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ORIGINAL ARTICLE

Early intervention with pulse dye and CO_2 ablative fractional lasers to improve cutaneous scarring post-lumpectomy: a randomized controlled trial on the impact of intervention on final cosmesis

Tamar Safra[1,2] · Waseem Shehadeh[3] · Amir Koren[3] · Fares Salameh[3] · Or Friedman[4] · Eli Sprecher[2,3] · Ofir Artzi[2,3]

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Abstract

Light-based modalities appear to be effective for ameliorating surgical scar appearance; however, protocols for achieving such outcomes have yet to be established. We studied the safety and efficacy of a combination of pulsed dye laser (PDL) and fractional ablative CO_2 laser (FACL) for the attenuation of post-lumpectomy scarring. We conducted a prospective, evaluator-blinded, comparative split-scar study in post-lumpectomy patients. One-half of the scar was treated with three sessions of 595-nm PDL and FACL at 1-month intervals, starting within 6 weeks after suture removal. The entire scar was also treated with standard moisturizers and silicone gels. Six months after the last treatment, the two halves of the scar were assessed by three uninvolved physicians who used the Observer Scar Assessment Scale as well as by the patients who used the Patient and Observer Scar Assessment Scale. Eighteen female patients (mean age, 51.3 years) with a mean scar length of 7.8 cm completed the treatment and follow-up. Six months after the last treatment, both the physician evaluators and the patients noted significant improvements for all assessed scar parameters in the laser-treated scar area compared with the untreated scar area. The treatment was well tolerated, and no remarkable adverse events were reported. All 18 participants were satisfied with the treated scar areas. A combination PDL and FACL protocol starting up to 6 weeks after suture removal is a safe and effective method for the attenuation of post-lumpectomy scar formation.

Keywords Scar · Lumpectomy · Pulsed dye laser · Fractional ablative carbon dioxide laser · Patient and Observer Scar Assessment Scale

Introduction

Breast-conserving surgery (lumpectomy) is the standard surgical treatment for early-stage breast cancer patients, providing equivalent long-term survival and much better cosmetic outcomes than mastectomy [1]. Most breast cancer patients require oncologic and reconstructive "onco-plastic" surgeries, which can result in unsightly scarring. Such scars may

Tamar Safra and Waseem Shehadeh contributed equally to this work.

✉ Ofir Artzi
ofira@tlvmc.gov.il; benofir@gmail.com

Tamar Safra
Safrat@bezeqint.net

Waseem Shehadeh
swasimsh@gmail.com

Amir Koren
koren1am@gmail.com

Fares Salameh
faressalameh@hotmail.com

Or Friedman
Or.friedman@gmail.com

Eli Sprecher
elisp@tlvmc.gov.il

[1] Department of Oncology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

[2] Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

[3] Department of Dermatology, Tel Aviv Sourasky Medical Center, 6 Weizmann Street, Tel Aviv, Israel

[4] Department of Reconstructive and Plastic Surgery, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

be esthetically unappealing and cause pain, pruritus, and considerable psychological distress. As a result, the patients may experience lowered mood and negative changes in their perception of their femininity, attractiveness, and body image [2–4]. Current scar minimizing procedures include the frequent use of moisturizers, silicone gel or sheet occlusion, pressure therapy, and sun avoidance [5], with variable results. The role of lasers in scar prevention has been highlighted in a steadily growing number of publications during the past two decades. Several types of lasers were shown to be efficient in reducing scar formation, including the pulsed dye laser (PDL) [6, 7] and fractional ablative and non-ablative lasers [7–13].

Fractional ablative CO_2 laser (FACL) has been shown to remodel the dermal matrix [14], while the effect of vascular-targeting lasers, such as PDL and diode lasers, on scar reduction has been shown to be mediated, at least in part, through upregulation of heat shock protein 70 in the vicinity of blood vessels, hair follicles, and sebaceous glands, which in turn may modulate transforming growth factor beta expression [15–19]. Better results were observed when the treatment was performed early after suture removal and up to 2–4 weeks from surgery [9, 20–22].

The purpose of this study was to analyze the effects of treatment with PDL combined with FACL on post-lumpectomy surgical scars starting within 6 weeks after suture removal.

Materials and methods

Study design and patients

This was a prospective, randomized, split-scar comparative study. Nineteen patients over 18 years of age who underwent lumpectomy were enrolled. Eighteen patients completed the study protocol. The study was approved by the Tel Aviv Sourasky Medical Center's institutional ethics committee, and all of the participants signed an informed consent prior to undergoing the described procedures. Exclusion criteria included recent use of retinoids, pregnancy or planned pregnancy, current breast feeding, and bleeding, collagen, or elastin disorders.

Treatment protocol

Treatment was initiated between 2 and 6 weeks after breast lumpectomy. All the scars were divided into two halves and designated "A" and "B." Following randomization, one half of the scar ("A" or "B") was treated with PDL followed immediately by focal FACL once monthly for 3 consecutive months. The entire wound was treated with moisturizers and a silicone-based product. All pre-scars and scars were photographed by a standardized high-definition digital camera prior to the first treatment and at the final assessment (6 months after the last treatment).

Laser procedures

Prior to laser treatment, the scar area was cleansed with 70% alcohol, and a topical eutectic mixture of 2.5% lidocaine hydrochloric acid and 2.5% prilocaine (EMLA, AstraZeneca, Cambridge, UK) was applied to the scar under occlusion for 30 min before therapy.

A randomized half of the scar was first treated with 595-nm PDL (Perfecta, Syneron-Candela, Wayland, MA) using a 7-mm spot size, 0.45-ms pulse duration, and energy fluence of 4–6 mJ/cm^2. The same part of the scar was then consecutively treated with 10,600-nm FACL (Ultrapulse Encore, Lumenis Ltd., Yokne'am, Israel) at the following settings: fluence 12.5–17.5 mJ and 5% density. The FACL treatment was performed only on the edges of the wound on areas of observed skin tension and on elevated or uneven surfaces. Each treatment lasted less than 10 min. Protective eyewear was utilized during treatments. The number of treatments, intervals, and laser parameters was chosen in accordance with previous publications [23, 24].

Outcome measures

The scars were evaluated using patient and observer scar assessment scales (Observer Scar Assessment Scale (POSAS) by the physicians and Patient Scar Assessment Scale (PSAS) by the patients). First developed and validated for the documentation of burn scars [20], these scales have since been used for the analysis of a variety of different scar types, where they proved to be reliable outcome measures [25]. Three uninvolved blinded physicians (two dermatologists and one plastic surgeon) who were unaware of the treatment area of the scar evaluated the scar at baseline (prior to any treatment) and 6 months after the last laser treatment. The study participants similarly evaluated the treated and untreated scar areas 6 months after the last laser treatment and also rated their satisfaction with the treated scar areas in comparison with the untreated area using a patient four-point satisfaction scale (0—unsatisfied, 1—slightly satisfied, 2—moderately satisfied, and 3—very satisfied).

Statistical analysis

The paired Wilcoxon signed-rank test was applied in order to test for the significance of the differences between the treated scar and the non-treated scar according to the scores of the POSAS parameters. The significance level was set at $\alpha = 0.05$. Analyses were carried out using the R software, version 3.4.3.

Results

Eighteen of the 19 participants who were enrolled in the study completed the treatment and follow-up. The subject who withdrew after the first laser treatment did so following the discovery of metastases. The demographics and clinical characteristics of the study group are summarized in Table 1. The women were generally healthy and had a mean age of 51.3 years (range 34–67) and a body mass index of 24.4 kg/m^2. Their skin Fitzpatrick type ranged from II to IV, and the mean scar length was 7.8 cm (range 5.9–10.1 cm).

Clinical scar assessment

The follow-up period ended 6 months after the last treatment, at which time the non-involved blinded physician evaluators noted improvements (i.e., lower OSAS scores) both in the treated and in the untreated scar areas in all of the scar parameters that were assessed. However, the improvements in scar parameters were significantly greater in the laser-treated scar area compared with the untreated scar area (Table 2). The intraclass correlation coefficient was 0.142 for the total score before treatment, 0.230 for the treated part post-treatment, and 0.326 for the untreated part post-treatment (Table 3).

The PSAS also showed significant overall improvement in the laser-treated scar area compared with the untreated scar area (Fig. 1). Patient-rated scar color, stiffness, thickness, and irregularity were significantly improved in the laser-treated scar area compared with the untreated scar area, while there was a trend towards a significant improvement in the level of pain and itching in the laser-treated scar area compared with the non-treated scar area.

All 18 participants were satisfied with the treated scar areas compared with the untreated area. Thirteen of them (72.2%) indicated that they were greatly satisfied with the laser-treated scar area, while the remaining five (27.8%) indicated that they were moderately satisfied.

Table 1 Demographic and clinical characteristics

Variable	Study population $n = 18$
Age (years)	51.3 ± 11.3
Body mass index (kg/m^2)	24.4 ± 4.54
Fitzpatrick skin type	
II	10 (55.6%)
III	6 (33.3%)
IV	1 (5.6%)
Hypertrophic scarring history	1 (5.6%)
Smoking history	
Past smoker	3 (16.7%)
Current smoker	2 (11.1%)
Previous breast surgery	3 (16.7%)
Cancer type	
Benign lesion	1 (5.6%)
Ductal carcinoma in situ	7 (38.9%)
Invasive ductal carcinoma	9 (50.0%)
Neuroendocrine tumor	1 (5.6%)
Excised tumor mass (g)	53.3 ± 27.4
Involved lymph nodes	
Involved lymph nodes	3 (16.7%)
Macro-metastasis in lymph nodes	1 (5.6%)
Neoadjuvant cancer-directed therapy	
Chemotherapy + biologic neoadjuvant therapy	1 (5.6%)
Adjuvant cancer-directed therapy	
Radiotherapy	8 (42.1%)
Chemotherapy + radiotherapy	2 (11.1%)
Biologic therapy	1 (5.6%)
Biologic therapy + radiotherapy	2 (11.1%)
Scar length (cm)	7.83 ± 1.25

Continuous variables are shown as mean ± standard deviation, and categorical variables are shown as frequency (percent)

Safety

Adverse events following laser treatment were limited to local irritation, erythema, and purpura in the laser-treated scar areas, and they all resolved spontaneously by the end of follow-up.

Discussion

Post-surgical scarring with its physical sequelae (pain, itching, and unattractive appearance) and resultant psychological stress can dramatically impact a patient's quality of life as well as overall patient satisfaction with medical procedures. These scars are a constant reminder of the patient's past or present disease and the related surgery and can be associated with extensive functional and psychosocial morbidities [26]. Many studies have been published on the role of lasers (PDL or fractional ablative laser) in the field of scar mitigation, and most of them indicated that early, pre-scar laser treatment close to suture removal (2–4 weeks post-surgery) had the most optimal final cosmetic result [27–30]. Recent publications demonstrated an advantage of using both lasers in successive manner to achieve a better outcome: three PDL treatments followed by three fractional ablative laser treatments [8, 31].

The purpose of this study was to determine the performance and potential benefits of a novel therapeutic approach that combines PDL and FACL simultaneously with the aim of reducing scar formation after a lumpectomy. Our results demonstrated that the treated scar areas showed improved esthetic appearance to better resemble that of the surrounding

Table 2 Evaluator assessment of the untreated and treated scar areas

Scar parameter	Observer Scar Assessment Scale (OSAS)					*P* value[b]
	Baseline[a]	6 months		Change		
		Treated	Untreated	Treated	Untreated	
Overall	19.10 ± 3.47	8.11 ± 1.75	12.91 ± 3.30	− 10.94 ± 3.73	− 6.16 ± 4.43	< 0.001
Vascularity	5.82 ± 1.40	1.94 ± 0.68	3.09 ± 1.14	− 3.84 ± 1.33	− 2.63 ± 1.45	0.001
Pigmentation	2.82 ± 0.87	1.76 ± 0.53	2.67 ± 0.78	− 1.08 ± 1.06	− 0.18 ± 1.05	< 0.001
Thickness	3.41 ± 0.65	1.31 ± 0.31	2.13 ± 0.81	− 2.08 ± 0.78	− 1.27 ± 1.13	0.002
Relief	3.94 ± 0.86	1.46 ± 0.31	2.50 ± 0.76	− 2.47 ± 0.95	− 1.45 ± 1.07	< 0.001
Pliability	3.10 ± 0.56	1.63 ± 0.34	2.37 ± 0.68	− 1.47 ± 0.66	− 0.78 ± 0.82	0.001

Values shown are mean ± standard deviation

[a] Pre-treatment

[b] Paired Wilcoxon signed-rank test for the difference between the treated and untreated scar areas

unaffected skin (Fig. 1). Overall, the study participants tolerated the treatments well, and none reported any remarkable adverse effects.

The beneficial effect of treating post-surgical scars with lasers early after the procedure has been documented [27]. PDL and FACL are commonly used for the treatment of post-surgical scars as monotherapies and in different visits [7, 8]. Significant adverse effects are rare in association with these two modalities [8, 11]. In order to achieve greater improvement in scar appearance, several studies have shown that laser treatment should be initiated early after tissue injury, during the inflammatory (1–3 post injury) or proliferation (1–4 weeks post-injury) phases of wound healing [27, 28]. In the present study, treatment was initiated between 2 and 6 weeks after injury. Our study successfully demonstrated the positive and lasting effects of the PDL and FACL combination on surgical scar attenuation in comparison with the control area.

The limitations of our study include the relatively small size of our cohort and the inability to blind the patients to the treatment site, which may influence their assessment of outcome. This issue was partially addressed by the blinded evaluation of three uninvolved physicians. Follow-up was performed at 6 months after the last treatment, while some studies have suggested that scars should be followed for at least 12 months to assess the true outcome of laser treatment of scars [14, 15, 27].

The issue of metastasis and laser treatment remains to be elucidated. There are no real data on long follow-up periods of cancer patients who have been treated with lasers. Notably, our study patients were followed for 16–26 months post-last treatment with no recurrences. The patient who withdrew from the study had been diagnosed with metastases during the weeks following suture removal and within a month of laser treatment initiation (i.e., before the second treatment). It can be assumed that the metastases were present before treatment initiation and were diagnosed only after a systemic work-up. Furthermore, the lasers and parameters used in this study allow laser penetration down to the papillary dermis, which is usually not the site of a primary cancer. In addition, the scar (and thus the treatment) was several centimeters away from the tumor in most cases.

Another limitation that warrants consideration is the anti-scarring effect of chemotherapy and tamoxifen [32–34]. This is a split scar study in which the final cosmesis of a half scar

Table 3 Interobserver reliability

Variable	Intraclass correlation coefficient	95% confidence interval
Pre-treatment		
Total	0.142	− 0.04, 0.422
Vascularity	0.332	0.007, 0.657
Pigmentation	0.048	− 0.12, 0.33
Thickness	0.091	− 0.058, 0.347
Relief	0.191	− 0.028, 0.492
Pliability	− 0.127	− 0.281, 0.156
Post-treatment—treated half		
Total	0.23	− 0.004, 0.525
Vascularity	0.412	0.132, 0.685
Pigmentation	0.163	− 0.037, 0.45
Thickness	0.081	− 0.099, 0.364
Relief	0.049	− 0.064, 0.261
Pliability	0.122	− 0.051, 0.392
Post-treatment—untreated half		
Total	0.326	0.01, 0.643
Vascularity	0.339	0.06, 0.631
Pigmentation	0.181	− 0.027, 0.469
Thickness	0.393	0.073, 0.685
Relief	0.248	− 0.012, 0.561
Pliability	0.275	0.017, 0.574

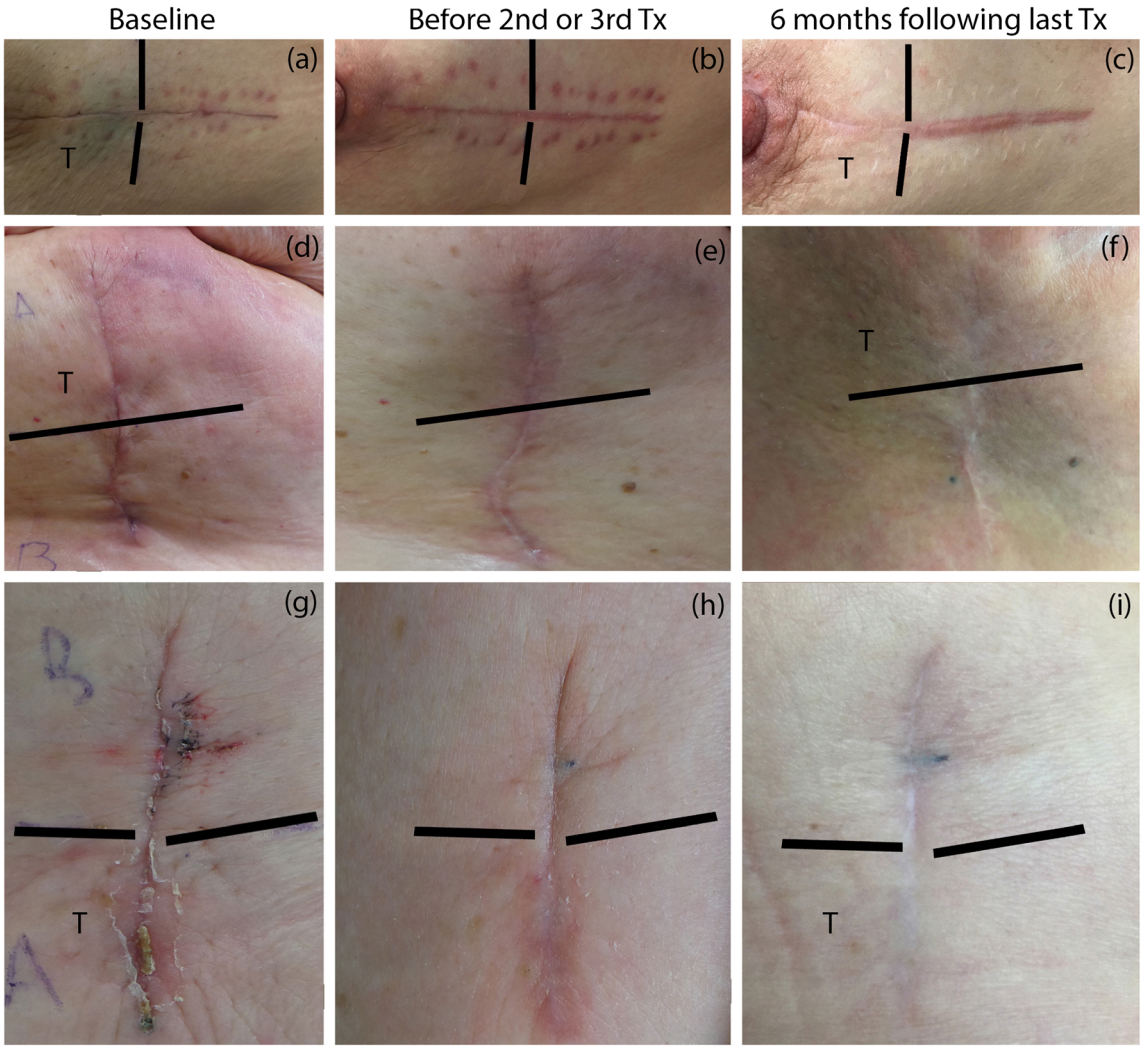

Fig. 1 Three representative treated (*T*) versus the untreated scars at baseline, before second or third treatment, and 6 months following three treatment sessions of combined pulsed dye laser (PDL) and ablative CO_2 laser (FACL) at one-month intervals, starting within 6 weeks after suture removal

treated with laser was compared with a half scar that had not been treated with laser. Given that systemic therapies affect both sides equally, the improvement that took place in the treated half still would have been demonstrated. Due to our small cohort study we were unable to compare the value of the tamoxifen-treated patients with those not treated with tamoxifen, which is a subject for future studies.

Another important issue is the timing of radiation and laser treatment initiation. Several studies [35–37] demonstrated that the risk of local relapse or distant metastases has no correlation to the interval between breast cancer surgery and radiotherapy treatment, and thus radiation to breast cancer after surgery can be postponed. In our current study, in order to exclude the influence of radiation, radiotherapy was postponed until the last laser treatment had been administered, with the approval of our department of oncology. The authors recommend a consultation with a breast oncologist prior to the initiation of laser treatment in order to discuss individual patient management.

Conclusions

We have demonstrated that three treatment sessions of combined PDL and FACL given at 1-month intervals and starting within 6 weeks after suture removal and ending up to 8 weeks from surgery significantly improved the clinical outcomes of the treated scars compared with the non-treated (control) scars and that they are associated with high patient satisfaction. As treatments with pulse dye laser and FACL during the inflammatory and proliferative phases of scar formation have been shown to independently mitigate scarring, a comparison between monotherapy (PDL or CO_2) with the described combined approach is warranted in future studies. In addition, it remains to be determined whether supplementary treatments or the use of other modalities, including laser-assisted drug delivery of anti-fibrotic agents, may afford additional benefits. Further comparative studies are also warranted to determine the best treatment protocol for optimal reduction of surgical scar formation.

Data availability statement The datasets generated and analyzed during the current study are not publicly available due to patient confidentiality but are available from the corresponding author upon reasonable request.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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