Title: A SINGLE-CENTER, RANDOMIZED, SPLIT-FACE, COMPARATIVE TRIAL EXAMINING NOVEL PLANT-BASED HYPOALLERGENIC OINTMENT VS PETROLEUM-BASED LANOLIN-CONTAINING OINTMENT FOLLOWING FRACTIONATED CARBON DIOXIDE LASER RESURFACING OF THE FACE

Authors: Yunyoung C. Chang, MD[1]; Jennifer Croix, MD, PhD[1]; Shannon Hernandez, RN[1]; Anne Chapas, MD[1]

Affiliation:
1. Union Square Laser Dermatology
19 Union Square West, 5th Floor
New York, NY 10003

Corresponding Author:
Yunyoung C. Chang, MD
Union Square Laser Dermatology
19 Union Square West, 5th Floor
New York, NY 10003
(P): 212-366-5400
(F): 212-366-5461
(E): drchang@unionderm.com

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Abstract

Purpose: Fractionated carbon dioxide (CO(2)) laser resurfacing uses fractional photothermolysis with an ablative 10,600-nm wavelength for treatment of rhytides and photodamage. Although associated with reduced side effect profile from traditional ablative lasers, fractionated lasers can lead to significant erythema, edema, crusting, and exudation for 14 days. Post-care includes regular distilled water soaks and healing ointment. This study evaluated efficacy and patient satisfaction of a novel plant-based hypoallergenic ointment (Doctor Rogers RESTORE® Healing Balm) compared to petroleum-based lanolin-containing ointment (Aquaphor® Healing Ointment) to accelerate wound healing post-laser resurfacing of the face.

Design: This was a single-center, prospective randomized, double-blinded, split-face comparative study of 10 subjects with photo-aging and rhytids who received treatment with fractionated CO2 laser between September 2017 and January 2018. Aquaphor and RESTORE Healing Balm were randomized to each half of the face and applied from Days 0 to 7 with an option to continue to Day 14. The primary outcome measures were Investigator-rated degree of erythema, edema, crusting, exudation, and percentage healing, with follow-up evaluations performed at Days 2, 4, 7, 14, and 30. The secondary outcome measure was patient satisfaction.

Summary:
Based on investigator post-resurfacing scores, Day 4 showed improved erythema (50%), edema (50%), crusting (40%) and percentage healing (60%) on the RESTORE treated side compared to Aquaphor, with the majority of remaining patients scoring the same as Aquaphor. On Day 14, RESTORE demonstrated improvement in erythema (50%), edema (30%), and percentage healing (30%) compared to Aquaphor, with all remaining patients scoring the same as Aquaphor. Crusting was the same on Day 14 between the two products. Ninety percent of patients preferred RESTORE over Aquaphor, found it easier to use and were more likely to use it in the future.

Conclusion: Doctor Rogers RESTORE® Healing Balm is a plant-based hypoallergenic ointment that is safe and effective post-laser treatment and is associated with high patient satisfaction and preference.

Introduction:

Ablative resurfacing of the skin using carbon dioxide (CO2) laser has been the gold standard for treatment of photoaging for more than 20 years[1]. Ablative fractional laser (AFL) using CO2 resurfacing applies the concept of fractional photothermolysis with an ablative 10,600-nm wavelength for the treatment of facial rhytids and photoaging. This laser technology delivers columns of thermal injury to a specific fraction of the epidermal and dermal tissue, leaving intervening areas of follicular units and fibroblasts unaffected thereby allowing for more rapid repopulation during the healing phase[2]. This leads to decreases in recovery time, side effects, and complications as compared to traditional non-fractionated ablative resurfacing treatments[1,2,3]. Nevertheless, AFL can still be associated with significant erythema, edema, crusting, exudation, secondary infections, and hypertrophic scarring[4,5]. The downtime associated with this procedure remains a hindrance to treatment.

A post-procedure skincare regimen is important to optimize the wound healing response post-AFL. In our practice, it typically consists of regular application of distilled water soaks and healing ointments during the following week. Many of the healing ointments currently used contain lanolin, which has seen an increased prevalence of contact allergy[6]. A novel healing ointment (Doctor Rogers RESTORE®Healing Balm) has been developed to help repair sensitive or damaged skin. It is a 100% plant-based, hypoallergenic ointment that is both lanolin and petroleum free, and has also been shown to inhibit the growth of bacteria and fungi.

The primary objective of this study was to compare the efficacy of a novel plant-based ointment to a petroleum ointment containing lanolin for wound healing and skin quality following AFL resurfacing of the face. Secondary objectives included safety and subject-graded improvement, satisfaction, and experience with both ointments.

Materials and Methods:

Study Design and Subjects:

This was a prospective, comparative double-blinded, split-face, randomized clinical study comparing a novel plant-based hypoallergenic ointment (RESTORE® Healing Balm) to a commonly used petroleum-based ointment containing lanolin (Aquaphor® Healing Ointment) after laser resurfacing. This study was approved by the Western Institutional Review Board (IRB).

Ten (10) healthy females and males meeting inclusion and exclusion criteria were included in the study. Subjects were 45 to 70 years of age, Fitzpatrick skin types I-III, and had a baseline wrinkle score of grade II or III in the Fitzpatrick Goldman Wrinkle and Elastosis Scale. The use of treatment skin care products including including alpha-hydroxy acids, salicylic acids, vitamins C or E, were instructed to discontinue use at least 14 days prior to participation in the study and for the

duration of the study. Subjects were excluded if they were pregnant or breastfeeding, had a known allergy to product ingredients or local anesthetics, had active infection or other active skin condition in the treatment area, had history of keloids or hypertrophic scars, had recent excessive sun exposure, had taken isotretinoin within the past year, had a chemical peel or other laser treatments within 3 months prior to study, or were receiving active topical products within 14 days prior to or during the study period.

Study Intervention:

Starting days 1 to 14 prior to treatment, subjects were screened for eligibility to participate in the study. If deemed eligible, informed consent to participate in the study as well as photography release forms were obtained. Subjects were instructed to stop any concurrent active skincare products. They were provided with supplies for the study, including 7-day courses of prophylactic antibiotic (dicloxacillin) and antiviral (valacyclovir) treatment to be started on the day of the procedure prior to treatment.

On the day of treatment, topical anesthesia using lidocaine 30% cream was applied for 60 minutes prior to fractionated CO_2 laser resurfacing of the face. Valium and Demerol were administered, and local nerve blocks with 1% lidocaine were performed immediately prior to the procedure to the supratrochlear, supraorbital, infraorbital, and mental regions. Fractionated CO_2 laser resurfacing was performed on the subject's face using the 10,600nm Fraxel Re:pair system (Solta Medical, Hayward, CA). The treatment settings were consistent with energy set to 40 mJ, treatment level 8, 30% coverage, and 4 passes. Uniform treatment settings were used for both sides of the face and for each patient.

Each side of the face was randomized by a non-blinded coordinator to RESTORE Healing Balm or Aquaphor ointment in a 1:1 fashion prior to the procedure, with the opposite side of the face receiving the other product. Immediately following the procedure (Day 0), the non-blinded coordinator applied RESTORE Healing Balm to one half of the face and Aquaphor ointment to the other half face. Subjects received blinded products with Aquaphor and RESTORE Healing Balm to be used post-procedure (blinded and labeled in similar jars to apply to each half of the face).

On post-procedure days 0 to 7, subjects were instructed to perform distilled water soaks every 4 hours while awake followed by application of blinded products to each side of the face. Subjects had an option to continue split-face application from days 8 to 14.

Clinical Evaluation:
Subjects returned for follow-up on post-procedure days 2, 4, 7, 14, and 30 for evaluation. The Canfield VISIA photography system was utilized to obtain

standardized photographs to document pre-treatment status and at each follow up visit.

At each post-procedure visit, a blinded investigator rated erythema, edema, crusting, and exudation on a 5-point scale (none [0] to severe [4]) as well as investigator-evaluated percentage healing (0-100%).

Subject Evaluation:
Subjects were given a take-home Subject Diary to document adverse effects for each ointment on post-procedure days 1-7 and 14, including erythema, oozing, crusting, pain, itching, and tightness (from 0-10 with 0 being none and 10 being the most severe). Subjects were also asked to compare ointment satisfaction and preference on post-procedure days 7 and 14.

Statistical Analysis:
Statistical evaluation was performed using Microsoft Excel and was conducted on an intent-to-treat basis.

Results:
Subject Demographics:
Of 10 total subjects, the mean age was 63.6 years, 100% subjects were Caucasian, and 80% of the patients were female and 20% were male [Table 1].

Investigator Scores of Healing:
Investigator-rated healing was graded based on erythema, edema, crusting, exudate, and percentage healing.

Erythema: On Day 4, RESTORE demonstrated superior improvement of erythema in 50% of subjects, and 30% of subjects showed equivalent improvement in erythema when compared to Aquaphor. On Day 7, RESTORE showed superior improvement in erythema in 60% of subjects with another 30% showing equivalent improvement as Aquaphor [Chart 1].

Edema: On Day 4, RESTORE demonstrated superior improvement of edema in 50% of subjects, with another 40% showing the equivalent improvement of edema when compared to Aquaphor. On Day 7, RESTORE showed superior improvement in edema in 30% of subjects, with another 60% showing equivalent improvement in edema as Aquaphor [Chart 2].

Crusting: On Day 4, RESTORE demonstrated superior improvement of crusting in 40% of patients, with another 50% showing equivalent improvement in crusting when compared to Aquaphor. On Day 7, RESTORE showed improved crusting in 20% of patients with another 70% showing the same crusting as Aquaphor [Chart 3].

Percentage Healing: On Day 4, RESTORE demonstrated superior healing in 60% of patients, with another 20% showing equivalent healing when compared to Aquaphor. On Day 7, RESTORE showed improved healing in 50% of patients with another 40% healing the same as Aquaphor [Chart 4]. Clinical photos of two subjects are shown [Photo 1].

Subject Scores of Healing:

Pruritis: On Day 2, 30% of subjects reported reduced pruritis using RESTORE. On Day 3, 40% of patients reported reduced pruritus with RESTORE. All other patients reported equivalent pruritis to Aquaphor.

Crusting: On Day 2, 50% of patients reported reduced crusting using RESTORE when compared to Aquaphor. On Day 3, 20% of patients reported reduced crusting. All other patients reported equivalent crusting to Aquaphor.

Tightness: On Days 2 and 3, 40% of patients reported improved tightness using RESTORE, with another 50% reporting equivalence to Aquaphor.

Redness: On Day 2, 60% of patients reported decreased redness using RESTORE when compared to Aquaphor, with another 30% reporting equivalence to Aquaphor. On Day 3, 40% of patients reported decreased redness with RESTORE, and another 50% reported equivalence to Aquaphor. On Day 4, 30% of patients reported decreased redness, with the remainder reporting the same redness as Aquaphor.

Pain: Subject scores of pain were similar for both sides throughout the duration of the study.

Subject Preference:

Ninety percent of subjects preferred RESTORE Healing Balm over Aquaphor Healing Ointment [Chart 5]. In addition, 90% of subjects found RESTORE easier to use, were more likely to recommend it to others after laser treatment, and were more likely to use it in the future. 50% of subjects were very satisfied or extremely satisfied with skin quality using RESTORE as compared to only 20% of subjects with Aquaphor.

Discussion:

Despite reduced healing times compared to traditional ablative lasers, AFL resurfacing techniques are still associated with significant downtime. As such, expediting recovery and optimizing results are paramount to the patient's experience. Post-AFL skincare typically includes a healing ointment. This study demonstrates the safety and efficacy of a novel, hypoallergenic, plant-based healing ointment for optimizing healing post-AFL.

We found that Doctor Rogers RESTORE® Healing Balm may be superior and is at least equivalent in regard to erythema, edema, crusting, and percentage healing compared to Aquaphor Healing Ointment. In addition, 90% of patients preferred RESTORE® Healing Balm to Aquaphor Healing Ointment.

RESTORE® Healing Balm is made with glycerin (derived from sustainably farmed oil palm trees), castor seed oil and castor wax. Glycerin is a humectant that binds and holds in moisture, which appears to have bactericidal effects and promote healing[7]. Castor seed oil is an emollient that hydrates the skin and decreases inflammation[8]. It is hypothesized these ingredients are better able to promote healing in injured skin than petroleum. The prevalence of contact allergies from ingredients such as lanolin, fragrance, formaldehyde and dyes has increased over the past decade[6]. The ingredients in RESTORE healing balm all have a low or unreported rate of allergy, reducing the risk of possible complications when used on injured skin. RESTORE Healing Balm is also free of petroleum, parabens, sulfates and phthalates.

The study results give credibility to using a new plant-based, petroleum and lanolin free ointment (RESTORE® Healing Balm) for post-AFL skincare, as well as consideration for use in other laser treatments, skin surgery, and other open wounds.

Limitations of this study include a small sample size and single-center protocol. The study was not powered to measure statistical significance, and larger studies may be helpful.

In conclusion, Doctor Rogers RESTORE® Healing Balm is a plant-based hypoallergenic ointment that is safe and effective post-laser treatment and is associated with high patient satisfaction and preference.

Legend:
Table 1: Patient Demographics
Chart 1: Investigator-graded Score of Erythema
Chart 2: Investigator-graded Score of Edema
Chart 3: Investigator-graded Score of Crusting
Chart 4: Investigator-graded Score of Percentage Healing
Chart 5: Patient Preferences
Photo 1: Clinical Photos of Subjects 2 and 5, at Baseline, Days 2, 4, 7, 14, and 30

Table 1: Patient Demographics

Patient Demographics	
Gender	80% female, 20% male
Mean Age	63.6 years old
Ethnicity	100% Caucasian

Chart 1: Investigator-graded Score of Erythema

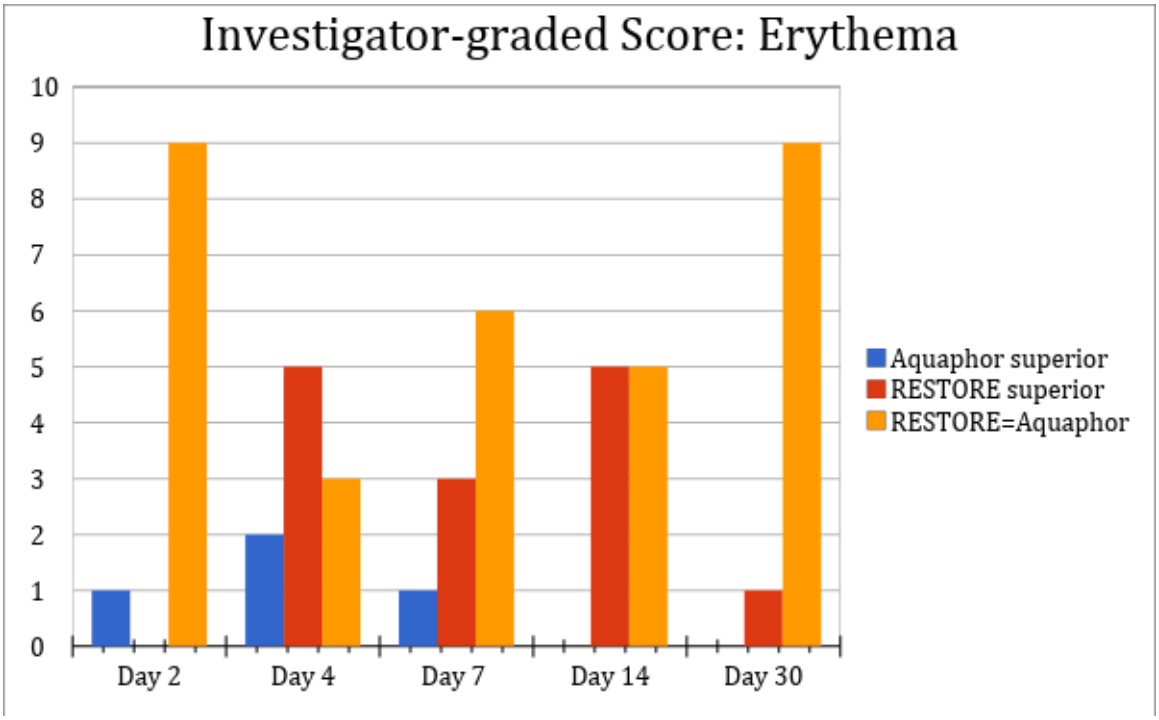


Chart 2: Investigator-graded Score of Edema

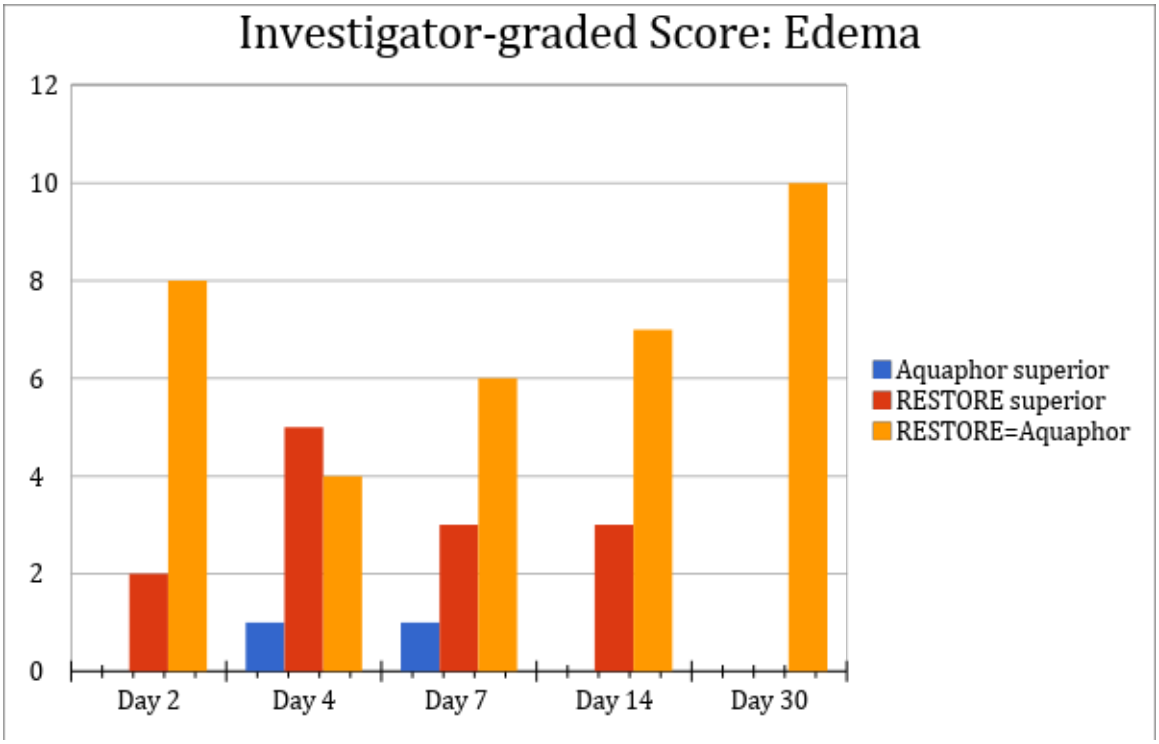


Chart 3: Investigator-graded Score of Crusting

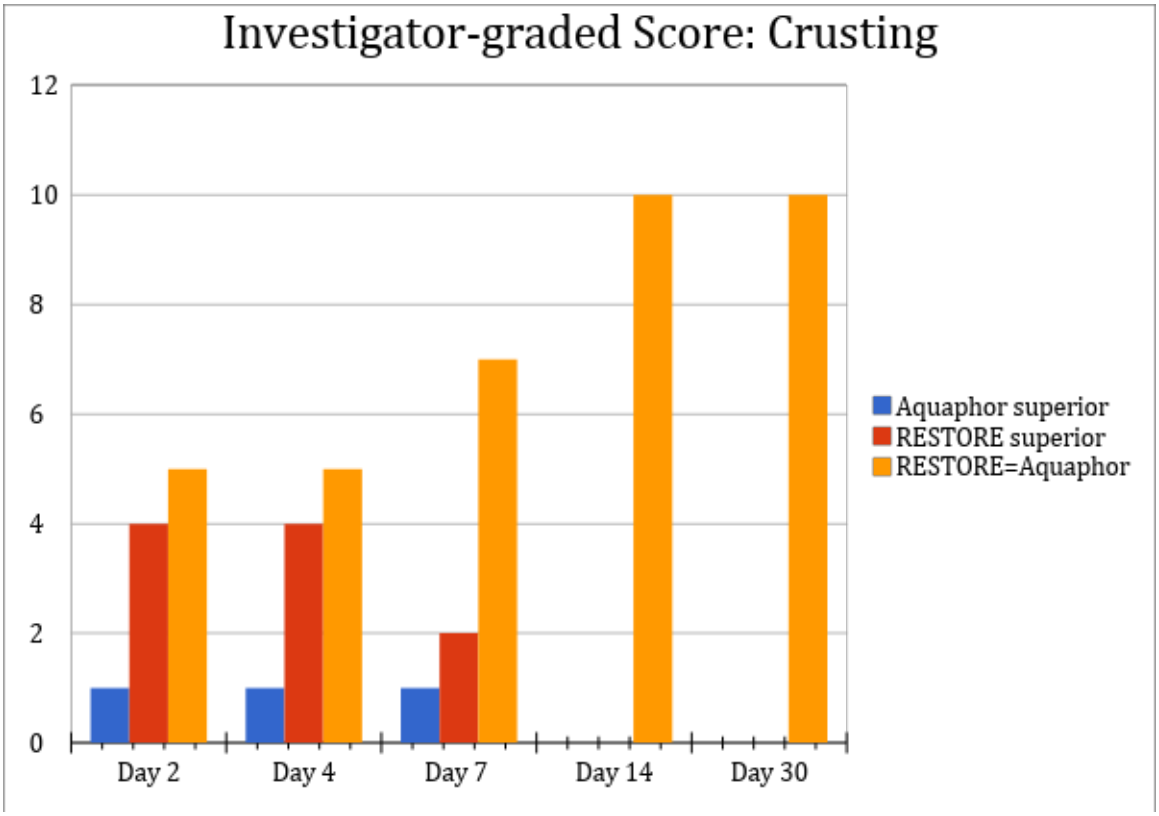


Chart 4: Investigator-graded Score of Percentage Healing

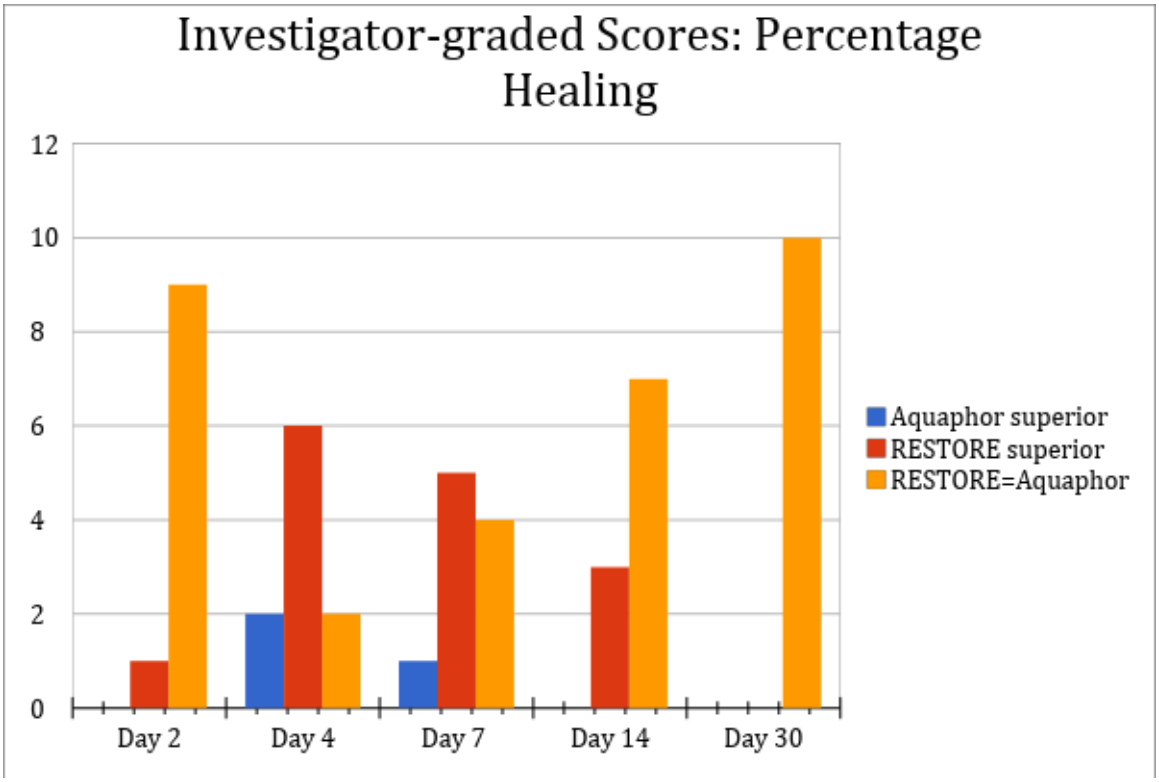


Chart 5: Patient Preferences

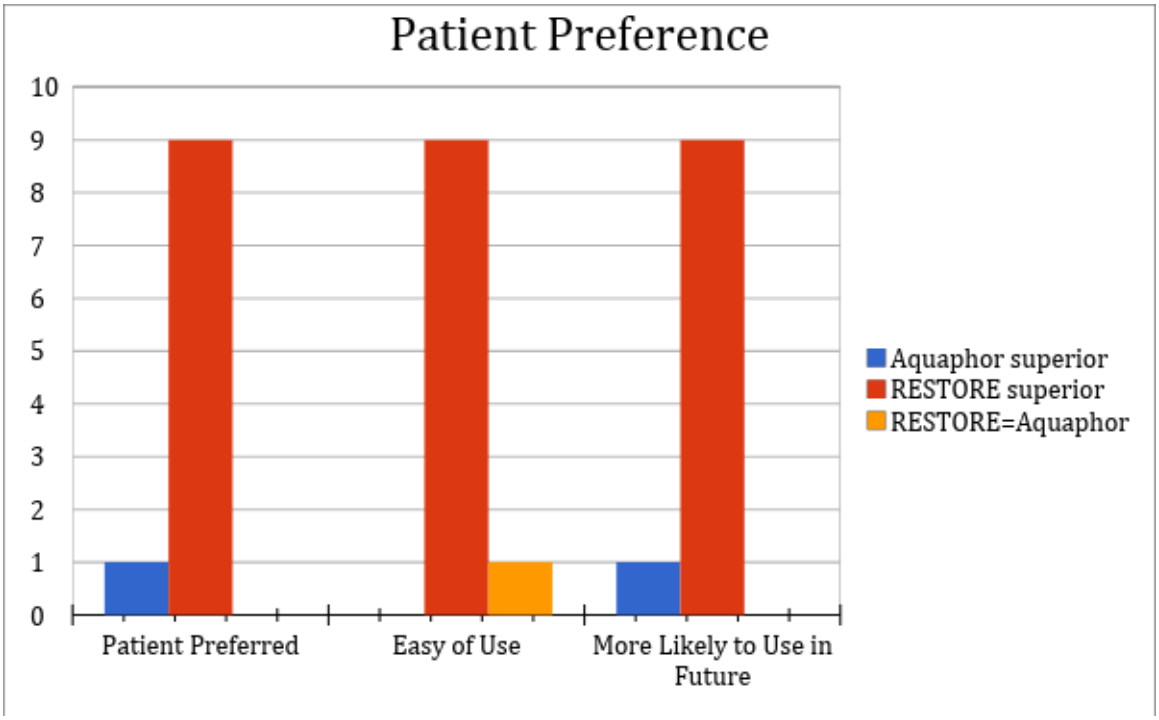
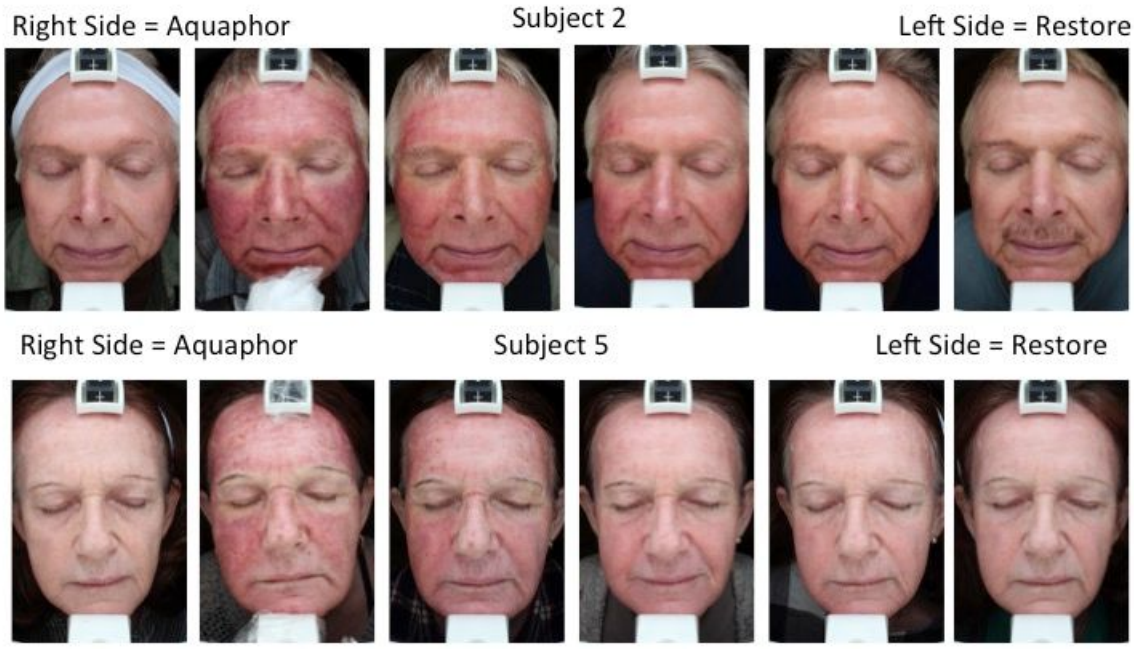


Photo 1: Clinical Photos of Subjects 2 and 5, at Baseline, Days 2, 4, 7, 14, and 30



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