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Proposal of New Parameters for Non-Ablative Fractional Er:Glass 1,550 nm Laser for Hypertrophic Scars: A Histological and Clinical Analysis

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Abstract

Introduction: Hypertrophic scars (HS) can be highly limiting, both functionally and aesthetically. Lasers serve as a middle ground between conservative treatments (such as silicone and injectables) and surgical revision.

Objectives: To evaluate improvements in HS and associated histopathological changes following treatment with non-ablative fractional laser (NAFL) Er: 1,550 nm glass.

Methods: Eight hypertrophic scars were treated with three monthly sessions of low fluence and high-density NAFL, applied to one-half of each scar. Clinical and symptomatic improvements, along with histopathological changes, were compared between the treated and control sides.

Results: Partial symptomatic improvement was noted. A statistically significant reduction in the proportional area of collagen fibers was observed in hematoxylin-eosin staining (p=0.009) and Masson's trichrome staining (p=0.001) on the treated side compared to the control. No significant differences were found in the proportional area of elastic fibers or epidermal thickness.

Conclusion: The histological changes suggest that low fluence and high-density NAFL is an effective treatment for HS. We recommend increasing the number of sessions or combining it with other techniques to achieve faster and more optimal results.

Keywords: ***Erbium: glass laser; Non-ablative laser; Hypertrophic scar; Keloid; Treatment outcome***

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1. Introduction

Hypertrophic scars (HS) are a type of scar that is characterized by their raised appearance. They are commonly associated with symptoms such as pruritus, hypohidrosis, or numbness. Unlike keloids, hypertrophic scars do not grow beyond the original wound borders, but they can still be equally challenging to treat. The etiology of hypertrophic scars is multifactorial, often linked to injury (such as full-thickness incisions or burns), and these scars frequently occur in areas of high mobility, such as the chest. Treatments such as intralesional steroids, 5-fluorouracil, pressure therapy, silicone gel sheeting, cryosurgery, radiotherapy, excisional surgery, ablative laser surgery, and pulsed dye laser (PDL) therapy have been reported to be effective [1,2].

Both hypertrophic scars (HS) and keloids (KL) are forms of excessive dermal fibroblast proliferation that arise during the wound-healing process following skin injury, infection, surgery, injections, or thermal/chemical injuries in predisposed individuals [3]. Although most scars are aesthetically and functionally acceptable, HS and KL can be unpredictable and cause significant distress to the patient. Symptoms such as pain, itching, and restricted movement can severely impact the patient's quality of life [4].

Histopathologically, HS is marked by thickened collagen bundles arranged in a parallel pattern to the epidermis, with little or no keloidal collagen present. The pathogenesis of HS and KL is complex and may involve multiple cellular and chemical mediators during the different phases of wound healing (inflammatory, proliferative, and remodeling) [5,6]. Several treatment modalities exist, including noninvasive methods such as silicone gels and invasive approaches like corticosteroid injections, bleomycin, 5-fluorouracil, cryotherapy, and surgical excision [5]. However, these treatments often have limited success and high recurrence rates.

Lasers offer a promising alternative, bridging the gap between conservative treatments and surgery [7]. Over the years, their use has increased significantly. Initially mentioned as case reports in the 2002 International Recommendations for Scar Treatments [8], lasers were formally introduced in the 2012 [9] and 2014 [10,11] expert consensus guidelines as key treatment options for scars. In the 2020 International Consensus [5], lasers were recognized as a first-line therapy for scar management.

Among the laser types, CO2 lasers have shown efficacy in reducing hypertrophic scars [12-15], although they carry a risk of complications like post-inflammatory hyperpigmentation. Non-ablative fractional lasers (NAFL) have emerged as a safer alternative for HS treatment, offering minimal side effects and less pain, albeit with a slower response compared to ablative fractional lasers (AFL). Choe et al. [16] observed reduced hypertrophy in post-thyroidectomy scars following four monthly sessions of NAFL (1,550 nm), initiated 2-3 weeks after surgery. Similarly, Karmisholt et al. [17] reported improvements in erythema and flexibility in half of the surgical wounds treated with three NAFL sessions (1,540 nm). NAFL induces an initial inflammatory response, which stimulates dermal remodeling through the release of pro-inflammatory cytokines (interleukin-1β and tumor necrosis factor-α). NAFL leads to dermal remodeling, which was observed using parameters with high or low energies [18]. This study aimed to evaluate the clinical and histological effects of NAFL (Er:glass 1,550 nm) on hypertrophic scars, using conservative parameters with low fluences and high density to induce collagen contraction and reduce scar prominence.

2. Methodology

Seven volunteers, aged 25 to 69, with surgical or traumatic scars, were enrolled. One volunteer had two scars, making a total of eight hypertrophic scars for analysis. The volunteers were recruited from the Dermatology Clinic at Santa Casa de São Paulo School of Medical Sciences. Their skin phototypes ranged from I to IV, and the time of scar development ranged from 45 days to 12 months. None of the patients had undergone prior treatment (e.g., silicone gels, intralesional steroids, radiotherapy, or laser therapy) for their scars.

The study was approved by the Ethics and Research Committee of Santa Casa de São Paulo (Approval Number 3,225,859), and all participants signed informed consent forms before enrollment.

Photographs were taken of each scar using a Sony Cyber-shot DSC-W690® camera (16.1 megapixels), maintaining consistent lighting and positioning. The scars were measured in length and width. Each scar was divided in half, and the half with the most pronounced tissue overgrowth or patient-reported discomfort was selected for treatment. Three monthly sessions of NAFL (Er: glass 1,550 nm) were applied to the selected side of the scar. Thirty days after the last session, two punch biopsies (2.0 mm) were taken, one from the treated side and one from the control side.

The Patient and Observer Scar Assessment Scale (POSAS) was administered before and after treatment to assess clinical changes. POSAS consists of the sum of two scales: the patient part, which contains six items (color, flexibility, stiffness, irregularity, itching, and pain), and the observer part, which contains five items (vascularization, pigmentation, pliability, thickness, and relief). All items on both scales are scored numerically [19]. The non-ablative fractional system used was the Lutronic Mosaic® (South Korea), employing a 1,550 nm Er: glass laser with four passes and energy settings of 10 mJ/pulse (Low fluence), 500 spots/cm² (High Density), and a static mode application, with 6,8 or 10 mm tip, depending on the scar´s size. No topical anesthetic was used due to the minimal pain associated with the procedure.

2.1 Histological analysis

Two skin biopsy samples (one from the treated side and one from the control side) were taken from each participant. The samples were stained with hematoxylin-eosin, Masson's trichrome, and Verhoeff's stains. The images of the colored sections were acquired using the Leica DMI8® microscope, equipped with LASX software (Leica Microsystems, Germany). A blinded pathologist performed subjective assessments of the collagen fiber characteristics, while quantitative analysis of epidermal thickness and collagen and elastic fiber areas was conducted using ImageJ software.

2.2 Statistical analysis

Descriptive statistics were performed for all variables. Quantitative variables were analyzed by calculating minimum and maximum values, means, standard deviations, and medians. The Shapiro-Wilk test t [20] was used to assess normality. The paired Student’s t-test was applied for comparisons between the treated and control sides. When normality assumptions were not met, the Wilcoxon non-parametric test [20] was used. Statistical significance was set at $p \leq 0.05$, and the data were analyzed using SPSS 17.0 for Windows.

3. Results

3.1 Clinical and symptomatic evaluation

POSAS scores indicated no significant difference between pre- and post-treatment assessments. When the observer and patient components of the POSAS were analyzed separately, no significant improvement was noted in the observer-reported components. However, the patient-reported components showed a statistically significant improvement from pre to post-treatment ($p = 0.033$). FIG. 1 and 2 illustrate pre and post-treatment photographs of a patient, highlighting a slight reduction in scar height and increased flexibility in the treated area.

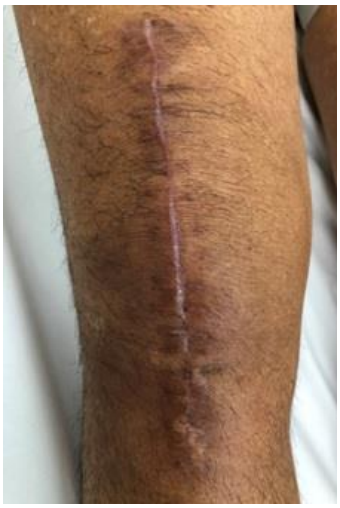

FIG. 1. **Surgical hypertrophic scar before treatment.**

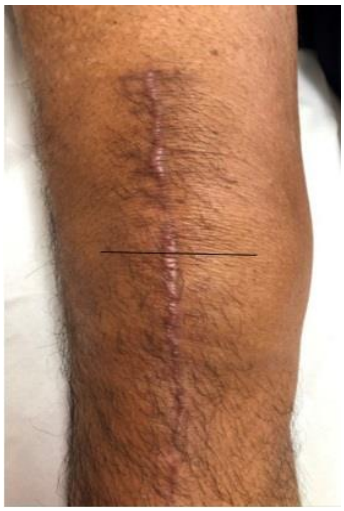

FIG. 2. **Surgical hypertrophic scar after treatment (treated area: lower half).**

3.2 Histopathological evaluation

Blinded histological evaluation revealed thinner, sparser, and less compact collagen fibers on the treated side compared to the control side (FIG. 3 and 4, Masson's trichrome stain). A statistically significant reduction in the proportional area of collagen

fibers was observed in both hematoxylin-eosin (p=0.009) and Masson's trichrome (p=0.001) staining (FIG. 5). No statistically significant differences were found in the proportional area of elastic fibers or epidermal thickness between the treated and control sides.

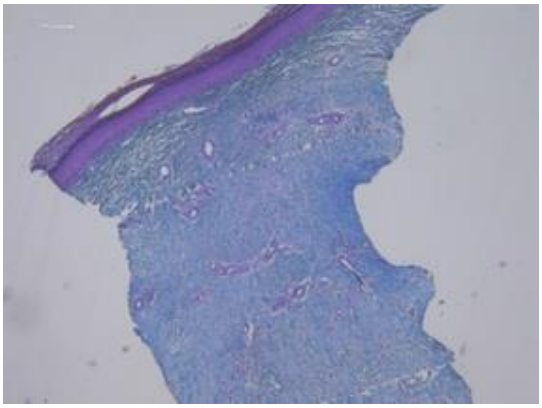

FIG. 3. **Representative figure of the histological specimen of hypertrophic scar on the control side (Masson staining).**

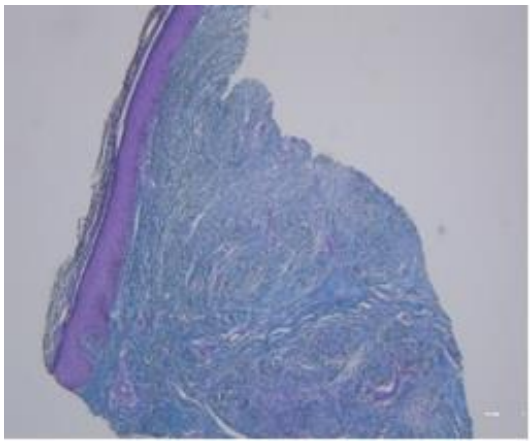

FIG. 4. **Representative figure of the histological specimen of hypertrophic scar on the treated side (Masson staining).**

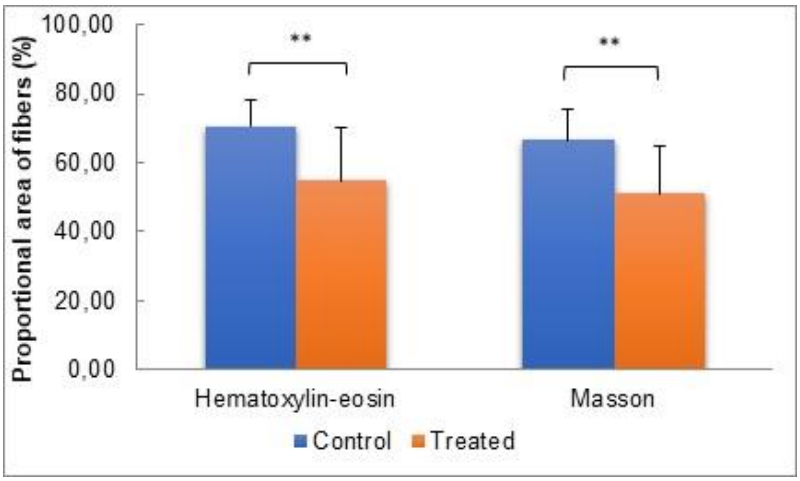

FIG. 5. **Values of the proportional area of the collagen fibers in the hematoxylin-eosin (p=0.009) and Masson staining (p=0.001), in the control and treated sides, expressed as mean and standard deviation.**

4. Discussion

Hypertrophic scars can be distressing for patients, significantly affecting their quality of life [4]. While extensive research has focused on the use of AFL and NAFL for hypertrophic scars, few studies have evaluated the histopathological changes that accompany clinical improvements. Studies on burn scars have demonstrated that CO_2 laser treatment results in the reorganization of collagen fibers, making them thinner and more fibrillar [21]. Similarly, NAFL treatment of burn scars has been shown to promote the formation of more prominent rete ridges and a denser, more interwoven collagen structure with higher vascularization [22].

The present study aimed to achieve clinical improvement in hypertrophic scars using a less painful technique, with fewer side effects and shorter recovery times. After three treatment sessions, histological findings indicated a reduction in the proportion of collagen fibers. While quantitative analysis of collagen changes following fractional laser treatment has been documented for other skin conditions such as striae [23], few studies have focused on hypertrophic scars, making direct comparisons difficult.

In this study, thinner and sparser collagen fibers were noted in the treated areas, with a significant reduction in their proportional area in both hematoxylin-eosin ($p=0.009$) and Masson's trichrome staining ($p=0.001$). Although the proportional area of elastic fibers showed a trend toward increase, no statistically significant difference was observed. Similarly, epidermal thickness remained unchanged. The proposed adjustment of parameters from low fluence and high density is grounded in the principles of physics, which demonstrate that increasing fluence leads to greater thermal damage and enhanced neocollagenesis. However, when the objective is to reduce collagen deposition in hypertrophic scars (HS), it is hypothesized that inducing minimal thermal damage is sufficient to stimulate the remodeling of higher-quality collagen within localized areas of the treated skin. This hypothesis was confirmed through histological analysis, which demonstrated the desired remodeling effect.

The POSAS evaluation before and after treatment did not reveal statistically significant overall improvement. However, when the patient-reported components (including symptoms and appearance) were analyzed separately from the observer-assessed components (focused solely on appearance), a statistically significant improvement was noted only in the patient-reported outcomes.

Although symptomatic relief was evident, no significant changes in the appearance of the scars were observed. This is likely due to improvements in the collagen structure without corresponding restoration of skin adnexal structures. Consequently, a larger number of treatment sessions may be required to achieve clinically noticeable aesthetic changes.

Unlike the well-documented clinical success of NAFL in treating atrophic scars, where the laser effectively stimulates collagen production, its application in hypertrophic scars (HS) often fails to produce visible clinical improvement, even when histopathological changes are evident. This disparity can be attributed to the pathological differences between the two types of scars. In atrophic scars, the thinner dermis permits the laser to reach the appropriate depth for effective dermal remodeling. Moreover, the higher energy settings typically employed in treating atrophic scars further enhance collagen proliferation, contributing to the more favorable outcomes observed in these cases [24].

5. Study Limitations

The small sample size of the study was largely due to the reluctance of participants to undergo biopsies, given the psychological trauma associated with scar formation. Additionally, while the follow-up period was 4 months, a longer duration might be necessary to observe more significant clinical improvements.

6. Conclusion

NAFL (Er: glass 1,550 nm), using low fluences and high density, demonstrated histological improvements in hypertrophic scars, with partial symptomatic relief after three sessions. However, these preliminary results suggest that more treatment sessions or combination therapies may be necessary for faster and more optimal results. NAFL appears to be a safe and effective treatment option for hypertrophic scars, offering minimal side effects.

7. Conflicts of Interest

The authors have no conflict of interest to declare.

8. IRB Approval Status

Reviewed and approved by Santa Casa de Sao Paulo School of Medical Sciences IRB, approval n.º 3,225,859.

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