound healing phase. This in turn translates into reduced downtime to achieve faster cosmetic enhancement which is crucial for patient's satisfaction with the procedure. The semi-occlusive nature of the gel allows the exchange of gases and prevents maceration, while enabling the wound's transpiration. This has been associated with a reduction of the inflammatory response, promoting of a fast recovery postprocedure, enhancing healing and reducing acute symptoms, and ultimately improving the overall visible treatment outcome.[14] It is postulated that this dressing enhances wound healing by balancing the pro-inflammatory processes induces by the procedure with its anti-inflammatory and chemical effects enhancing granulating tissue formation.

In contrast, petrolatum-based ointments have more occlusive properties that may promote wound maceration and are related to erythema and inflammation, likely as a consequence of contact dermatitis.[16]

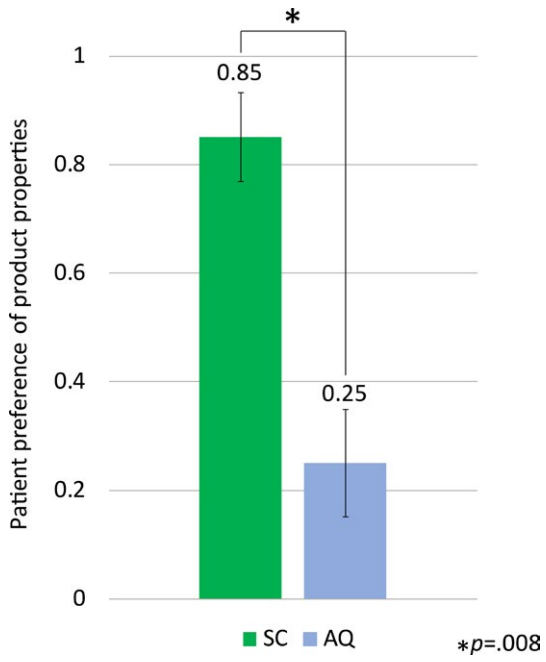

FIGURE 2 Patient preference of product properties at visit 3 (day 7 postprocedure). Bars are presented as mean values ± standard error mean

A decrease of the inflammatory response starting from a very early stage of the wound healing process may reduce the risk of post-inflammatory hyperpigmentation. It is therefore possible to speculate that a wound dressing that normalizes inflammation, reducing patient downtime, might play an important role in the treatment of darker skin types, representing an important and safe option.

Moreover, patients favorably perceived the product properties (feel on skin, drying time, and stickiness) of the innovative wound dressing over the standard therapy; as a result, the treatment journey was improved. Although no consensus exists regarding the ideal topical wound care product, based on the results of the current clinical trial, a dressing enabling a significant inflammation reduction coupled with enhanced product properties should be considered as one of the newest and perhaps best ways to enhance downtime reduction in such procedures and should be considered first-line

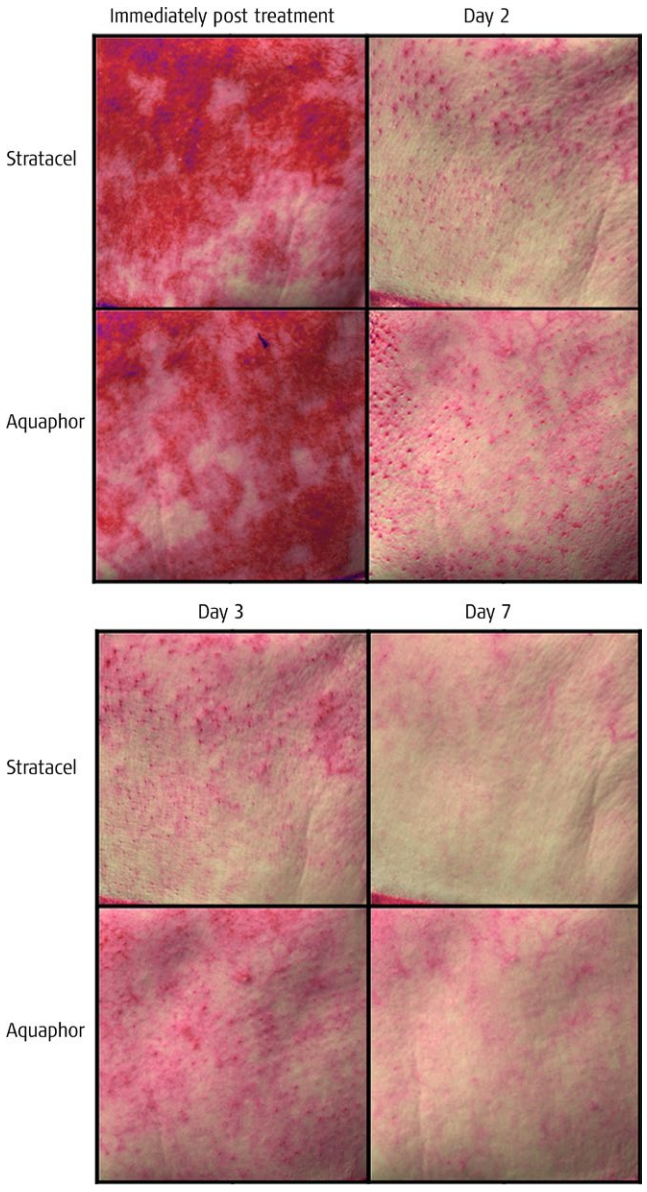

FIGURE 3 Evolution of erythema with the use of the two study products across visits

therapy following FRFM or other fractional and ablative energy-based procedure.

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