Fractional Deep Dermal Ablation Induces Tissue Tightening

Zakia Rahman, MD,[1] Heather MacFalls, MS,[2] Kerrie Jiang, MSN, NP,[2] Kin F. Chan, PhD,[2] Kristen Kelly, MD,[3] Joshua Tournas, MD,[3] Oliver F. Stumpp, PhD,[2] Vikramaditya Bedi, MS,[2] and Christopher Zachary, MD[3]*

[1]*Department of Dermatology, Stanford University, Stanford Medical School, Stanford, California 94305*

[2]*Reliant Technologies, Mountain View, California 94043*

[3]*Department of Dermatology, School of Medicine, University of California Irvine, Irvine, California 92868*

Background and Objective: Due to the significant risk profile associated with traditional ablative resurfacing, a safer and less invasive treatment approach known as fractional deep dermal ablation (FDDA^{TM}) was recently developed. We report the results of the first clinical investigation of this modality for treatment of photodamaged skin.

Study Design/Materials and Methods: Twenty-four subjects received treatments on the inner forearm with a prototype fractional CO_2 laser device (Reliant Technologies Inc., Mountain View, CA) at settings of 5–40 mJ/MTZ and 400 MTZ/cm^2. Clinical and histological effects were assessed by study investigators 1 week, 1 month, and 3 months following treatment. Thirty subjects were then enrolled in a multi-center study for treatment of photodamage using the same device. Subjects received 1–2 treatments on the face and neck, with energies ranging from 10 to 40 mJ/MTZ and densities ranging from 400 to 1,200 MTZ/cm^2. Study investigators assessed severity of post-treatment responses during follow-up visits 48 hours, 1 week, 1 month, and 3 months following treatment. Using a standard quartile improvement scale (0–4), subjects and investigators assessed improvement in rhytides, pigmentation, texture, laxity and overall appearance 1 and 3 months post-treatment.

Results: Clinical and histologic results demonstrated that fractional delivery of a 10,600 nm CO_2 laser source offers an improved safety profile with respect to traditional ablative resurfacing, while still effectively resurfacing epidermal and dermal tissue. Forearm and facial treatments were well-tolerated with no serious adverse events observed. Eighty-three percent of subjects exhibited moderate or better overall improvement (50–100%), according to study investigator quartile scoring.

Conclusions: FDDA^{TM} treatment is a safe and promising new approach for resurfacing of epidermal and deep dermal tissue targets. Lasers Surg. Med. 41:78–86, 2009.

Key words: fractional deep dermal ablation (FDDA); ablative resurfacing; fractional photothermolysis; photodamage; CO_2 laser

INTRODUCTION

The efficacy of ablative laser skin resurfacing is well-substantiated [1–6]. Specifically, ablative resurfacing with pulsed CO_2 or "hot" Er:YAG lasers are considered a highly effective treatment option for severe photodamage and tissue laxity [6]. Significant tissue tightening is consistently achieved with immediate collagen shrinkage followed by long-term collagen remodeling contributing to the predictability and sustainability of the results [7–9].

However, the risks for significant treatment complications following traditional CO_2 resurfacing eventually reduced the utilization of this technique. Although treatment efficacy was reproducible, the risks of protracted wound healing, persistent redness, delayed-onset permanent hypopigmentation, infection and scarring were all major deterrents to its use [10–12]. These limitations led to the development of new treatment modalities capable of providing safer, more reproducible results [13–16].

The concept of fractional photothermolysis (FP) was initially developed to address the shortcomings of traditional ablative and non-ablative device modalities. Instead of delivering homogeneous bulk thermal damage, FP is a modality characterized by the creation of microscopic zones of thermal damage with spatial separation between damaged tissue. The first device to implement this concept utilized a 1,550 nm laser source for the coagulation of soft tissue [15]. Although this device does not result in instantaneous ablation of tissue, it has previously been shown to result in safe and effective biological resurfacing [17], suited for treatment of pigmentary dyschromia, acne scarring, periorbital rhytides and non-facial photodamage.

As with the non-ablative systems, fractional delivery of an ablative CO_2 laser source results in a microscopic

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*Correspondence to: Christopher Zachary, MD, Department of Dermatology, University of California Irvine, Irvine, CA 92868.
E-mail: czachary@uci.edu

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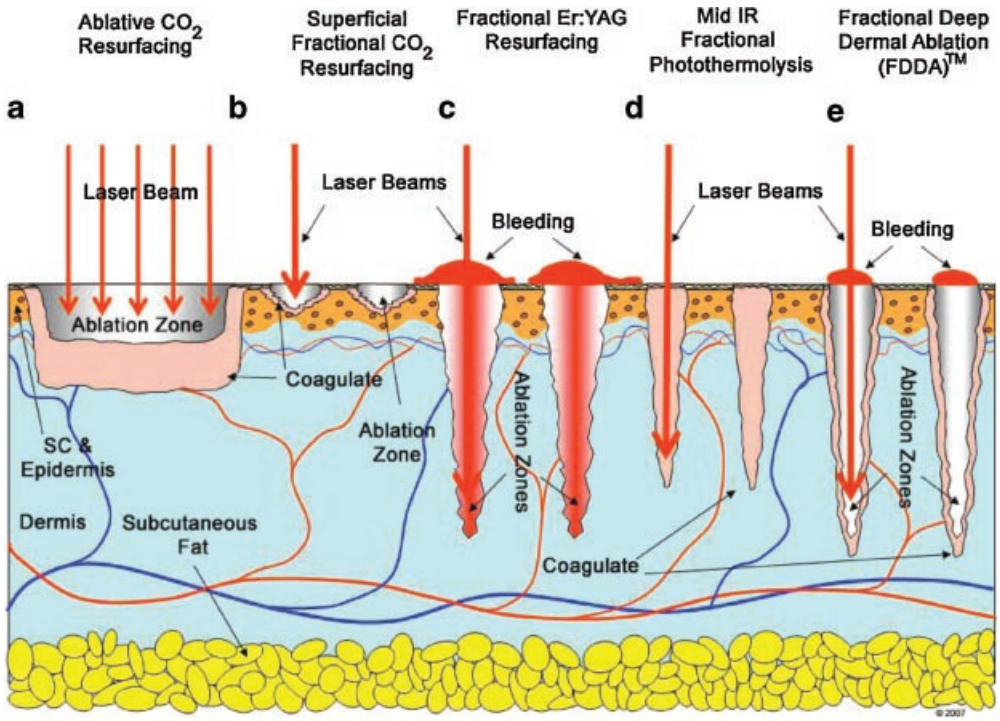

Fig. 1. Comparison of (**a**) traditional ablative resurfacing, (**b**) superficial pseudo-fractional CO_2 resurfacing, (**c**) fractional Er:YAG resurfacing, with (**d**) mid-IR fractional photothermolysis and (**e**) fractional deep dermal ablation (FDDA™) by a CO_2 laser.

pattern with spatial separation of columns of thermally affected epidermal and dermal tissue [16]. A comparison between the thermal damage patterns achieved with ablative resurfacing, superficial pseudo-fractional CO_2 resurfacing, fractional Er:YAG resurfacing, mid-IR Fractional Photothermolysis and FDDA™ are shown in Figure 1.

Within this report, we summarize the results from two separate clinical studies and present the first clinical examination of fractional deep dermal ablation (FDDA™). A pilot study characterized the laser-tissue interaction and wound healing profile following FDDA™ treatment with a fractional array-generating CO_2 laser system. The subsequent pivotal clinical investigation, using a prototype laser, examined the safety and efficacy of this modality for treatment of photodamaged skin. Results from both studies confirmed the clinical utility of FDDA™ treatment.

METHODS

Forearm Study Methods

Twenty-four healthy subjects were enrolled in a pilot study to evaluate the clinical and histological effect of an investigational 30 W, 10,600 nm CO_2 laser system (Reliant Technologies Inc., Mountain View, CA). The laser beam was delivered through multiple deflective and refractive elements and focused to a diffraction-limited $1/e^2$ spot size of 120 μm at incidence to the skin using the fractional approach, depositing a microscopic array of laser beams across the surface.

Subjects were excluded on the basis of active localized or systemic infections, history of keloid scar formation, recent chemical peeling procedures, or other cosmetic procedures on the area to be treated within 12 months of enrollment, Accutane use within 12 months of enrollment, or if they were smokers or were pregnant.

Four forearm test sites measuring approximately 1.5× 1.0 cm^2 were selected for each subject. Treatment sites were separated by at least 2 cm and placed in a straight line parallel in direction with respect to positioning of the radius/ulna (i.e., not perpendicular). Topical anesthetic was applied in a thick layer to treatment sites prior to the laser exposure and allowed to penetrate the skin for up to 60 minutes.

Different treatment energies (5–40 mJ) were selected by the study investigator and laser exposure was performed for each site. Treatments were administered using a single pass at a density of 400 MTZ/cm^2. Immediately following treatment, pain was assessed according to the 10-mm visual analog scale (VAS).

The test sites were evaluated for clinical appearance and post-treatment responses, including erythema, edema, the presence of petechiae and any side effects. The severity of post-treatment responses was assessed immediately post-treatment, 48 hours post-treatment and 1 week post-treatment using the following 3-point scale: 0 = none, 1 = minor, 2 = moderate, 3 = marked/severe.

Up to 2 punch biopsies were obtained from each subject. Biopsy procurement was performed at different post-treatment intervals (immediately, 48-hour, 1-week, 1-month, and 3-month post-treatment) in order to analyze the wound healing response over time.

Pivotal Study Methods

Following completion of 1- and 3-month follow-up visits within the forearm study, with evidence of safety and an understanding of the wound healing process following FDDA™ treatments, the pivotal study was initiated. The primary aim of this study was to evaluate the safety and efficacy of the prototype 10,600-nm CO_2 fractional laser system (Reliant Technologies Inc.) for the treatment of photodamage and laxity on the face and neck.

Ten subjects provided their informed consent and were enrolled at each of three study sites, for a total of 30 study subjects. Treatments were performed at the Fraxel Laser Clinic (Mountain View, CA), the R. Laurence Berkowitz Clinic (Campbell, CA) and the University of California at Irvine Department of Dermatology (Irvine, CA) with approval obtained from the Food and Drug Administration (FDA), the Western Institutional Review Board (WIRB) in Olympia, Washington and the UC-Irvine Institutional Review Board prior to study initiation.

Subjects were excluded from participation if they had active localized or systemic infections within 6 months of enrollment, had a compromised ability for wound healing, reported a history of keloid scar formation, received other cosmetic procedures within 6 months of enrollment, recently used Accutane, were smokers or were pregnant. Upon enrollment, subjects were prescribed an anti-viral medication (Valacyclovir) initiated the day of surgery and up to 7 days post-procedure. Compounded topical anesthetic (23% lidocaine/7% tetracaine or 30% lidocaine) cream was applied in a thick layer over the entire treatment region and allowed to penetrate the skin for up to 60 minutes. Oral hydrodocone bitartrate/acetaminophen tablets and lorazepam were administered one hour prior to the procedure. The topical anesthetic was then removed using a gentle, non-irritating cleanser.

Treatments were administered to the face and neck using parallel, overlapping treatment passes in the horizontal and vertical direction. With a fixed spot size of 120 μm, laser treatments were primarily administered at treatment energies of ≤20 mJ/pulse and total treatment densities ≤1,200 MTZ/cm^2 on facial skin and total treatment densities of ≤800 MTZ/cm^2/pass on the neck. The pulse width or dwell time varied with micro-pulse energy, and was maintained between 0.2 and 5 milliseconds. Each treatment density at any pulse energy level is associated with a percentage value for surface area coverage. For instance, densities of 800 MTZ/cm^2 were equivalent to 20% coverage, while 1,000 MTZ/cm^2 resulted in 25% surface area coverage. Table 1 lists the three sites' most frequently used energy and percent coverage setting, for the face and neck treatment area. During treatments, pain was assessed according to the 10-mm visual analog scale.

TABLE 1. Energy (mJ) and Corresponding Coverage (%) for Face and Neck Treatment Areas

Energy (mJ)	Face coverage (%)	Neck coverage (%)
12	46	26
15	40	23
20	35	18

Clinical appearance and post-treatment responses were assessed immediately upon treatment completion and at 48 hours, 1 week, 1 month, and 3 months post-treatment. Post-inflammatory hyper-pigmentation and hypopigmentation were assessed 1 month and 3 months post-treatment using the 0–3 severity scoring system.

The effectiveness of the deep dermal fractional ablative laser system for the treatment of photodamage, including rhytides, pigmented lesions, skin texture, vascular dyschromia, skin laxity and overall appearance was subjectively evaluated by blinded independent investigators 3 months post-treatment. Scoring was performed using the Fitzpatrick Wrinkle Scale (0–9) and a standard quartile improvement scale (0–4), with 0 = No Improvement (0%), 1 = Minor Improvement (1–25%), 2 = Moderate Improvement (26–50%), 3 = Marked Improvement (51–75%) and 4 = Very Significant Improvement (76–100%). In order to standardize investigator assessment of the relative changes in skin laxity, the term was defined as the presence of loose, sagging or redundant skin. Subject and investigator scoring 1 month and 3 months post-treatment were performed using the same quartile improvement scale (0–4) and methodology for each of the characteristics mentioned above.

Statistical Analysis

Statistical analysis was performed using the SAS Statistical package, version 8.10 (SAS Institute, Cary, NC). The improvement assessments at study follow-up visits were presented as mean score changes. Pearson correlation coefficients were used to assess the relationships between subject and investigator improvement scoring.

RESULTS

Forearm Study Clinical Results

Forearm exposures were performed without any adverse sequelae and the tested treatment energies were well tolerated. Mild (=1) to moderate (=2) erythema and edema were noted within a few minutes after exposure. Very slight petechial bleeding was noted in approximately 20% of subjects during the period immediately post-treatment until 48 hours post-treatment. Table 2 provides a summary of erythema and edema scores assessed by the investigators at different time points.

Post-treatment edema was completely resolved among 87% of subjects within 1 week post-treatment, and the remaining subjects were reported to have only very minor

TABLE 2. Post-Treatment Responses According to Treatment Energies

	Erythema (0–3)				Edema (0–3)			
Energy (mJ)	Immediately post-tx	1 week post-tx	1 month post-tx	3 months post-tx	Immediately post-tx	1 week post-tx	1 month post-tx	3 months post-tx
5 mJ ($n = 24$)	0.85 ± 0.2	0.48 ± 0.3	0.3 ± 0.2	0	0.95 ± 0.2	0	0	0
10 mJ ($n = 17$)	0.88 ± 0.2	0.59 ± 0.4	0.41 ± 0.2	0	1.00 ± 0.3	0.19 ± 0.4	0	0
20 mJ ($n = 24$)	1.06 ± 0.3	1.03 ± 0.3	0.72 ± 0.3	0	1.06 ± 0.3	0	0	0
30 mJ ($n = 17$)	1.17 ± 0.4	1.25 ± 0.3	1.08 ± 0.4	0	1.17 ± 0.8	0	0	0
40 mJ ($n = 6$)	1.25 ± 0.4	1.16 ± 0.4	0.83 ± 0.6	0	1 ± 0	0	0	0

edema at that visit. Minor to moderate erythema was apparent immediately post-treatment; however for treatments of $\leq$20 mJ/pulse, the intensity of erythema diminished to a score of less than "1" (minor) on average. Although the positive correlation between treatment energy and erythema was noted, even at higher energies the maximum intensity of erythema was, on average, categorized as "minor" to "moderate." No cases of delayed wound healing response were observed, even up to energies of 40 mJ/pulse.

Forearm Study Histological Results

Hematoxylin and Eosin staining was performed on biopsies taken from multiple treatment sites at various time points post-treatment. Lesions ranged from 125 to 250 μm in diameter extending up to 300–1,100 μm deep, for pulse energies of 5–40 mJ, respectively. For all treatment energies, there was an approximately 50-μm zone of coagulation adjacent to the ablated zone, promoting hemostasis for this treatment.

Epidermal cell migration occurred during the reepithelialization process for the 20 mJ treatments. Forty-eight hours following treatment, reepithelialization was almost completed for all treatment settings. After 1 week, complete healing and reepithelialization was confirmed by histological data. Interestingly it was observed that a pseudo-rete ridge pattern was created by epidermal invagination into the ablated zones. By 1-month post-treatment, the pseudo-rete ridge has regressed to the normal level of dermal-epidermal junction, retaining a physiologically normal rete ridge. At this time point, the previously ablated sites have been remodeled and replaced by new collagen. At 3 months post-treatment, prolonged dermal remodeling process was consistently observed as previously reported [5]. The rete ridge pattern remained at 3-month post-treatment, providing or improving the tinctorial characteristics of younger and healthier skin. These confirmed and correlated well with clinical observations during the treatment follow-up period.

Pivotal Study Results

The subject population included 30 subjects with Fitzpatrick skin types I–IV between the ages of 31 and 66 (average 55.4 ± 7 years). Subjects received one to two laser treatments with the prototype laser system. Subjects were treated at settings of $\leq$20 mJ/pulse and $\leq$400 MTZs/cm^2 per pass treatment density. According to mid-treatment assessments, subjects found pain to be moderate to very significant, with an average score 4.4 ± 2.5 on a 10 point scale.

Safety Data

Erythema and edema were observed in all subjects immediately post-treatment. Oozing with sparse petechial bleeding was observed in all subjects immediately post-treatment. Subjects cleansed the treatment area using Cetaphil cleanser and applied Aquaphor to moisturize the skin. Subjects were instructed to continue cleansing the area using distilled water and vinegar soaks, followed by reapplication of Aquaphor, during the first 3 days post-treatment.

Forty-eight hours post-treatment, subjects continued to exhibit mild to severe erythema (1.95 ± 0.6), with slightly milder edema (1.71 ± 0.5). Oozing and petechial bleeding was reported to have subsided in all but one subject within 24 hours of treatment. This slight pinpoint bleeding was observed in 1 subject 48 hours post-treatment. Crusting, possibly a secondary response to prior oozing, was observed in approximately 73% of the study subjects (22/30) 48 hours post-treatment. When crusting was observed, it was reported to have developed between 24 and 48 hours post-treatment. Some patients also noted a delayed superficial desquamation at 1 week following treatment. There was no correlation between other post-treatment responses, such as erythema, edema or the presence of crusting. It is possible that this response may be attributed to subject compliance with instructions for post-operative wound care.

Erythema and edema continued to resolve from 2 to 7 days post-treatment, with both responses diminishing to the point of being mild in severity by 1 week post-treatment. In addition, no oozing or petechial bleeding was observed in any subject at the 1-week follow-up visit. Two subjects sustained physical abrasions (both reported at the 1 week follow-up visits) on the neck, with subject's confirming that occurrence followed contact with abrasive clothing surfaces. Topical antibiotics were prescribed and successfully mitigated symptoms associated with these abrasions, resulting in complete healing without adverse sequelae. None of the subjects exhibited oozing or petechial bleeding 1 month post-treatment.

One month post-FDDA^{TM} treatment, no oozing or petechial bleeding was observed in any subject. The incidence of erythema and edema was 33% and 10%, respectively, though mild in severity with an erythema severity score of 0.93 ± 0.6 and an edema severity score of 0.66 ± 0.2. Mild post-inflammatory hyper-pigmentation (PIH) was observed in six subjects (20%), three of which were Fitzpatrick skin type II and three of which were Fitzpatrick skin type III. No association between skin type and PIH was observed within this subject population.

By the 3-month follow-up visit, complete resolution of edema and post-inflammatory hyper-pigmentation was demonstrated. There was no recurrence of previously exhibited responses, such as crusting, oozing or petechial bleeding. Table 3 provides a summary of post-treatment responses.

To further confirm the safety of the prototype laser system, additional follow-up visits were conducted for the forearm study subjects 2 years post-treatment and the ten subjects treated at the Fraxel Laser Clinic 1 year post-treatment. 67% (16 of 24) and 100% (10 of 10) subjects, respectively, were available for evaluation. Upon evaluation, none of the subjects exhibited any symptoms; specifically no patients reported scarring or hypopigmentation. Confirmation that there was no incidence of delayed onset hypopigmentation was of particular importance.

Efficacy Data

Subject and investigator quartile improvement scoring (0–4) confirmed the consistent improvement in each of the characteristics of photodamage. Eighty-three percent of subjects exhibited moderate or better improvement in the overall appearance of the photodamaged skin treated (50–100% improvement). Subject and study investigator improvement scoring was well-correlated for overall improvement and each sub-characteristic. As confirmation of the collagen remodeling process associated with CO_2 laser ablation, continued improvement was observed throughout the 3-month follow-up period, particularly in the appearance of laxity and rhytides. Table 4 depicts subject and investigator quartile improvement scoring.

Blinded, independent investigators further confirmed the efficacy of the prototype laser system for the same indications.

All subjects treated were included in the blinded scoring analysis for a total set of 30 baseline and 3-month follow-up visit photographs which were assessed independently by two blinded investigators. Photos were randomly arranged and coded with an alpha-numeric identifier for the purposes of a blinded assessment.

Each investigator assigned a Fitzpatrick Wrinkle Score to represent the severity in photodamage reflected in each

TABLE 3. Post-Treatment Responses and Severity Scoring

Post-treatment responses	Number of subjects (%)	Mean post-treatment response score (0–3)
Erythema		
48 hours post-treatment	30 (100%)	1.95 ± 0.6
1 week post-treatment	30 (100%)	1.23 ± 0.4
1 month post-treatment	10 (33%)	1 ± 0
3 months post-treatment	2 (7%)	1 ± 0
Edema		
48 hours post-treatment	30 (100%)	1.71 ± 0.5
1 week post-treatment	22 (73%)	0.8 ± 0.5
1 month post-treatment	3 (10%)	0.66 ± 0.2
3 months post-treatment	Not observed	Not observed
Oozing		
48 hours post-treatment	1 (3%)	1 ± 0
1 week post-treatment	Not observed	Not observed
1 month post-treatment	Not observed	Not observed
3 months post-treatment	Not observed	Not observed
Petechial bleeding		
48 hours post-treatment	1 (3%)	1 ± 0
1 week post-treatment	Not observed	Not observed
1 month post-treatment	Not observed	Not observed
3 months post-treatment	Not observed	Not observed
Post-inflammatory hyperpigmentation		
1 month post-treatment	6 (20%)	1 ± 0
3 months post-treatment	Not observed	Not observed
Delayed onset hypopigmentation		
1 month post-treatment	Not observed	Not observed
3 months post-treatment	Not observed	Not observed

TABLE 4. Number of Subjects Demonstrating Moderate or Better Improvements (≥2)

Characteristic	1 month	3 months
Overall improvement		
By subject	25/30 (83%)	23/30 (83%)
By investigator	22/30 (73%)	25/30 (83%)
Improvement in texture		
By subject	25/30 (83%)	24/30 (80%)
By investigator	25/30 (83%)	26/30 (87%)
Improvement in appearance of wrinkles		
By subject	21/30 (70%)	22/30 (73%)
By investigator	22/30 (73%)	22/30 (73%)
Improvement in laxity		
By subject	18/30 (60%)	20/30 (67%)
By investigator	12/30 (40%)	21/30 (70%)
Improvement in appearance of pigmentation		
By subject	17/30 (57%)	22/30 (73%)
By investigator	21/30 (70%)	23/30 (77%)

photograph. Baseline Fitzpatrick Wrinkle Scores were averaged to obtain the baseline Fitzpatrick Wrinkle Score. Three-month follow-up Fitzpatrick Wrinkle Scores were averaged to obtain the post-treatment Fitzpatrick Wrinkle Score. Overall, photodamage, as indicated by the Fitzpatrick Wrinkle Scale, improved by an average of 1.47 ± 1.1 on a scale of 1–9 during the 3-month follow-up period (Table 5). In addition, investigators were asked to select one photo within a set (blinded as to which photo was taken at baseline and which was taken at follow-up) as being "better overall". Investigator 1 selected the post-treatment photograph as being "better overall" for all subjects, while investigator 2 selected the post-treatment photograph as being "better overall" for 29/30 subjects (97%). For the purposes of calculations for that subject, improvement scores were recorded as the negative value (of the same magnitude as recorded by the investigator as positive improvement for the baseline photograph) for every characteristic.

The average Fitzpatrick Wrinkle Score assigned by the blinded investigators (5.13 ± 1.6) was correlated to the score assigned by the study investigator at baseline assessment (5.82 ± 1.8). This served to further validate the Fitzpatrick Wrinkle Score assignment process. The primary endpoint of this investigation is the reduction in Fitzpatrick Wrinkle Score as determined by blinded investigator analysis. No direct comparison was made between study investigator and blinded investigator scoring using the same scale.

Changes in the overall appearance of photodamage, as well as rhytides, pigmented lesions, vascular dyschromia and skin laxity were assessed for each photograph according to the same quartile improvement scoring system used by subjects and investigators. Consistent improvement in the indices of photoaging was exhibited in the vast majority of subjects, as evidenced by the frequency distribution for overall improvement ≥1. Improvement in the appearance of each of the characteristics of photodamage, including

TABLE 5. Independent Investigator Scoring Using a Quartile Improvement Scale (0–4) and the Fitzpatrick Wrinkle Scale (0–9)

	Average quartile improvement scores (0–4)				
	Rhytides	Pigmentation	Texture	Laxity	Vascular
Investigator 1	2.37 ± 1.0	2.43 ± 1.0	2.70 ± 0.6	2.23 ± 0.8	2.30 ± 1.1
Investigator 2	2.23 ± 1.6	2.23 ± 1.6	2.13 ± 1.2	1.07 ± 0.7	2.20 ± 0.9
	Average investigator score				
	2.30 ± 1.4	2.33 ± 1.3	2.42 ± 0.9	1.65 ± 1.0	2.25 ± 1.0

Average Fitzpatrick Wrinkle scores (0–9)*

Pre-treatment, Fitzpatrick Wrinkle score (0–9): 5.13 ± 1.6

3 Months post-treatment, Fitzpatrick Wrinkle score (0–9): 3.67 ± 1.4

Average reduction in Fitzpatrick Wrinkle score: 1.47 ± 1.1†

*Pearson correlation coefficient between independent investigators' assessments of the change in Fitzpatrick Wrinkle score $r = 0.62$ ($P < 0.001$).

†Paired t-test analysis demonstrated statistical significance ($P < 0.001$).

Bold—primary study endpoints.

rhytides, pigmentation, texture, laxity and vascular dyschromia was confirmed by blinded investigators for 90% of the subjects treated.

To reflect the magnitude of improvement exhibited for each characteristic, the mean improvement scores were calculated for each investigator separately and as an average for both investigators (Table 5). The distinct scoring (0–4) performed by each investigator for each characteristic confirmed average improvement scores for rhytides, pigmented lesions, texture, skin laxity, and vascular dyschromia.

Blinded investigator quartile scoring was presented individually and as combined evaluation by the two investigators. Their independent score frequency distributions show strong agreement (in the occurrence of improvement) in each of the sub-categories. Some degree of incongruence in *magnitude* of improvement is expected during blinded investigator analysis of photographs as a result of different interpretations of the quartile scoring system. The agreement between investigator 1 and 2 over *occurrence* served to confirm the consistency in identification of response.

Clinical photographs are shown in Figure 2 to depict the progression of wound healing during the 3-month follow-up period, with resolution of clinical downtime within the first week following treatment. In addition, as reflected in Figure 3, consistent long-term improvement was sustained 1 year following treatment with the prototype laser system.

DISCUSSION

The method whereby carbon dioxide laser leads to cosmetic improvement has been demonstrated [6]. The zone of residual thermal damage (RTD) combined with ablation led to the expected cosmetic outcomes. It was observed that although ablation depths were much less than wrinkle depths, the zone of collagen that was altered in the residual thermal damage zone was as thick as 250 um. Previously it has been postulated that the depth of ablation and collagen alteration determined the efficacy of carbon dioxide laser resurfacing. Subsequently, numerous studies comparing CO_2 resurfacing to Er:YAG resurfacing revealed that the depth of injury correlated to clinical results [18–20]. When traditional multiple pass CO_2 laser resurfacing is compared to Er:YAG resurfacing, more tightening and clinical improvement was observed with CO_2 laser resurfacing [21,22]. Thus both amount of tissue ablation and zone of RTD play an important role in the efficacy of ablative laser resurfacing.

Fractional non-ablative resurfacing has been shown to be a safe and effective modality for the treatment of wrinkles and photodamage [23,24]. We postulated that extending the concept of fractional resurfacing with deep dermal ablation of tissue would maximize the efficacy of traditional ablative resurfacing while minimizing the side effect profile associated with non-fractional ablative treatments. To achieve the same volume of collagen contraction and increase the depth of residual thermal damage, we choose

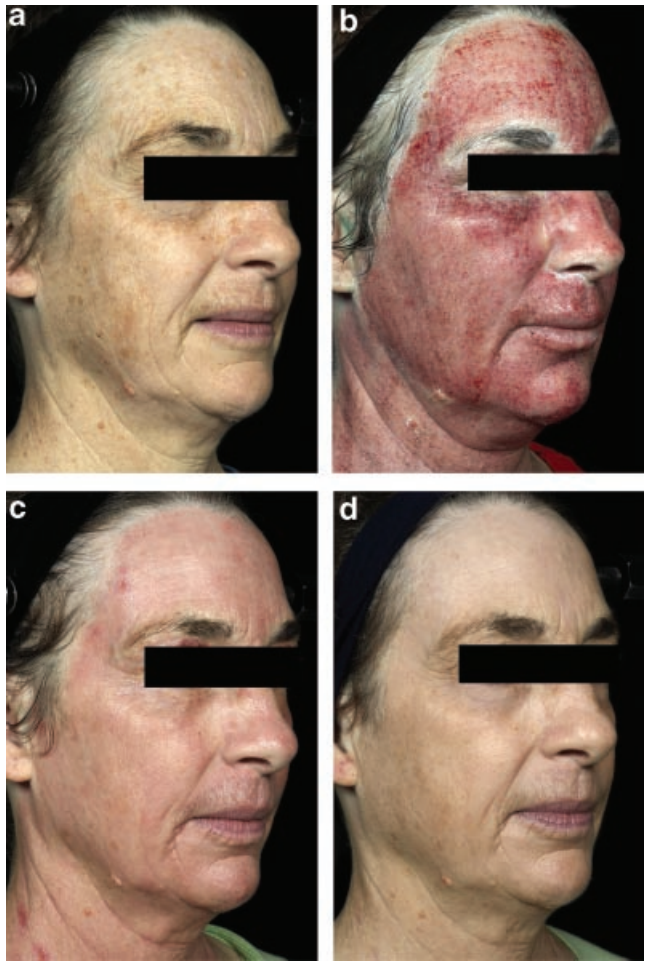

Fig. 2. Baseline (**a**), 24 hours post-treatment 2 (**b**), 1 week post-treatment 2 (**c**), and 3 months post-treatment 2 (**d**). Treatments were performed at settings of 15 mJ and 47% coverage on the face and 15 mJ and 27% coverage on the neck, with 90 days between treatments 1 and 2.

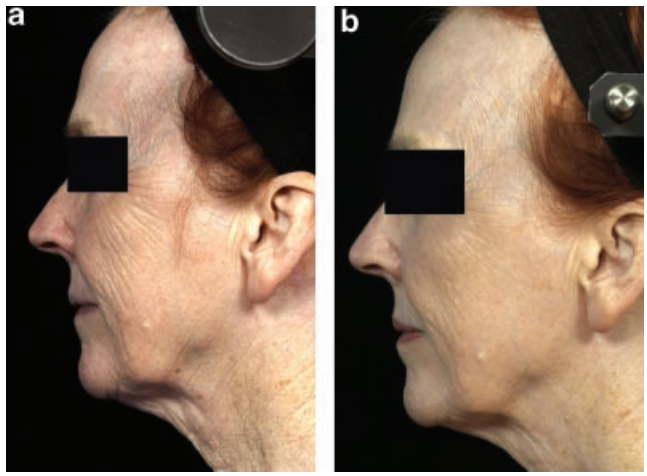

Fig. 3. Baseline (**a**), 1 year following a single FDDA treatment at settings of 15 mJ and 47%!coverage on the face and 15 mJ and 27% coverage on the neck (**b**).

the CO_2 laser to perform the evaluation. The size of the vessels in the dermis increases with increasing depth of penetration. This was observed as increased bleeding during treatments. The zone of collagen denaturization around the zone of vaporization assists in sealing off some of these vessels to limit the bleeding. This might provide a significant advantage as compared to Er:YAG ablative resurfacing which lacks a significant zone of coagulation to promote hemostasis as observed clinically by significant bleeding. We postulate that pure vaporization without a zone of collagen denaturization with a Er:YAG laser would lead to significantly more bleeding at comparable depth of deep ablation. The smaller zone of RTD would also limit the efficacy of Er:YAG resurfacing compared to CO_2.

Traditional CO_2 resurfacing provides significant improvement of skin laxity and deep rhytides. The depth of ablation and RTD is less than 500 μm. We postulated that treating the same volume of tissue fractionally in a vertical plane would lead to the same efficacy as horizontal nonfractional treatment. We observed improvement that was comparable to traditional multiple-pass CO_2 resurfacing without the associated prolonged wound healing response or hypopigmentation. Although 20% of subjects exhibited post-inflammatory hyperpigmentation, this was less than the incidence rate documented by Schwartz et al. [25] following retrospective review of non-fractional full CO_2 resurfacing outcomes.

Facial treatment energies and total skin surface coverage were significantly higher than neck parameters. The high density of pilosebaceous units on the face makes it more forgiving and therefore able to tolerate higher coverage. We report the 3-month results of all 30 subjects in this investigation. Nine subjects were also evaluated at 12 months. The unique wound healing process of the FDDA treatment was indicative of the importance of sparing epidermal melanocytes in preventing delayed onset hypopigmentation, which can be observed with high incidence in traditional ablative modalities. The FDDA treatment also appears to be unique as an ablative resurfacing modality that can be applied off the face clinically without causing any adverse sequelae. With an encouraging safety profile and the ability to stimulate a pseudofollicular pattern followed by sustained rete ridge modulation, FDDA treatment may have significant potential for facial and nonfacial photodamaged skin or striae where the epidermis is atrophic and flattened.

CONCLUSIONS

Clinical and histologic evaluation of fractional deep dermal ablation with a prototype fractional CO_2 laser reveals safe and efficacious treatment of skin laxity and for the signs of photoaging. Positive treatment outcomes were confirmed by blinded investigators, study investigators and subject assessments. Clinical results correlated with histologic collagen remodeling and rapid reepithelialization. The pilot forearm study demonstrated complete histologic reepithelialization by 48 hours. This was clinically correlated in the face and neck study with resolution of exudate by 48 hours. No adverse sequelae were reported in any of the forearm subjects or the face and neck subjects throughout the study up to 2 years following completion of study. Two important risks that are associated with traditional ablative resurfacing, scarring and hypopigmentation, were not reported for up to 2 years.

Treatment success for improvement of pigmentation, rhytides as well as skin laxity was demonstrated through statistically significant reduction in the Fitzpatrick Wrinkle Score and the consistent improvement for each indication as demonstrated by standard quartile improvement scoring. The improvement of skin laxity confirmed our hypothesis that volume reduction through deep dermal ablation of tissue leads to clinically observed skin tightening. Further studies and long-term safety data are needed to elucidate optimal treatment parameters.

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