The Use of CO_2 Fractional Photothermolysis for the Treatment of Burn Scars

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A recent advancement in the treatment of burn scars has been the use of the carbon dioxide (CO_2) laser to perform fractional photothermolysis. In this analysis, we describe our results and patient-reported outcomes with the use of fractional CO_2 laser for the treatment of burn-related scarring. We performed a retrospective study of all patients who underwent CO_2 laser procedures for treatment of symptomatic burn scars and skin grafts at one accredited regional burn center. Burn injury and laser treatment demographics, as well as complications, are reported. A questionnaire was administered to all patients and included patient-reported outcome measures aimed at understanding the patient experience and their subjective response to treatment. A total of 387 CO_2 laser procedures were performed on 131 patients for the treatment of symptomatic burn scars and skin grafts between October 1, 2011, and May 1, 2014 (average, 2.95 procedures/patient; range, 1–11). Average time between injury and first laser was 597.35 days (range, 60–13,475). Average time between laser treatments (when multiple) was 117.73 days (range, 22–514). There were no infections requiring treatment with oral antibiotics. Overall patient satisfaction with laser therapy was 96.7%. Patients reported reductions in neuropathic pain, tightness (contracture), and pruritus (54.0, 50.6, and 49.0%, respectively). Fractional photothermolysis utilizing the CO_2 laser is a safe and effective modality for the treatment of symptomatic burn scars, donor sites, and skin grafts. Patient satisfaction with this procedure is high, and complications are low. Significant improvements in scar appearance, pliability, tightness, neuropathic pain, and pruritus were commonly reported. (J Burn Care Res 2016;37:106–114)

Hypertrophic scarring (HTS) after burn injury remains a significant clinical challenge and continues to present providers with difficult treatment decisions. HTS is a common complication of burn injury that is described as a fibroproliferative disorder. Authors have documented its incidence as high as 80% in injured military personnel with a high prevalence in burn injuries.[1] HTSs are red, firm, raised, and remain confined within the original area of the wound. On a molecular level, HTSs result from disorganized and excessive collagen deposition through abnormalities in the wound healing phases of inflammation, proliferation, and remodeling.[2] They tend to form early after the inciting injury, often within the first 2 to 4 months and slowly improve over the course of 6 to 9 months after that point few changes are observed.[3]

Risk factors for HTS can be categorized into three broad categories: 1) injury related: depth of burn, microbiological burden, and location of burn; 2) patient related: genetics, race, skin color, and age; and 3) treatment factors: type of wound closure, time to healing, and associated wound tension. One common mechanism for many HTSs is the presence of a prolonged inflammatory state, which can be incited by a variety of factors. HTSs that occur after surgery are thought to be caused by excessive tension along the incision site.[4] If

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tension exists across a scar that is hypertrophic, the key treatment typically involves surgical release of the tension through a scar lengthening procedure. Scar lengthening procedures can include the use of local tissue (Z-plasty, Y-to-V flaps, and local flaps) or distant tissue (split thickness skin grafts, full thickness skin grafts, or free tissue transfer). Once tension is released, inflammation resolves, and the hypertrophic nature of the scar will often improve. More recently, the use of certain lasers, with and without surgical release, has been shown to be beneficial in the treatment of HTSs, as well as their associated symptoms.[5–13]

Laser treatment of HTS, in particular pulsed dye and fractional CO_2, has been shown to improve abnormal pigmentation, pruritus, pain, tightness, and the abnormal appearance of a previously meshed skin graft.[6,8,10,14–17] Mechanistically, the idea has been proposed that the laser, like the knife in a Z-plasty, breaks up the disorganized collagen fibrils that create the contracture. By breaking down the collagen with organized columns of microthermal injury, the body has the ability to heal in a more organized fashion; as presumably, the surrounding tension that has been acquired as a result of the healing process is no longer present. Thus, local remodeling occurs in a more favorable fashion allowing for less scar contracture after laser treatment. Studies on the effect of fractional CO_2 laser on scar have shown alterations of types I and III procollagen; matrix metalloproteinase (MMP)-1; transforming growth factor (TGF)-b2,-b3, and -bFGF, and miRNAs miR-18a and miR-19a expressions.[18] In a subsequent study, gene expression profiling revealed induced expression of Wnt5a, CYR61, and HSP90 in human skin during the early remodeling phase after fractional CO_2 laser treatment.[19] All these proteins play an important role in collagen remodeling. Regardless of the specific mechanism, numerous papers have described positive clinical outcomes with the use of this laser for various scars, including acne, atrophic, incisional, hypertrophic, and burn scars.[8,9,20]

Despite exciting preliminary data seen with ablative fractional CO_2 laser treatment of hypertrophic burn scars, there is a paucity of high-level evidence to validate its use. Scar appearance, scar tension, and pruritus are difficult to quantify objectively, and patient-reported outcomes studies are needed to verify the improvement seen by surgeons. In this study, we set out to review our experience, as well as to assess patient-reported outcomes, in our cohort of patients treated with fractional CO_2 laser for the treatment of symptomatic HTSs related to burns.

METHODS

Study Design

A retrospective analysis of all burn patients with symptomatic, hypertrophic burn scars treated with a fractional CO_2 laser at Massachusetts General Hospital (MGH) from October 2011 to March 2014 was performed. An internal review board approved questionnaire was administered through phone or in person, in the outpatient clinic setting, by a staff member not involved in the care of the patient. All deidentified data were then entered into a database. This study was approved by the MGH Internal Review Board.

Setting

The Sumner Redstone Adult Burn Center at MGH is an accredited, verified burn center in the Northeastern United States with approximately 350 admissions per year and 2000 annual outpatient clinic visits per year.

Patient Population

Data extracted from our laser treatment registry included date of admission, patient age, sex, Fitzpatrick score, mechanism of burn injury, TBSA burned, time from burn injury to laser treatment, average interval between treatments, locations of treatment, and complications. All patients treated during the study period were included in the analyses. An attempt was made to contact all patients for completion of the questionnaire. No patients were excluded from the study.

Treatment Protocols

All patients were treated with the fractional CO_2 laser (Ultrapulse, Lumenis Ltd., Yokneam, Israel) by two surgeons (J.G. [91%] or S.F. [9%]). The majority of patients were not treated with the laser until they were at least 3 months after burn, and most patients were not treated until at least 6 months after burn to allow for normal scar maturation. Preoperative, perioperative, or postoperative antibiotics were not used. Because of the large treatment areas and high energy levels utilized, the majority of procedures were performed in the operating room using general anesthesia. Procedures performed in the clinic were completed after injection of 1 or 2% lidocaine with epinephrine for local anesthesia. Posttreatment protocol included bacitracin ointment (Fera Pharmaceuticals, LLC Locust Valley, NY), adaptic non-adhering

dressing (Systagenix, Gargrave, North Yorkshire, U.K.), and Kerlix or dry gauze dressing changed daily for 1 week or until lasered areas were reepithelialized. Moisturizer was then applied three times daily and as needed. Patients were allowed to shower 24 hours postoperatively. A 1-week course of nonsteroidal anti-inflammatories and oral narcotics were prescribed for postoperative pain control. Patients were encouraged to minimize sun exposure and were required to wear sunblock for several months, or at least as long as scars remained hyperemic. Treatments were repeated if good response was noted by patient and surgeon. At least 1-month intervals were allowed for wound healing between laser treatments.

Laser Settings

HTS was first treated with the Deep Fx handpiece. Energy level is increased to the point where dermal bleeding is noted from more than 50% of columns, signifying penetration through the scar. For the majority (>90%) of hypertrophic burn scars, this required 150 mJ, which allows for penetration to approximately 4 mm in depth. This amount of energy requires a lower density (<5%) to limit collateral damage to surrounding epithelium. Density settings are set to 3%, and as we have gained experience with these settings and the outcomes, we have begun to overlap treatment areas between 10 and 30%.

The Superficial, or Active FX, handpiece was used after the Deep Fx treatment. Settings with the superficial handpiece were typically between 70–100 mJ and 80–200 Hz.

Questionnaires

All patients enrolled were at least 2 months out from their most recent laser treatment. Letters were mailed to all patients treated with the CO_2 laser during the study time period. This letter briefly explained the study and gave patients the opportunity to decline participation. Patients seen in the outpatient clinic were asked to fill out questionnaires during their visit. Those who were not scheduled to be seen in clinic were contacted by telephone and had the questionnaire administered by a study staff member. There were a total of 54 questions in the survey (Survey Supplemental Digital Content 1, http://links.lww.com/BCR/A29). The first 18

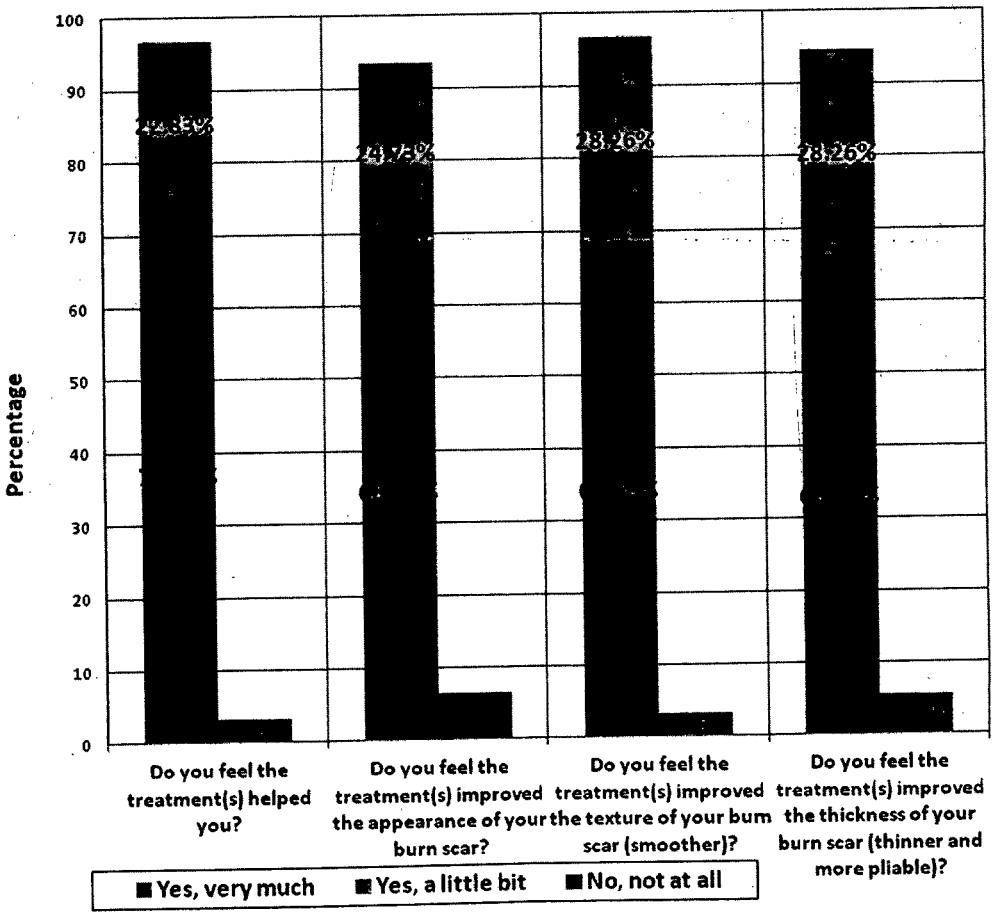

Figure 1. Patient-reported outcome of scar characteristics. Patients reported improvements in appearance, texture, and thickness.

questions addressed the patient experience using treatment and patient-reported outcome measures. The final 36 questions consisted of the Short Form 36 as a general measure of functional health status (Survey, Supplemental Digital Content 1, http://links.lww.com/BCR/A29). Questions regarding symptoms such as pruritus, tightness, and pain were all subjective and based on patient-reported outcomes.

Statistical Analysis

Descriptive statistics were computed for the study cohort. Continuous variables were summarized by the mean, SD, and histogram. Sign test was used to compare difference in patient-reported scores before and after laser treatment.

RESULTS

Demographics

A total of 387 CO_2 laser procedures were performed on 131 patients for the treatment of symptomatic burn scars and skin grafts between October 1, 2011 and May 1, 2014 (average, 2.95 procedures per patient; range 1–11). Patients were all adults with an average age of 43.0: 67 men and 64 women. The majority of patients treated sustained flame burns (N = 62, 47.3%), and scald was the second most common injury (N = 37, 28.2%), followed by motor vehicle collision (N = 9, 6.9%), chemical (N = 9, 6.9%), contact (N = 6, 4.6%), electrical (N = 4, 3.1%), and other (N = 4, 3.1%). Average TBSA for patients treated with laser was 15.2% (median, 9; range, <1 to 90). Fitzpatrick scores ranged from I to VI with the majority of patients being type III (N = 79, 60.3%), followed by types II and IV (N = 14, 10.7% each). The average number of laser treatments per patient was 2.95 (median, 3.0; range, 1–11). Average time between injury and first laser treatment was 597.3 days (median, 185.5; range, 60–13,475). Average time between laser treatments (when multiple) was 117.7 days (median, 77.0; range, 22–514). A total of 336 (85.93%) procedures were performed in the operating room, and 55 (14.07%) procedures were performed in the outpatient burn clinic. Laser treatments

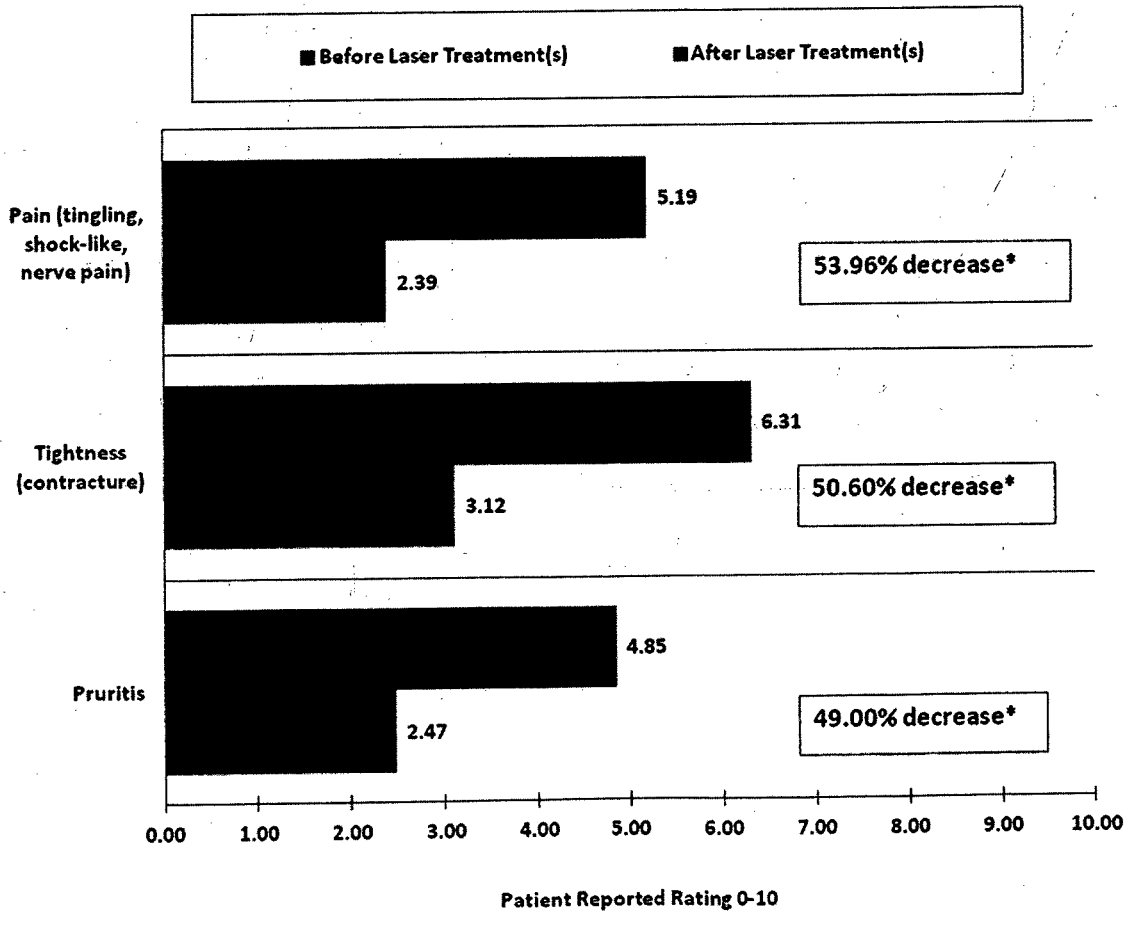

Figure 2. Patient-reported scale of pain, tightness, and pruritus prelaser and postlaser treatment on a 0 to 10 scale with 10 being the most severe. $^*P < .0001$.

were performed across all anatomic regions, with the upper extremity being the most common location (27%) and the lower extremity as second (23%), followed by torso/trunk (20%), hands (19%), and head/neck (11%).

Patient-Reported Satisfaction Outcomes

An attempt was made to contact all 131 patients, 93 completed the questionnaire (71%). Of the no-responders, 10 declined to participate (7.6%) and 26 could not be contacted (20%). Overall patient satisfaction with laser therapy was 96.7% (Figure 1), with 73.9% of patients reported that the laser treatments helped them "very much." Improvements in scar thickness and pliability were seen in 94.6% of patients. 96.7% of patients reported that their scars were smoother after laser treatment, and 93.6% of patients responded that laser treatments improved the appearance of their burn scars.

Patient-Reported Pain, Tightness, and Pruritus Scores

Common complaints associated with HTS: pain, tightness, and pruritus, were significantly decreased after laser treatment ($P < .0001$). With respect to self-reported pain from scarring, a 54% reduction in pain scores was noted before and after treatments. In addition to pain relief, patients reported a 51% decrease in the tightness of their scar. Lastly, a 49% decrease in pruritus after laser treatment was reported by patients in our cohort (Figure 2).

Complications and Postprocedural Pain

There were no infections requiring treatment with oral antibiotics. No patients required additional clinic follow-up appointments, and no patients were readmitted

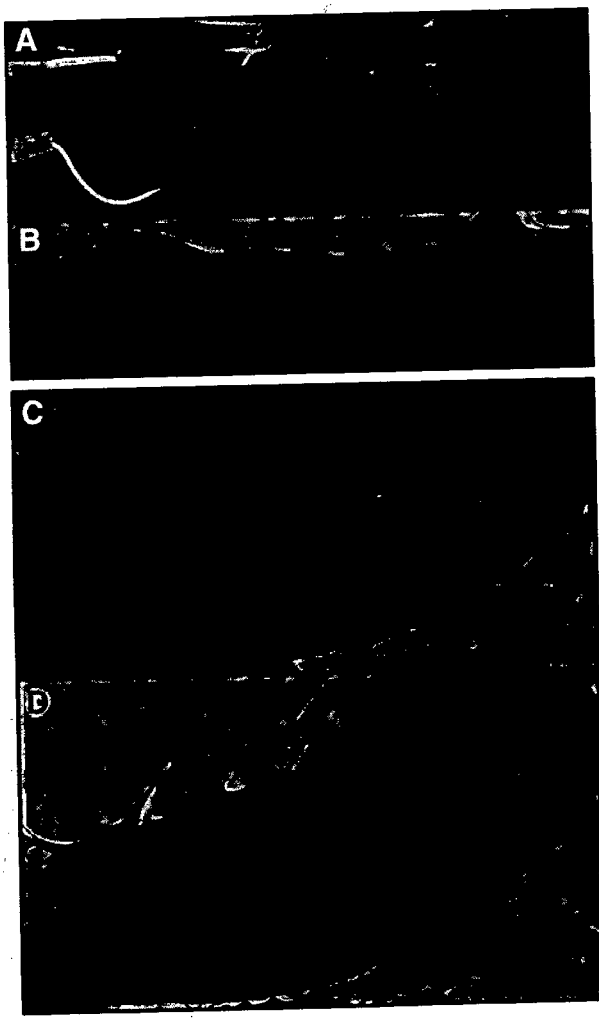

Figure 3. Healthy 21-year old man involved in an apartment fire who jumped from a second story window sustained 25% TBSA burns requiring excision and grafting, L1/L4 burst fractures, and bilateral calcaneal fractures. A and C, Pretreatment results, approximately 21 months after burn. B and D, Posttreatment results after two CO_2 laser procedures (21 and 37 months after burn).

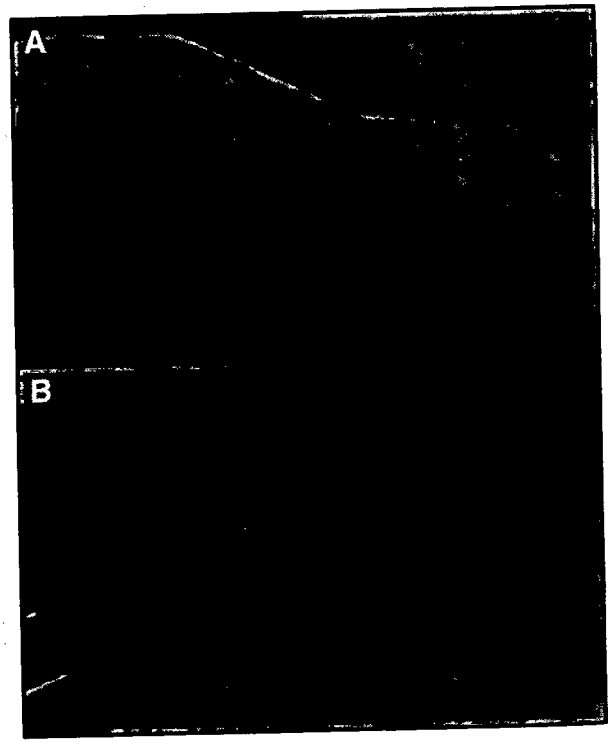

Figure 4. Healthy 44-year-old Asian woman sustained a 6% TBSA scald from hot oil to bilateral hands and feet requiring excision and grafting. Figures illustrate the ability of the CO_2 laser to remove overgrafted areas, in this case on the wrist. A, Photograph taken approximately 5 months after burn just before her first laser procedure. B, Photograph taken after she underwent a total of three laser treatments (5, 7, and 9 months after burn).

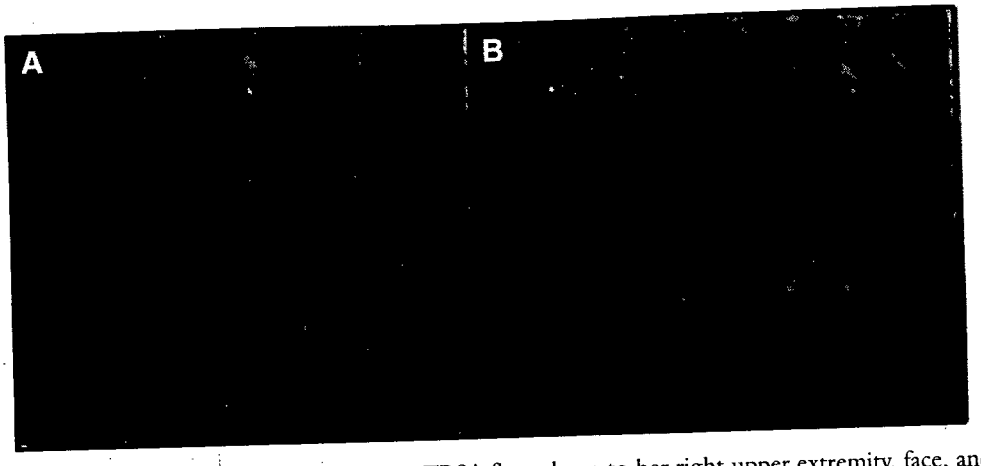

Figure 5. Healthy 50-year-old woman sustained a 7% TBSA flame burn to her right upper extremity, face, and neck from a candle. She required excision and autografting to her right hand and forearm; however, the burns to her face and neck were partial thickness and healed with conservative measures in less than 14 days. A and B, The results of treatment with CO_2 laser to an area of hypertrophic scar on her chin. A, Photograph taken just before first laser, approximately 4 months after burn. B, Photograph taken after five treatments (5, 8, 9, 11, and 13 months after burn).

because of their laser treatments. Twenty-one (22.6%) patients reported at least one area of blistering after laser procedure for an average of 1.5 days (SD, 3.43), and 45 (48.4%) patients reported having at least one open area for an average of 3.3 days (SD, 4.57). Overall, 25 patients (26.9%) reported no pain in the first 24 hours after laser procedure. The average pain score (0–10 scale) in the first 24 hours after laser procedure, for those who did experience pain, was 4.24 (SD, 3.29). The average number of days after laser that patients experienced pain was 2.6 (SD, 3.33). Fifty-three (57.0%) of the patients utilized prescribed narcotics for postprocedural pain for an average of 2.8 days.

Short Form 36 Results

The Short Form 36 was administered as part of the patient questionnaire to assess the general physical, emotional, and social health of our patient population. Overall our patient population fell within the norm for general health, pain, physical functioning, and emotional and social well being.

Representative Photographs

Figures 3 to 8 demonstrate representative improvements in burn scars over time and on different anatomical points of the body. Figure 3A, B demonstrates

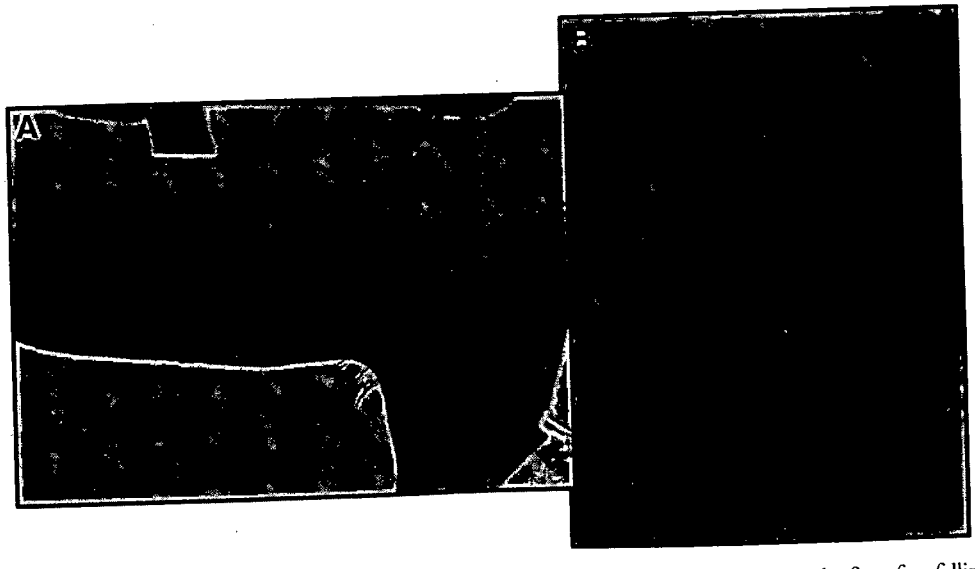

Figure 6. Forty-four-year-old woman sustained a 4% TBSA flame burn when her nightgown caught fire after falling asleep with a lit cigarette. She required excision and grafting of her right upper extremity. A, Photograph taken 6 months after burn before laser treatments. B, Photograph taken 23 months after burn and after four treatments with CO_2 laser (6, 8, 12, and 14 months after burn).

before and after laser treatments to the forearm and upper extremity in the same patient. A dramatic reduction in scar erythema and improvements in scar pliability are noted. Figure 4 demonstrates the utility of the laser to remove and smooth areas of overgraft. Figures 5 to 7 demonstrate before and after laser treatments to the lower lip/chin, upper arm, and bilateral hands, respectively. Figure 8A, B (same patient) demonstrates the ability of fractional photothermolysis on a well-matured burn scar on the upper arm and chest.

DISCUSSION

As a result of advances in the critical care of massive burn injuries, the lethal dosage 50 for burns based on TBSA affected is approximately 90%.[21] Given such a low overall mortality rate, increased attention can now be placed on postacute burn reconstructive surgery and the minimization of morbidity from burn scars and skin graft contracture. Scars are the body's natural response to a breach in the epidermis and dermis. Teleologically, the scar response exists to allow for closure of open wounds as rapidly as possible, which may not always favor an aesthetically acceptable result. The wound bed, as well as the environment surrounding the wound, plays a substantial role in the final appearance and nature of the scar. For example, wounds with infection, contamination, or excess tension are particularly prone to poor wound healing, chronic inflammation, and HTS.[22–24] Mechanical cues such as tension have become increasingly shown to play a central role in the signaling cascade that incites a HTS.[22,25] Healed burns, as well as skin grafted wounds and burns, have an ultimate lack of tissue often inciting the body's scar response over a large area.

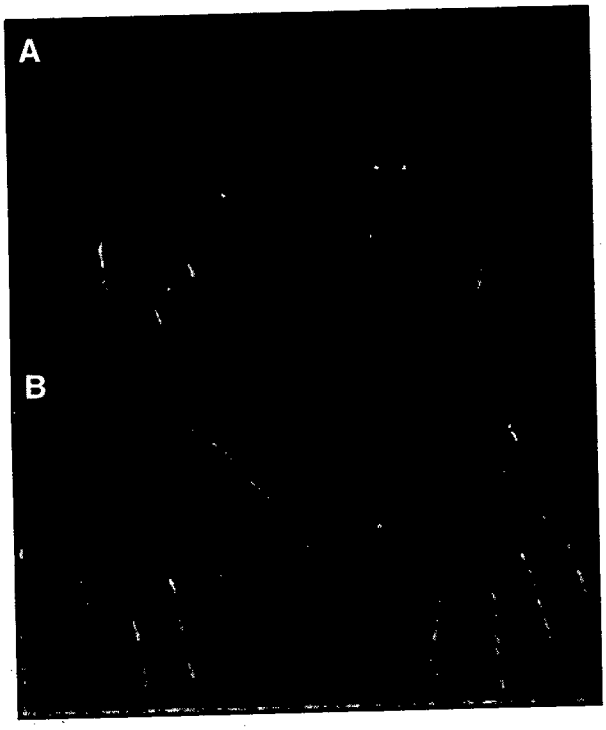

Figure 7. Fifty-one-year-old man with a past medical history significant for hypertension, hyperlipidemia, and pulmonary sarcoidosis sustained a 10% TBSA electrical flash burn to bilateral hands and face while working on a high voltage grid. He required excision and grafting to bilateral hands for full thickness burns. A, Photograph taken 6 months after burn and demonstrates this patient's significant hypertrophic response. In addition to CO_2 laser, he required multiple reconstructive procedures including releases of all webspaces bilaterally with a combination of adjacent tissue rearrangements and full thickness grafting. B, Photograph taken 25 months after burn after all releases and after four treatments with CO_2 laser (8, 12, 15, and 18 months after burn).

Even with early excision and skin graft coverage of burn wounds, patients are often left with unsightly, HTSs. Additionally, the use of meshed grafts to expand coverage area and decrease graft loss from hematoma, seroma, and infection can also lead to HTSs with an unsightly meshed pattern. Strategies to combat these unsightly scars have been limited. Scar excision and repeat grafting goes against basic plastic surgical principles and creates a new wound that may heal in a similarly hypertrophic manner. Scar lengthening procedures, such as a Z-plasty, can be used to alleviate existing tension, incite scar remodeling, and result in dramatic reduction in scar hypertrophy. Such procedures, however, require a more invasive operation and do not improve the existing superficial meshed pattern.[26,27] The fractional CO_2 laser is a relatively new modality that attempts to break up the tension across a hypertrophic wound, incite collagen turnover, and allow for a more "normal" wound healing process to take place.[10,14–17] Similar to a Z-plasty, the laser breaks up the thick, disorganized collagen fibrils that created the scar, allowing these regions to reheal in a more organized fashion.[16,26,27]

Objective assessment of scars is notoriously difficult, and existing scales, such as the Vancouver scar scale, are difficult to standardize. Furthermore, the time course for scar maturation is inconsistent and dependent on multiple known and unknown variables. As the majority of scars improve somewhat over the course of time, the ability to objectively evaluate the effect of a specific treatment is extremely difficult. Thus, in this study, we have chosen to focus primarily on patient-reported outcomes. We believe that, ultimately, one of the most important outcomes remains patient satisfaction with treatment. In this

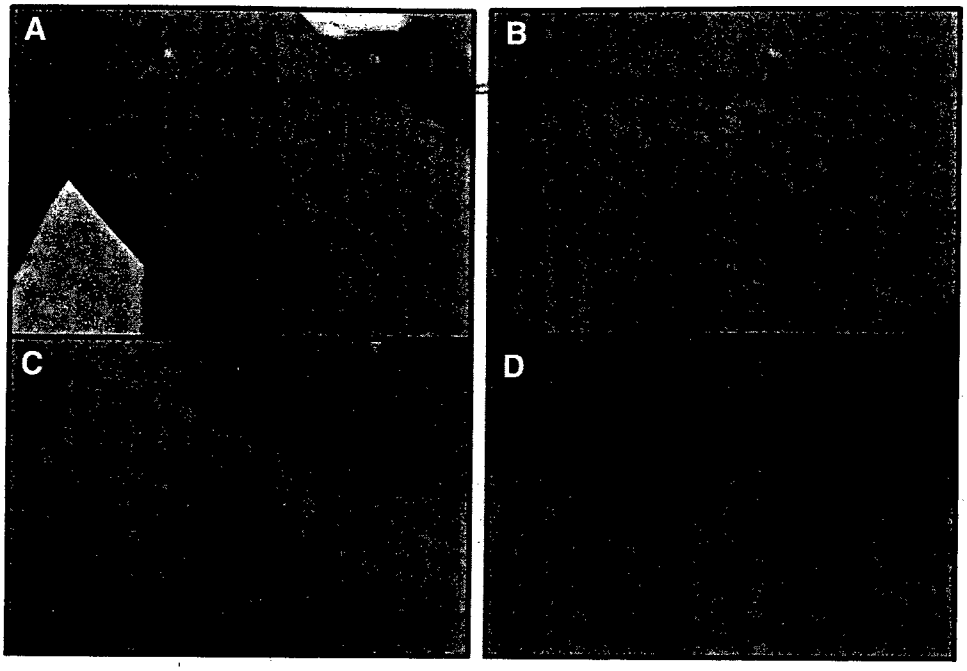

Figure 8. Healthy 25-year-old woman sustained a flame burn to the chest and left upper arm requiring excision and grafting. A and B, Photographs taken 23 months after burn and after treatment with dermabrasion and kenalog injections by another surgeon. C and D, Photographs taken after four treatments with CO_2 laser (24, 28, 31, and 34 months after burn).

study, we demonstrate that our patients have a significantly high percentage of satisfaction with the outcome from their laser procedures. Specifically, they report 54, 51, and 49% improvements in their scores for neuropathic scar pain, pruritus, and tightness, respectively; and 94% of patients reported improvements in the appearance of their scars. Furthermore, there were no major complications, readmissions, or reoperations, resulting from this treatment, making this a very safe procedure. The only negative effect patients reported was pain during the first 24 to 36 hours postoperatively.

This study has several limitations. The most notable limitation being a nonprospective study design and thus the absence of a control group in which no laser treatment was performed. Given the heterogeneity of burn scars and the fact that patients often specifically request CO_2 laser for treatment, an untreated, matched control group is extremely difficult to obtain. A further limitation of this study is that it is a retrospective review at a single center, and all patients were treated by two surgeons. Additionally, as most scars mature during the first 1 to 2 years after burn, we acknowledge that patient satisfaction may not be solely attributable to laser therapy. For those patients whose initial burn care was through our burn center, we were able to have most return in 6 months after their initial injury to initiate laser therapy. For referrals, however, we could not always control the timing, postinjury, for laser therapy. In general, we attempt to allow some amount of scar maturation to occur from months 0 to 6 to appreciate the maturation trajectory, which is why we did not intervene before this. Beyond 6 months, we did not appreciate a difference between early and late treatment with regards to patient-reported outcomes. Nevertheless it has been shown that early treatment of incisional scars with fractional CO_2 laser leads to improved appearance, and therefore, it is possible that this can be extrapolated to the immature burn scar.[28]

Another limitation of this study is that we have relied completely on patient self-assessment and have not offered an objective assessment by the surgeon or outside observer. One way to address many of these limitations would be to perform a randomized, split-scar, controlled trial with a pretreatment and posttreatment questionnaire and standardized photographs with scored assessment. This would improve our ability to accurately assess the direct benefits of this technology while minimizing the effect of time and scar maturation. Such a trial is currently being designed for implementation in our institution.

As with any new technology, we as surgeons must remain cautiously optimistic until we have more high-level evidence and longer follow-up. Furthermore,

future studies are needed to determine the most effective timing (postburn) of intervention, most effective treatment intervals, and the most effective laser treatment settings for a specific scar. This study, however, sets precedent and demonstrates that fractional CO_2 laser can be safely performed on burn patients and that patients are highly satisfied with outcomes. This study represents a major step forward in the treatment of the symptomatic hypertrophic burn scar.

CONCLUSION

HTS remains a significant source of morbidity for burn survivors. Until recently, treatments have been limited to corticosteroid injections, dermabrasion, and operative scar release. Recent studies have shown ablative fractional CO_2 laser treatments to be a promising new modality. We demonstrate that this operation is safe, with minimal side effects, and that patients report improvements in several of the symptoms associated with HTS. Finally, patients reported an improvement in the appearance of their burn scars and were pleased overall with their results. Controlled and rigorous studies are needed to better understand the mechanism of action and to optimize dosimetry and timing of treatments.

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