

Treatment of CO₂ Laser Induced Hypopigmentation With Ablative Fractionated Laser Resurfacing: Case Report and Review of the Literature

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ABSTRACT

Background: The carbon dioxide laser (CO₂) has been proven to be an effective device for the treatment of photoaging. However, it is associated with adverse side effects including prolonged erythema, edema, burning, milia, acne, crusting and hypo-/hyperpigmentation. Delayed onset hypopigmentation after CO₂ laser resurfacing can markedly detract from clinical outcomes. To overcome the disadvantages of traditional ablative and non-ablative resurfacing, fractional photothermolysis (FP) has been introduced. FP has been demonstrated in early case reports and case series to produce significant improvement in hypopigmentation of acne and surgical scars.

Case Report: A 53-year-old Caucasian female with Fitzpatrick type I skin presented with a nine-month history of delayed onset hypopigmentation following ablative CO₂ laser resurfacing. After a series of three treatments at eight-week intervals with an ablative fractionated CO₂ laser device, the hypopigmentation and line of pigmentary demarcation between the face and neck improved by 75 percent.

Conclusion: Ablative fractional resurfacing is a safe and potentially effective modality for the treatment of CO₂ laser induced hypopigmentation on the face.

INTRODUCTION

Background

Traditional Ablative CO₂ Laser Resurfacing

The carbon dioxide laser (CO₂) has been proven to be an effective device for a wide range of dermatologic conditions, including the skin signs of photoaging (rhytides, dyschromia, mottling and skin texture abnormalities), and scarring (acne scarring, surgical scarring, thermal burns, etc.).^{1,2} High-energy, short duration exposure to the 10,600 nm wavelength of the CO₂ laser light vaporizes intra- and extracellular water, causing tissue ablation.^{1,2} The exposure of CO₂ light is rapid enough to limit extraneous dermal injury and thus, reduces the likelihood of scarring.^{1,2} It has been demonstrated that this pattern of superficial and rapid removal of epidermis and dermis, stimulates collagen and elastin formation and mediates subsequent improvement in skin texture and contour.^{1,2}

While significant clinical improvements can be achieved with CO₂ laser resurfacing, the risks are significant and deter patients from undergoing this treatment modality.³⁻⁷ Patients undergoing CO₂ facial resurfacing can anticipate post-treatment erythema which lasts from weeks to months, depending upon the depth of ablation. More significant complications have also been reported, including infection, permanent scarring or alterations in skin texture. Post-inflammatory hyperpigmentation, especially in patients of darker skin phototypes, has been reported in up to 40–50 percent of cases.³⁻⁸ Another adverse consequence of

CO₂ resurfacing is delayed onset hypopigmentation, particularly given that this side effect is usually not transient and can markedly detract from overall clinical outcomes.³⁻⁸

Non-ablative Laser Resurfacing

To overcome these adverse effects of ablative skin resurfacing, non-ablative resurfacing devices were introduced as a means to improve photodamaged skin while preventing the significant epidermal damage associated with ablative devices.^{4,9-12} Lasers utilized for non-ablative resurfacing procedures have a much deeper optical penetration than ablative CO₂ and Er:YAG lasers.^{4,9-12} With non-ablative resurfacing, selective damage to dermal tissue occurs to induce a wound response, but without damage to the epidermis.^{4,9-12} The wound response to thermally damaged dermal tissue results in the formation of new dermal collagen and the repair of tissue defects related to photoaging.^{4,9-12} While it has been demonstrated that non-ablative devices have a more benign side effect profile than ablative devices, they have more limited efficacy.^{4,9-12}

Fractional Photothermolysis

To overcome the disadvantages of conventional ablative and non-ablative laser technologies, researchers have introduced fractional photothermolysis (FP), which has revolutionized laser surgery by delivering energy in a novel beam pattern.¹³ Utilizing a non-ablative-erbium-doped 1,550 nm laser, full thickness columns of coagulation are created in a pixilated

pattern (termed microthermal zones or MTZs) just beneath the surface of the skin, leaving healthy skin between MTZs.¹³⁻¹⁵ The density and depth of the MTZ may be adjusted in order to target the intended tissue in a precise manner.¹³⁻¹⁵ Because of the focal nature of wounding in FP, each wound is surrounded by healthy tissue and healing is rapid and recovery time is dramatically reduced.¹³⁻¹⁵

FP has been utilized for a broad spectrum of skin conditions, beyond the initial studies demonstrating improvement in periorbital rhytids and skin contraction in forearm skin. Indications for FP reported in the literature include mild-to-moderate acne scarring, dyschromia, fine wrinkling and texture changes associated with photoaging on the face, chest, neck and hands,¹⁶⁻¹⁹ Poikiloderma of Civatte,²⁰ acne scarring,^{21,22} melasma,²³⁻²⁵ nevus of Ota,²⁶ minocycline-induced hyperpigmentation,²⁷ hyper/hypopigmented scars,²⁸⁻³⁰ residual hemangiomas,³¹ telangiectatic matting,³² granuloma annulare,³³ colloid milium³⁴ and disseminated superficial actinic porokeratosis.³⁵⁻³⁷

One of the novel effects of FP has been the observation of normalization of pigmentary variance after treatment with this technology. The effects of FP on epidermal pigment are of interest because few of the currently available non-ablative laser treatments in the infrared spectrum (IR) have significant effects on epidermal pigmented lesions. In contrast, traditional ablative laser resurfacing completely removes the pigmented layer, which can result in permanent hypopigmentation. In the initial report by Manstein et al.,¹³ there were several dark-skinned patients who demonstrated little or no significant pigmentary change after FP at low or medium MTZ densities per treatment. Histology revealed that there is a localized, well-controlled melanin release and transport mechanism using micro epidermal necrotic debris (MENDs) as the vehicle for pigmentary re-distribution.¹³ Furthermore, unwanted localized accumulations of pigment (i.e., solar lentigines) appeared to be effectively removed in a precise and gradual manner as originally described in the prototype device by Manstein et al.¹³ Further recent investigation regarding this aspect of FP has led to novel concepts for treatment of conditions characterized by pigment abnormalities, such as melasma,²³⁻²⁵ nevus of Ota,²⁶ minocycline induced hyperpigmentation²⁷ and hyper/hypopigmented scars.²⁸⁻³⁰

Treatments for Hypopigmentation

Current treatment modalities for hypopigmentation are of limited scope and efficacy. These treatment modalities include cosmetic tattooing, medium-depth chemical peels, carbon dioxide and erbium laser resurfacing, dermabrasion, skin grafting, cosmetic camouflage and various forms of phototherapy and laser therapy.⁴⁴⁻⁴⁸ FP has been demonstrated in early case reports and case series to produce significant improvement in hypopigmentation of both acne and surgical scars.^{21,22,28-30}

Given these reports of success in the literature of improvement of hypopigmented surgical scars with FP, the authors performed treatment of a patient with delayed hypopigmentation which occurred after traditional ablative CO₂ resurfacing with a fractionated CO₂ laser device. Herein, the authors report a case of significant improvement in facial hypopigmentation after treatment with an ablative fractionated CO₂ laser device (Dermal Optical Thermolysis, DOT Laser, Eclipse Med, Dallas, TX).

Case Report

A 53-year-old Caucasian female with Fitzpatrick type I skin presented with a nine-month history of delayed onset facial hypopigmentation following traditional ablative CO₂ laser resurfacing. Hypopigmentation developed approximately three months after traditional ablative CO₂ laser resurfacing for desired cosmetic improvement of photoaging. While the patient was pleased with the improvement in skin texture and rhytides after ablative CO₂ resurfacing, she was very concerned with the hypopigmentation and wished to undergo further treatment to resolve the pigmentary variation. At clinical presentation, a well defined pigmentary line of demarcation was present along the base of the mandible separating the hypopigmentation of the face from the normal pigmentation of the neck (Figure 1a). Her past medical history was unremarkable. The patient denied any personal or family history of keloid formation, vitiligo or other pigmentary disorder. She had one course of isotretinoin for nodulocystic acne as a teenager.

The treatment area was thoroughly cleansed before the procedure with a gentle, skin cleanser. A bupivacaine/lidocaine/tetracaine mix was applied 30 minutes before treatment. A series of three treatments was performed at eight-week intervals with an ablative fractionated CO₂ laser device (Dermal Optical Thermolysis,

FIGURE 1. Frontal facial view. Pre- and post-treatment of CO₂ laser induced hypopigmentation with ablative fractional CO₂ laser (DOT Laser, DEKA, Calenzano Italy). Photos used with permission from C. William Hanke MD MPH.



DOT Laser, Eclipse Med, Dallas, TX) at settings of 30 Watts, 500 pitch, 500 milliseconds for the face and 20 Watts, 500 pitch, 500 milliseconds for the neck. Improvement was quantified on a quartile scale (0–4) to assess the percentage of improvement with each treatment as well as after the completion of a series of treatments. Cold air anesthesia was administered with the Zimmer Cooler at a setting of 5, at a distance of three to four inches from the skin surface. During treatment, the patient reported minimal pain that was alleviated with the use of the cold air anesthesia. Minimal post-operative erythema and edema was noted which resolved within 72 hours.

Follow-up results at two months after each treatment revealed a significant clinical degree of improvement in the hypopigmentation of the patient's face. The hypopigmentation of the patient's face improved by 75 percent at two months after the series of three treatment sessions (Figures 1a, 1b, 2a, 2b, 3a and 3b). Additionally, the line of demarcation between the pigmentary variation of the face and neck significantly improved after the series of treatments (Figures 1a, 1b, 2a, 2b, 3a and 3b). The background dyschromia and textural abnormalities of the patient's neck and chest improved after the series of treatments with the dermal optical thermolysis (DOT) Laser (Figures 4a and 4b). The patient's degree of satisfaction paralleled the physician's assessment of improvement.

DISCUSSION

Ablative Versus Non-ablative Fractional Photothermolysis

FP has recently become one of the most popular laser based technologies given the significant improvements in the cutaneous signs of photodamage coupled with its safety and side effect profile.¹³ FP was designed to overcome the limitations in efficacy of non-ablative resurfacing and adverse side effect profile of ablative resurfacing, where the microscopic, pixilated pattern of wounding into the dermis results in both significant skin pigmentary and textural improvements.¹³ FP creates microscopic thermal wounds and specifically spares tissue surrounding each wound.¹³ This focal nature of wound healing promotes rapid recovery, preventing the prolonged erythema and swelling which occur with traditional ablative facial resurfacing.¹³

The original prototype FP devices were “non-ablative” in that epidermal integrity is preserved and columns of coagulation are created underneath the skin with an intact stratum corneum barrier on the skin surface.¹³ While NAFF demonstrated modest improvements in conditions, such as photoaging,^{16–19} periorbital wrinkling,¹³ mild to moderate acne scarring^{21,22} and Poikiloderma of Civatte,²⁰ patients required multiple treatments to achieve significant results and even with multiple treatments, patients with significant textural and pigmentary abnormalities were only minimally improved with non-ablative energies.

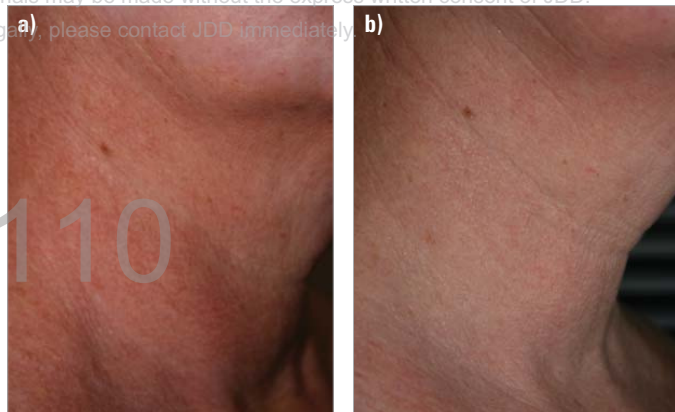
FIGURE 2. Left lateral facial view. Pre- and post-treatment of CO₂ laser induced hypopigmentation with ablative fractional CO₂ laser (DOT Laser, DEKA, Calenzano Italy). Photos used with permission from C. William Hanke MD MPH.



FIGURE 3. Right lateral facial view. Pre- and post-treatment of CO₂ laser induced hypopigmentation with ablative fractional CO₂ laser (DOT Laser, DEKA, Calenzano Italy). Photos used with permission from C. William Hanke MD MPH.



FIGURE 4. Neck. Pre- and post-treatment of poikiloderma of civatte and dyschromia of the neck with ablative fractional CO₂ laser (DOT Laser, DEKA, Calenzano Italy). Photos used with permission from C. William Hanke MD MPH.



A novel "ablative" FP was then introduced by Hantash et al in 2007.³⁸ This AFP device deposited a pixilated pattern of microscopic ablative wounds surrounded by healthy tissue in a similar fashion as the previous generation of NAFP devices.³⁸ The critical distinction between AFP and NAFP, is that with FP, a confluent column of ablation and thermal injury was seen which extended from the dermis and epidermis through the stratum corneum.³⁸

Utilizing human forearm skin *in vivo*, Hantash et al.³⁸ demonstrated that with AFP, a controlled microthermal zone of injury could be induced with stimulation of the wound healing response by adjacent intact skin. In several recent studies, significantly greater improvement in the cutaneous signs of photoaging have been demonstrated with AFP technology relative to the original generation of NAFP devices.^{39–42}

Weiss et al. reported a comparative split-face trial with one half treated with fractionated CO₂ laser and the contralateral half treated with 1550 nm non-ablative fractional Er:YAG laser.³⁹ Significantly greater improvement in peri-ocular rhytids (75% improvement) were observed in 10 patients treated with fractionated CO₂ laser relative to the 1550 nm erbium side (25% improvement) on blinded photographic analysis.

Lomeo et al.⁴⁰ reported the results of a split-face comparative trial of a non-ablative microfractional Er:YAG versus an ablative microfractional CO₂ laser device in 10 patients. A significantly higher improvement in skin texture and color (+15%) was observed on the side treated with the ablative microfractional CO₂ laser relative to the non-ablative microfractional Er:YAG laser.

Ross et al.⁴¹ published the results of a comparative study evaluating the efficacy of a 2940 nm microfractional Er:YAG laser relative to a standard ablative Er:YAG laser in the treatment of facial rhytids and dyspigmentation. On comparative analysis, traditional Er:YAG laser resurfacing demonstrated equivalent wound healing times as microfractional Er:YAG; however, microfractional CO₂ demonstrated significantly greater improvement in wrinkle reduction.

Improvement in Pigmentation With Fractional Photothermolysis

The pattern of wounding in FP has been well characterized histologically, whereby through laser-induced tissue heating, microcolumns of dermal and epidermal debris are selectively eliminated.^{13–15} It is postulated that the pigmentary improvement after treatment with FP is achieved through these channels in the skin, which selectively eliminate epidermal and dermal contents and allow new keratinocytes and melanocytes from surrounding intact skin to re-populate these channels of cellular damage.^{15–18} This hypothesis has been termed the "melanin

shuttle."^{15–18} It is this non-selective extrusion of epidermal and dermal melanocytes which has been postulated to be the mechanism of improvement of a variety of pigmentary disorders, including dyschromia of photoaging,^{16–19} melasma,^{23–25} minocycline induced hyperpigmentation²⁷ and Nevus of Ota.²⁶

This hypothesis has been proven by histologic analysis by Goldberg DJ et al.,⁴⁹ where after treatment of patients with melasma with a NAFP device, there is a decrease in the number of melanocytes and the amount of melanin granules within keratinocytes on both light and electron microscopy.

Izickson and Anderson²⁷ recently published a novel finding whereby minocycline-induced hyperpigmentation was markedly improved with the use of non-ablative FP. The authors reported the case of a 66-year-old woman with a two-year history of minocycline use for rosacea with resulting bluish pigmentation of cheeks and upper lip treated with FP using a 1550 nm FP laser (Fraxel SR, Reliant Technologies, Hayward, CA) over four treatment sessions.²⁷ Two months after the last treatment, near complete resolution of blue pigmentation on the face was observed. The authors postulated that the mechanism of improvement was likely analogous to improvement of deeper pigmentation in photoaging and melasma, with gradual clearance of drug induced dermal pigment, as well as deposition and remodeling of healthy new dermal collagen.

Kouba et al.²⁶ published a case report detailing treatment of a Nevus of Ota treated successfully with FP. A fractionated 1440-nm Nd:YAG laser (Affirm; Cynosure Inc., Westford, MA) was utilized with the end point of treatment of the entire field, as measured by a confluent, immediate erythema. The nevus of Ota completely resolved within six weeks after a series of two treatments. It was proposed that, similar to the effects of FP of minocycline hyperpigmentation, selective microthermal zones resulted in destruction of the superficial dermal pigment.

Treatment of Hypopigmentation With Fractional Photothermolysis

Fractional photothermolysis has been demonstrated in early case reports and case series to produce improvement in hypopigmentation of acne, surgical and burn scars.^{21,22,28–30}

Behroozan et al.²⁸ reported 75 percent overall improvement in a surgical scar on the chin after a single treatment with the 1550-nm Fraxel SR. In 2007, Glaich et al.²⁹ established the efficacy of the 1550-nm Fraxel SR in a series of seven patients with hypopigmented facial scars, resulting from acne (six patients) and a thermal burn (one patient). After a series of two to four treatments, 51–75 percent improvement in hypopigmentation was observed in six of seven patients. Improvement was also noted in the overall texture of the scar and surrounding area treated with FP.

In a study performed by Tierney et al.³⁰ comparing the efficacy of FP for the cosmetic improvement of surgical scars relative to the pulsed dye laser (PDL), greater improvements were noted with FP relative to PDL. Fifteen scars were treated on one-half of the scar with 1550-nm fractionated Er:YAG laser (Fraxel SR, Reliant Technologies Inc.) and on the contralateral half with the 595 nm PDL (V-Beam, Candela Corporation Inc., Wayland, MA). A total of four scars with significant hypopigmentation were improved after a series of four treatments with FP (mean improvement 65%,) with no improvement after treatment with PDL (mean improvement 0%,) ($P < 0.001$).

Most recently, Waibel and Beer⁵⁰ provided a novel case report of the efficacy of FP for hypopigmented burn scars. Postulated mechanisms of the unique efficacy of this technology include the greater depth of penetration and stimulation of wound healing properties.

The mechanism of action of fractionated laser resurfacing in hypopigmentation is purely speculative, but may include repopulation of resurfaced tissue with normal melanocytes from surrounding tissue, resulting in increased overall pigmentation. By treating a hypopigmented area of skin in with a pixilated fashion of ablation, the migratory pathways for healing are short and thus, melanocytes can migrate from pigmented, normal skin into the hypopigmented areas. Further histologic studies are highly needed to elucidate the healing process and confirm the movement of melanocytes into the treated areas. Fractional resurfacing may also result in improvement of pigmentary variation through collagen remodeling and up-regulation of collagen production, where smoothing out of skin texture gives the illusion of color, lessening the prominence of hypopigmentation.

CONCLUSION

It has been previously reported that treatment with NAFD devices results in significant improvement in hypopigmentation.^{21,22,28-30} The authors present the first case of improvement in hypopigmentation with AFP technology. The authors found that with AFP technology, rapid improvement in hypopigmentation was achieved after a series of three treatment sessions. Also, treatment with AFP of the neck and chest in this patient resulted in significant improvement of the background dyschromia in these areas, resulting in greater blending of cosmetic results of the face with the neck and chest.

The case of this patient highlights the significant adverse side effect of delayed onset hypopigmentation associated with the previous generation of traditional ablative CO₂ laser resurfacing devices. The side effects of hypo- and hyperpigmentation associated with traditional ablative laser resurfacing significantly limits the tolerability and patient satisfaction associated with these procedures. The use of non-ablative laser resur-

facing devices for the treatment of photoaging have become increasingly more common, given their protective effects on epidermal pigment. The advent of FP technology represents a significant milestone, whereby similar effects achieved on tissue tightening and skin texture as those seen with ablative resurfacing, with the safety and side effect profile of non-ablative resurfacing. Uniquely, both NAFD and AFP devices have also demonstrated significant improvement in disorders of skin pigmentation which are significantly greater than those achieved with the previous generation of resurfacing devices. Further investigation into the utility of fractional photothermolysis technology for a diverse array of conditions characterized by hypopigmentation are needed.

DISCLOSURES

The authors have no relevant conflicts of interest to disclose.

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