Treatment of Burn Scars With the 1,550 nm Nonablative Fractional Erbium Laser

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Background: Scarring is a major source of morbidity in patients with burns. Burn scars are difficult to treat and are among the worst scars seen in clinical medicine. Fractional laser resurfacing is a promising treatment option because of its unique wound healing response and depth of penetration.
Objective: To evaluate the efficacy of nonablative fractional resurfacing as a therapeutic option for extensive cutaneous scarring in burn patients.
Methods: Prospective, single-arm, pilot study. Ten subjects with second and third degree burn scars were treated with five nonablative fractional resurfacing treatments given at 4-week intervals. Three independent investigators evaluated subject outcomes at 3 months post-treatment (primary outcome); patients also provided subjective assessments of improvement (secondary outcome).
Results: Nonablative fractional resurfacing resulted in overall improvement in 90% of subjects, as determined by independent investigators; improvements were moderate to excellent in 60%. Ninety percent of subjects had improved skin texture, 80% had improved dyschromia, and 80% had improved hypertrophy/atrophy. Patients' self-reports also revealed moderate to excellent improvements (on average) in burn scar area, and significant improvements in self-esteem at 3 months post-treatment ($P = 0.03$).
Limitations: Small sample size and lack of control group.
Conclusions: Fractional resurfacing is a promising new treatment modality for burn scars. We should continue to identify novel approaches and management strategies for the spectrum of diverse burn scars so that we can better treat this patient population. Lasers Surg. Med. 44:441–446, 2012. © 2012 Wiley Periodicals, Inc.

Key words: burn scars; nonablative fractional laser; keloid scars; hypertrophic scars; atrophic scars

INTRODUCTION

Scarring is a major source of morbidity in patients with burns. Burn scars have both functional and cosmetic morbidity. Besides being disfiguring, burn scars also cause pain, burning, itching, decreased function, and reduced range of motion. Effective reconstructive surgery is thus of paramount importance to the quality of life of the burn patient [1]. The long-term care of burn patients seeks to optimize the functional and aesthetic outcome for each patient. However, current state-of-the-art treatments address only a subset of burn characteristics, and additional therapies are needed to help with mature burn scar reconstruction [2].

Burn scars are currently managed with surgical reconstruction, pressure therapy, silicone gel sheets, temporary

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pressure garments, and adjuvant topical drug treatments [3–6]. Since the 1970s, several laser treatment modalities have also been tried, with varying levels of success [6–12]. The continuous wave lasers, including continuous wave carbon dioxide, argon, and Nd:YAG achieved some improvement; however, their use was limited by the inherent problems of continuous mode lasers [6]. These continuous lasers produced variable results secondary to both proficiency of the operator as well as the properties of the laser, which in some cases caused adverse pigment changes and worsening of scars. Scanning CO_2 lasers have been used to debride burn wounds, but without clinically improved scar outcome [10]. The most successful outcomes to date have been achieved with pulsed dye lasers. Alster [11] reported an average improvement of 57% after the first treatment and 83% after the second treatment with pulsed dye lasers for hypertrophic surgical and traumatic scars. This study also noted reductions in erythema, flattening, itching, and pain [11]. Pigment-specific Q-switched and long-pulsed lasers have also shown good improvement for pigmented scars [12].

The fractional resurfacing laser is a relatively new laser treatment modality [13], and has not been well studied for the treatment of burn scars. Recent case reports and studies are showing the promise of fractional lasers in severely burned patients [14–16]. The fractional lasers may have potential advantages over other devices due to their ability to penetrate deep within the dermis. We believe that this is critically important for burn scars, which go deep, often through the entire dermis and even into the bone. In 2008 and 2009, we published initial case reports on the use of fractional lasers (both ablative and nonablative) for burn scars, which showed significant decrease of hypertrophic scars, decreased hyperpigmentation, decreased erythema, and textural improvements. This warranted further investigation [14,15]. Haedersdal et al. [16] published a study showing 1,540 laser improved burn scar texture.

In this prospective study, we evaluated the use of nonablative fractional resurfacing as a therapeutic option for improving skin texture, dyschromia, hypertrophy, and atrophic scarring in burn patients.

METHODS

Subject Population

The study population inclusion criteria consisted of 10 patients 18–75 years old who had sustained scarring from deep second or third degree burns. Exclusion criteria were pregnancy, breastfeeding, oral retinoids 6 months prior to treatment, active infection, or lesions suspicious for malignancy. The first 10 participants to meet inclusion criteria for the study were enrolled. No patients dropped out. The protocol and informed consents were approved by Western Investigational Review Board, Inc. (Olympia, WA) and written informed consent was obtained from each patient.

Study Design

This was a prospective, single-arm, pilot study conducted to determine the efficacy of nonablative fractional resurfacing as a therapeutic option for the extensive cutaneous scarring in burn patients. A total of five nonablative fractional resurfacing treatments were performed on 10 patients with second and third degree burns at 4-week intervals. The primary outcomes were objective improvements in scar appearance at 3 months post-treatment, as evaluated by independent investigators. The secondary outcomes were patients' self-reported improvements in self-esteem and burn scar area, reported at 1, 3, and 6 months post-treatment.

Treatment Parameters

Patients were treated with a 1,550 nm nonablative fractional laser (Fraxel ReStore, Solta, Hayward, CA). The energy (mJ) level ranged from 40 to 70 mJ/pulse with treatment density range from 6 to 13 (17–38% tissue coverage). Adjunctive cooling was performed via an air chilling system (Zimmer Cryo 5, MedizinSystems, Irvine, CA). After treatment the treated areas were cooled with ice packs for 10 minutes. Patients were instructed to use a moisturizer three times a day for a week with regular application of a UVA/B sunscreen as well as sun avoidance throughout the study.

Clinical Assessments/Endpoint Evaluations

Photographs were obtained using identical camera settings, lighting conditions, and patient positioning (Nikon D300, total pixels 13.1 million, effective pixels 12.3 million). Three blinded independent physicians evaluated clinical improvements at 3 months following the final laser treatment for each subject. Pre-treatment and three-month post-treatment photos were randomly presented to the investigators for comparison. Investigators first ordered the photographs as "before" and "after"; then they evaluated improvements in overall appearance, texture, dyschromia, and degree of atrophy or hypertrophy using a quartile scale: 0 = none, 1 = mild (1–33%), 2 = moderate (34–66%), 3 = excellent (67–100%). There were 3 cases (out of 30) where the investigators ordered the photographs incorrectly; in these cases, scores of 0 (no improvement) were assigned for all categories. For each subject, scores were averaged between the three independent investigators to provide a final score. The intra-class correlation coefficient (a measure of inter-rater reliability) for the average rating was 0.65 [16].

At 1, 3, and 6 months post-treatment, subjects provided self-assessment of subjective improvements in burn scar area, also graded on a quartile (0–3) scale. They also rated their self-esteem on a 1–10 scale (with 10 being highest) before treatment as well as at 1, 3, and 6 months post-treatment. All subjects provided data for the 3-month post-treatment evaluation, but one subject provided no data at 1 month and three subjects provided no data at 6 months.

Statistical Analyses

Statistical analyses were performed using SAS 9.1 (SAS Institute, Cary, NC). Subjects were grouped into categories based on their average objective improvement score: their objective improvement was considered moderate to excellent if their average score was ≥ 2; mild to moderate if their average score was <2 but ≥ 1; and none if their average score was <1. Subjective improvements in scar area and self-esteem ratings were presented as means and standard deviations. Pre and post-treatment self-esteem scores were compared using a Wilcoxon sign-rank test; this non-parametric test was used because the change in self-esteem scores was not normally distributed.

RESULTS

The subject population comprised 10 patients aged 23–68 years old, eight females and two males (Table 1). Treatment areas included the face, neck, chest, arms, hands, abdomen, legs, and foot. Patients had a combination of scar types, including atrophic, hypertrophic, and contracture scars.

The independent investigators correctly differentiated between pre and post-treatment Photos 27 out of 30 times. Investigator 1 correctly identified pre and post-treatment photographs in 10 out of 10 cases ($P < 0.0001$); investigator 2 was correct in 9 of 10 cases ($P < 0.002$); and investigator 3 was correct in 8 out of 10 cases ($P < 0.02$). Of the three instances where the post-treatment photograph was

TABLE 1. Demographic and Clinical Characteristics of the 10 Subjects

Patient	Age/ Gender	Skin type	Type of scar	Age of scar	Area of scar (cm^2)	Previously treated?
1	23/F	VI	Hyperpigmented scar Hypertrophic scar	22 years	Dorsal hand: 5.4 × 4.1 cm^2 Dorsal forearm: 15.0 × 4.0 cm^2	None
2	27/F	II	Erythematous scar Hyperpigmented scar Hypertrophic scar Contracture scar	1 year	Left forearm: 64 × 10.5 cm^2 Right arm: 66 × 13 cm^2	Skin grafts: both upper extremities
3	51/F	II	Erythematous scar Hyperpigmented scar Atrophic scar Hypertrophic scar	22 years	Left foot: 16 × 9 cm^2 Left thigh: 17 × 7 cm^2 Right leg and foot: 26 × 5 cm^2 Left forearm: 15 × 4 cm^2 Left lower back: 20 × 6 cm^2	Skin graft: left leg
4	68/F	II	Erythematous scar Hypertrophic scar Hypopigmented scar	20 years	Chest: 11 × 15 cm^2	Debridement
5	67/F	II	Hypopigmented scar Hyperpigmented scar Atrophic scar	65 years	Chest: 5.5 × 3.0 cm^2 Left arm: 27 × 13 cm^2	None
6	44/F	II	Erythematous scar Hypopigmented scar Hyperpigmented scar Atrophic and hypertrophic scar	39 years	Lower face: 10 × 4 cm; Right neck: 10 × 4 cm^2 Abdomen: 23 × 2 cm^2 Right arm: 34 × 6 cm^2 Right flank 20 × 11 cm^2	Skin grafts, multiple scar revision surgeries 30 years ago
7	32/M	III	Hyperpigmented scar Hypertrophic scar	3 months	Left dorsal hand: 10 × 5.5 cm^2	None
8	49/M	II	Hyperpigmented scar Atrophic scar	48 years	Right lateral cheek: 15 × 2.5 cm^2 Right lateral superior neck: 5 × 9 cm^2 (atrophic) Right lateral inferior neck: 5 × 9 cm^2 Right chest: 9 × 5 cm^2	None
9	40/F	II	Hyperpigmented scar Hypopigmented scar Hypertrophic scar	7 years	Right inner calf: 7.5 × 3.5 cm^2	Pulsed Dye Laser × 6 times done 1 month post-burn 7 years prior
10	28/F	II	Hypopigmented scar Atrophic scar	22 years	Left leg: 80 × 40 cm^2	Skin graft
Avg	42.9			24.6 years	672.14 cm^2	

TABLE 2. Objective Improvement at 3 Months Post-Treatment (Percent of Subjects in Each Category)

Extent of improvement[a]	Overall ($n = 10$)	Texture ($n = 10$)	Dyschromia ($n = 10$)	Atrophy or Hypertrophy ($n = 10$)
Moderate to excellent	60%	40%	50%	20%
Mild to moderate	30%	50%	30%	60%
None	10%	10%	20%	20%

[a]Improvement was rated by three independent investigators on a 0–3 scale: 0 = no improvement, 1 = mild improvement, 2 = moderate improvement, 3 = excellent improvement. Subjects were classified into improvement categories based on their average score from the three investigators: average score ≥ 2 is moderate to excellent improvement; average score < 2 but ≥ 1 is mild to moderate improvement; and average score < 1 is no improvement.

incorrectly identified, two were the same patient. This patient experienced minimal improvement from the fractional nonablative treatment.

Based on the average score from the three judges, 90% of the patients experienced an improvement in overall appearance after nonablative fractional resurfacing; 60% of the patients had moderate to excellent improvement (Table 2). Ninety percent of subjects demonstrated improvements in skin texture, 80% in dyschromia, and 80% in degree of atrophy or hypertrophy (Table 2). Of the different types of scars treated, including atrophic, hypertrophic, and contracture, all types had improvements in overall appearance (Figs. 1 and 2). The average overall improvement in burn scar was 2.07 as determined by the three blinded observers (Tables 3 and 4).

The average subjective (self-rated) improvement in burn scar areas was 2.2 (SD $\pm$ 0.8) at 3 months, corresponding to an average self-rated improvement between moderate and excellent (Table 5). Subject assessment of self-esteem increased from 7.3 ± 2.1 at baseline to 8.2 ± 2.1 at 3 months ($P = .03$, Wilcoxon sign-rank test; Table 3). Average changes in self-esteem were similar in magnitude at 1 and 6 months post-treatment, but these changes failed to achieve statistical significance, likely due to missing data at these time points.

Most subjects experienced mild to moderate erythema and edema immediately post-treatment; no subjects experienced severe erythema or edema after any treatments. In one subject, mild erythema persisted at 3 months post-treatment. No other adverse events were reported.

DISCUSSION

In this prospective, single-arm, pilot study, treatment with a nonablative fractional erbium laser resulted in at least mild improvement in scar appearance in 90% of subjects and moderate to excellent improvement in 60% of subjects. Improvements were seen in all scar types, including atrophic, hypertrophic, and contracture scars. Ninety percent of subjects had improvement in skin texture, 80% in dyschromia, and 80% in atrophy or hypertrophy. In addition, patients perceived subjective improvements in scar area that were, on average, moderate to excellent, and reported an average 1-point increase in self-esteem (on a 10-point scale), which was statistically significant at 3 months.

Laser treatment provides removal of scar tissue and remodeling of new collagen via precise wounding and healing of the laser wound, even for extensive burn scar surfaces. Other laser modalities have been tried, with varying levels of success [6–12]. Fractional laser

Fig. 1. Baseline photograph of an atrophic and hyperpigmented burn scar (left panel); and photograph of the same scar three months following five fractional resurfacing treatments at 50–65 mJ and 8–10 treatment levels (right panel), strict sun avoidance.

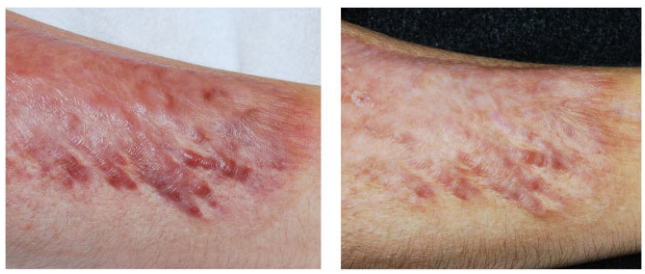
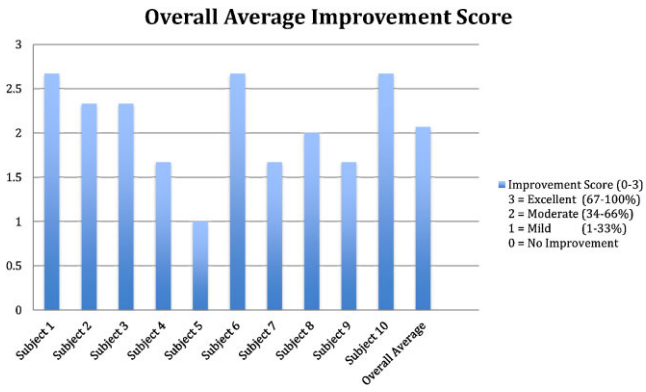


Fig. 2. Baseline photograph of an erythematous, hyperpigmented, hypertrophic contracture burn scar (left panel); and photograph of the same scar three months following five fractional resurfacing treatments at 70 mJ and 8–11 treatment levels (right panel), strict sun avoidance.

TABLE 3. Average Scoring of Each Patient on a 0–3 Scoring Scale in Various Categories as Determined by Blinded Observers (0—No Improvement, 1—Mild Improvement (1–33%), 2—Moderate Improvement 33–67%), 3—Excellent Improvement (67–100%)

Patient number	Overall improvement score	Dyschromia score	Degree of atrophy/hypertrophy improvement score	Texture improvement score
001	2.67	2.33	1.67	2.00
002	2.33	2.67	1.67	1.67
003	2.33	1.33	2.33	2.33
004	1.67	1.00	1.67	1.33
005	1.00	0.67	0.67	1.33
006	2.67	2.33	1.67	2.00
007	1.67	1.33	1.67	1.33
008	2.00	2.00	1.33	1.67
009	1.67	1.33	1.00	1.33
010	2.67	2.00	2.33	2.00
Average	2.07	1.70	1.60	1.70

TABLE 4. Objective Overall Improvement Score at 3 Months Post-Treatment Determined by Blinded Observers (0—No Improvement, 1—Mild Improvement (1–33%), 2—Moderate Improvement (33–67%), 3—Excellent Improvement (67–100%)



resurfacing may be particularly well suited for treatment of burn scars because of the depth of penetration it achieves. Based on our clinical experience, the aesthetic and functional outcomes of fractional laser may be superior in efficacy to other laser options, though direct comparison studies are needed. The nonablative fractional laser also has many additional benefits for the patient and doctor: it is easy to perform under topical, local or tumescent anesthesia; is bloodless; causes minimal pain; and results in rapid wound healing within a few days. The laser may also be repeated monthly, is performed on an outpatient basis, and has no absolute contraindications.

Multiple therapeutic options have been explored to improve scars. When nature, time, and surgery have taken its course, fractional laser is now a new option for further scar improvements in function, symptoms and cosmesis. Although all types of scars seem to improve with fractional laser therapy, hypertrophic scars seem to improve the most. Both fractional and nonablative lasers are excellent with decreasing erythema (pulsed dye laser 595 nm) and hyperpigmentation (thulium 1927 nm). The fractional devices can be used anywhere on the body, although it is recommended to decrease both depth and density when treating off-face body locations, especially in thinner areas of skin, such as the neck.

The optimal time frame to improve scars by fractional ablative laser therapy has not yet been determined. The

TABLE 5. Subjects' Self-Assessment of Improvement in Burn Scar Areas Post-Treatment, as well as of Self-Esteem Before and After Treatment (Mean ± SD)

	Pre-treatment ($n = 10$)	1 month post-treatment ($n = 9$)	3 months post-treatment ($n = 10$)	6 months post-treatment ($n = 7$)
Improvement in burn scar area[a]	n/a	2.4 ± 0.9	2.2 ± 0.8	2.3 ± 0.4
Self-esteem[b]	7.3 ± 2.1	8.1 ± 2.6[c]	8.2 ± 2.1[d]	8.4 ± 2.1

[a]Subjective improvement was rated on a 0–3 scale: 0 = no improvement, 1 = mild improvement, 2 = moderate improvement, 3 = excellent improvement.

[b]Self-esteem was rated on a 0–10 scale, with 0 being the lowest and 10 being the highest.

[c]$P = 0.06$, Wilcoxon sign rank test, comparing pre-treatment to 1 month post-treatment.

[d]$P = 0.03$, Wilcoxon sign rank test, comparing pre-treatment to 3 months post-treatment.

current consensus states that laser therapy should occur predominantly after surgery in large burn and traumatic scar patients. Consideration may be given if there is a role for laser pre-operatively to soften scar. It is important to have a stable, epithelized wound prior to laser therapy. Acne and surgical scars can be able to treated as early as 30 days. Recently, Drs. Ozog and Moy published a small clinical trial showing improvement of Mohs surgical scars treated with fractional carbon dioxide laser intra-operatively appeared to improve both appearance and texture [17]. This warrants further investigation to determine if treating an early developing scar with fractional lasers may help minimize the ultimate scar. Large burn and traumatic wounds are treated with a collaboration of medical experts including acute burn surgeons, burn reconstructive surgeons, physical therapists, and laser surgeons. The optimal time to treat with laser scar resurfacing may vary patient to patient but appears to be months—1 year after the injury.

Many questions remain about the use of fractional laser treatments for burn scars. Also, this study considered only monotherapy, however, combinations of therapeutic methods may lead to the best treatment outcomes. For example, intralesional corticosteroid injections are a mainstay in the treatment of hypertrophic scars and keloids alone or in combination with other therapeutic procedures [18–21]. Hypertrophic and keloidal scars could be treated with fractional lasers followed immediately by intralesional corticosteroid injections; the laser beam "holes" created by the fractional laser may maximize drug absorption and improve outcomes. Fractional nonablative laser therapy could also be combined with pressure, pulsed dye lasers, and fractional ablative lasers. Finally, this study considered only nonablative fractional resurfacing, but we speculate that the use of ablative fractional devices may be more efficacious for severe scars and also require fewer treatment sessions.

Since this was a pilot study, it was a small study and lacked a control group. Particular caution is warranted when interpreting the subjective results; self-reported self-esteem is highly variable, so the observed improvements in this study could be due, at least in part, to a placebo effect, random fluctuation, or other factors unrelated to the improvement in burn scars. Larger randomized clinical trials are needed to establish the efficacy of fractional laser resurfacing relative to existing treatments. Future studies should also address the optimal timing of treatment, the optimal laser parameters, combination therapies, and the use of ablative fractional devices. Imaging, histological, and biochemical studies are also needed to evaluate the direct biological effects of fractional laser resurfacing on burn scar remodeling.

In conclusion, fractional resurfacing is a promising new treatment modality for burn scars. We should continue to identify novel approaches and management strategies for burn deformities. The best results will likely be achieved through multi-specialty collaboration, innovative technology, and a combination of therapeutic treatments.

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