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ORIGINAL CONTRIBUTION

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# Fractional CO2 laser versus combined platelet-rich plasma and fractional CO2 laser in treatment of acne scars: Image analysis system evaluation

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## Summary

**Background:** Fractional CO2 laser and platelet-rich plasma (PRP) treatments have been used in the treatment of acne scars. However, an objective method of assessment has been lacking.

**Objective:** To evaluate the efficacy of CO2 laser versus the combination of PRP and fractional CO2 laser in treatment of acne scar.

**Patients and methods:** Thirty patients with atrophic acne scar lesions were included in this study. Patients were randomized to receive fractional CO2 laser therapy to one side of the face while the other side of the face was treated with fractional CO2 laser followed by intradermal PRP injection. Follow-up using the skin analysis camera system and photography was done for three months.

**Results:** A dramatic improvement was observed in the scar depth on both sides of the face. However, the combined fractional CO2 laser and PRP showed more significant improvement. Improvements in the scar appearance and skin texture were reported by the patients. Although 70% of our patients were of a dark skin type, no hyperpigmentation was reported.

**Conclusion:** The combined use of fractional CO2 laser and PRP achieved better results. It reduced the downtime of the fractional CO2 laser. The use of the skin analysis camera provided an objective assessment of the results.

KEYWORDS

acne scarring, acne scarring-laser-PRP, fractional CO2, platelets rich plasma

## 1 | INTRODUCTION

Postacne scarring is a notorious problem for both physicians and patients. The prevalence of acne scarring is 14% in women and 11% in men.[1] Facial atrophic acne scarring can occur with any type of acne, not just in nodulocystic disease.[2] The proper choice of treatment modalities remains a great challenge. The severity of lesions, side-effect profiles, patient expectations, and the psychological impact of the treatment procedure on the patient should all be considered by the physician. A single treatment, multiple treatments, or combined therapy may be required.[3] Many studies have revealed the efficacy of fractional ablative $CO_2$ laser (FCL) therapy in treatment of acne scarring.[4-6] FCL therapy is based on the theory of fractional photothermolysis, where microthermal treatment zones are generated at specific depths in the dermis. These microthermal treatment zones provide deep penetration and, subsequently, collagen remodeling and dermal regeneration can be achieved. Moreover, the tissue surrounding each column is spared, which leads to faster re-epithelization and better wound healing than traditional $CO_2$ ablation.[7] Platelet-rich plasma (PRP) therapy is an autologous preparation of platelets in concentrated plasma. PRP contains significant amounts of platelet-derived growth factor, transforming growth

  

factor, vascular endothelial growth factor, epidermal growth factor, and fibroblast growth factor.[8] This may account for the efficacy of PRP therapy for skin rejuvenation, acne scar treatment, and enhancement of wound healing.[9,10,12] Previous studies have compared the results of a combination of autologous PRP and FCL with those of FCL alone in the treatment of atrophic acne scars.[12,13] However, a noninvasive objective method to evaluate the treatment efficacy remained a questionable issue. This study has two goals. The first is to compare the efficacy of fractional CO2 laser therapy versus the combined use of PRP and fractional CO2 in the treatment of facial atrophic acne scars. The second goal is to evaluate the results of both treatment modalities quantitatively using a skin image analysis system.

## 2 | PATIENTS AND METHODS

Thirty patients with atrophic acne scar lesions were included in this randomized, split-face study. Patients were randomized to receive fractional $CO_2$ laser therapy to one side of the face, while the other side of the face was treated with fractional CO2 laser followed by intradermal PRP injection. The randomization was done by tossing a coin. The study was conducted according to the principles of the Declaration of Helsinki and was approved by the ethical committee of the National Laser Institution review board at Cairo University. Signed informed consent was obtained from each patient before enrollment in the study. Exclusion criteria included patients with a history of keloid or hypertrophic scar formation, recurrent active facial acne, isotretinoin intake within the preceding 6 months, diabetes, and collagen or vascular diseases. Pregnancy and a high level of exposure to sunlight or ultraviolet light (tanning) were also exclusion criteria. The quantitative global acne scarring grading scale adopted by Goodman and Baron[14] was applied in this study. This scale is based on evaluation of both the type and number of scars.

## 3 | TREATMENT PROTOCOL

A SmartXide DOT Fractionated CO2 Laser (DEKA, Florence, Italy) was used, with a smart stack scanning method with a power of 15 W, spacing of 800 mμ, a 600 sμ dwell time, and stack2. Local anesthetic cream was applied under occlusion 45 minutes prior to treatment. The cream used was EMLA® cream (lidocaine 2.5%, prilocaine 2.5%) from AstraZeneca Pharmaceuticals LP, Wilmington, DE. Patients received three sessions at 1-month intervals.

Preparation for PRP was done as follows: Four 8 mL of aliquots of peripheral blood from each patient was placed sterilely into collection tubes prefilled with sodium citrate as anticoagulant. The tubes were then placed in a centrifuge (DRE Slandered, Korea) for 6 minutes at 1200 *g*. The supernatant serum containing PRP was then withdrawn with a pipette m sterile syringe. Autologous PRP injection was done under strict sterile conditions. Intradermal injections with nappage technique were performed at different points along imaginary horizontal and vertical lines. Excess drops were rubbed gently on the skin. Cold compresses were applied after injection to decrease edema and pain. Patients were instructed to apply sunscreen for three months following the end of treatment. Follow-up using the skin analysis camera system and regular photography was done every 3 months for one year.

## 4 | ASSESSMENT OF TREATMENT EFFICACY

### 4.1 | Objective evaluation

The skin analysis camera system (Antera 3D™, Ireland), which uses light-emitting diodes (LEDs) and complex software, provided a quantitative assessment and measurements in microns. The overall roughness of the skin and the depth and severity of the atrophic scars were measured. Fine indentions and wrinkles appeared as orange and green dots and lines on the image, whereas very deep indentions and wrinkles appeared purple in color. Pigmentation and redness were assessed using the Antera camera, which uses LEDs and complex software to make a qualitative assessment.

Photographs were taken at baseline and 3 months after treatment. Patients were classified into groups reflecting mild, moderate, good, and excellent improvement in scarring, with each category reflecting an additional reduction in scar depth of 5 microns. Regular photography (using a Samsung 10-megapixel camera) was also done for all patients at baseline and after each session for 3 months. Additionally, patients were asked to rate their satisfaction regarding each type of treatment and to report any side effects. Patient satisfaction was assessed and graded using a three-point Likert scale with the three anchors being *satisfied*, *partially satisfied*, or *dissatisfied*. After a full explanation of the satisfaction scale, patients answered questions in an unstructured interview. All patients were followed up with 3 months after their final laser session.

### 4.2 | Statistical methods

The data are presented as the mean ± standard deviation (SD). Range, frequency (number of cases), and percentage are included when appropriate.

A Paired *t* test was used for comparison of numerical variables within groups. A Wilcoxon signed-rank test was used for paired (matched) samples. Correlation between various variables was assessed using the Spearman rank correlation equation for non-normal variables. The Mann-Whitney *U* Test was used to assess the statistical significance of the difference in a nonparametric variable between the two groups. The Kruskal-Wallis test was used to assess the difference between more than two groups of ordinal variables. Linear regression was used to test and estimate the dependence of a quantitative variable based on its relationship to one or more independent variables. *P*-values < 0.05 were considered statistically significant. All statistical calculations were performed using the

**TABLE 1** Description of scar characteristics among study cases

| | Mean | ±SD | Minimum | Maximum | Medium | IQR[a] |
|---|---|---|---|---|---|---|
| Duration of scars | 10.4 | 3.1 | 4.0 | 16.0 | 11.0 | 8-12 |
| Number of scars | 12.6 | 5.8 | 5.0 | 25.0 | 12.0 | 8-16 |
| Goodman global score before | 5.7 | 5.5 | 1.0 | 18.0 | 4.0 | 2-6 |
| Type of scars | | | | | | |
| Ice picks scar (n%) | 9 | 30.0% | | | | |
| Boxcar scar (n%) | 16 | 53.3% | | | | |
| Rolling scar (n%) | 5 | 16.7% | | | | |

[a]Interquartile ratio.

**TABLE 2** Comparison between Goodman global score before and after treatment for both sides

| | Before | | | After | | | | |
|---|---|---|---|---|---|---|---|---|
| Good global score | Mean | ±SD | Medium | Mean | ±SD | Medium | *P* | Sig |
| FCL | 5.7 | 5.5 | 4.0 | 3.3 | 2.8 | 2.0 | 0.0001[a] | HS |
| FCL with PRP | 5.7 | 5.5 | 4.0 | 2.2 | 2.4 | 1.0 | 0.0001[a] | HS |
| FCL versus FCL withPRP after treatment | 3.27 | 2.78 | 2.00 | 2.20 | 2.37 | 1.00 | 0.0001 | HS |

[a]Wilcoxon signed-rank test.

**FIGURE 1** The right side of the face of a male patient who was treated with combined FCP and PRP

Statistical Package for the Social Sciences (SPSS Inc, Chicago, IL, USA) release 15 for Microsoft Windows (2006).

## 5 | RESULTS

Thirty patients, 21 females (70%) and 9 males (30%), completed the treatment protocol. Their ages ranged from 20 to 42 years (with a mean of 26.7 ± 4.7). Patients of dark skin types (IV & V) represented 70% of the patients. The highest percentage of scars were boxcar scars (16%), whereas the lowest percentage were rolling scars (5%). The duration of scars ranged from 4 to 16 years with a mean of 10.4 ± 3.1 years (Table 1). The Goodman global score showed a statistically significant reduction for both sides of the face ($P < 0.0001$) after treatment. Nevertheless, greater reduction was found on the sides of the face that were treated with combined laser and PRP (Table 2 & Figures 1 and 2). Linear regression was done to study the effect of independent variables such as age, sex, type, and duration of scars on the Goodman score after treatment with each treatment modality. A highly significant correlation was found between the age, ice pick scar, the duration of the scar, and the Goodman score after treatment with laser only (Table 3). Assessment of the depth of the scars was done using the Antera Camera. A significant improvement was observed in the scar depth on both sides of the face (Figure 3). There was improvement in redness and pigmentation as well (Figure 4).The improvement of these parameters was significant for both treatment modalities. However, the combined FCL and PRP showed greater significant improvement ($P < 0.0001$) (Table 4). According to the Antera scoring system, 30% of patients showed good or excellent improvement on the FCL treated side, compared to 70% of patients on the FCL and PRP treated side (Table 5).

Improvement in scar appearance and skin texture, as well as decreased pores and pigmentation were reported by the patients (Figure 5). Patient satisfaction was higher for the sides that were treated with combined laser and PRP (Figure 6). Fifteen patients (50%) were very satisfied with the combined treatment versus only one patient (3.3%) for the laser treatment only (Figure 2).

**FIGURE 2** The right side of the face which was treated with FCP only

**TABLE 3** Linear Regression to study effect of independent variables on Goodman score after FCL treatment

| | Regression coefficients | *P* | Sig. | 95% CI for Regression coefficients | |
|---|---|---|---|---|---|
| Age | 0.244 | 0.0001 | HS[a] | 0.139 | 0.349 |
| Sex | −0.068 | 0.867 | NS[b] | −0.901 | 0.764 |
| Duration of Scars | −0.346 | 0.0001 | HS | −0.514 | −0.178 |
| Scar type | 0.124 | 0.596 | NS | −0.353 | 0.601 |
| Rolling | −0.436 | 0.365 | NS | −1.413 | 0.542 |
| Ice pick | 0.982 | 0.011 | S | 0.241 | 1.724 |
| Goodman scale before treatment | 0.454 | 0.0001 | HS | 0.394 | 0.513 |

[a]Highly significant.
[b]Nonsignificant.

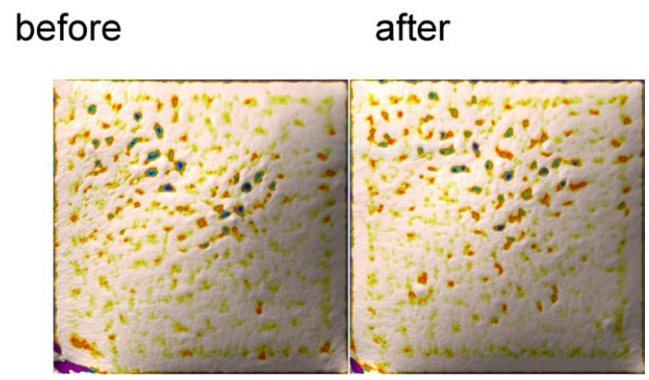


**FIGURE 3** A dramatic improvement was observed in the scar depth on the face by Antera camera

Erythema, edema, and crust formation were reported by all the patients, which faded away 5-7 days after the session on the laser treated side. On the other hand, these transient side effects faded more quickly (within 3 days) on the sides that were treated with combined treatment. Although 70% of the patients were of a dark-skinned type, no hyperpigmentation was reported.

## 6 | DISCUSSION

This study aimed to compare two treatment modalities for postacne scars, namely FCL or combined FCL and PRP, in the same patient by applying one treatment modality on each side of the face. Such

**FIGURE 4** Improvement of postacne scar hyperpigmentation as well

**TABLE 4** Comparison between FCL and FCL+PRP as regards improvement of scar depth, pigmentation, and redness by objective image analysis system

| | Group | | | | | |
|---|---|---|---|---|---|---|
| | FCL | | FCL+PRP | | | |
| | Mean | ±SD | Mean | ±SD | *P* | Sig |
| Scar | 40.71 | 12.98 | 35.23 | 12.54 | 0.0001[a] | HS[b] |
| Pigmentation | 6.44 | 1.46 | 6.09 | 1.52 | 0.0001[a] | HS[b] |
| Redness | 7.01 | 2.10 | 6.73 | 2.00 | 0.001[a] | HS[b] |

[a]Paired *t* test.
[b]Highly significant.

a split-face study could allow better evaluation of results and avoid individual variability in assessing the results.

Fractional ablative $CO_2$ laser has long been known for its safety and efficacy in the treatment of postacne scars and scars with different etiologies.[5] The micro-pores generated by the FCL allow accumulation of materials involved in wound remodeling, such as heat shock protein, procollagen, and dermal elastin, which finally lead to scar remodeling with a change of shape and texture.[6] Fractional photothermolysis: a new concept for cutaneous remodeling using microscopic patterns of thermal injury.[4] FCL resurfacing of photoaged facial and nonfacial skin: histologic and clinical results and side effects.[15] Erythema and melanin indices increased after FCL treatment due to elimination of microscopic epidermal necrotic debris (MEND). MEND was eliminated transepidennally by keratinocytes, and its migration upward and through the stratum corneum was facilitated by subepidermal clefting.[16] The rationale behind using the combination of FCL and PRP is due to the ability of PRP to induced rapid healing after ablative resurfacing.[13] The fact that many mitogenic and chemotactic growth factors are present in the platelet granules explained this result.[9] Moreover, erythema and pigmentation might be reduced by this combined therapy.[10]

Recently, Min et al [10]revealed that expressions of TGFβ and c-Myc were higher on the PRP-treated sides of faces compared to control sides. This result suggests that both TGFβ and c-Myc may contribute to increasing collagen deposition following PRP injection. Increased collagen deposition could lead to improvement in scar depth and appearance.[12]

**TABLE 5** Grade of scar improvement by Antera

| | FCL | FCL+PRP |
|---|---|---|
| Mild | 23.3% | 6.7% |
| Moderate | 46.7% | 23.3% |
| Good | 26.7% | 43.3% |
| Excellent | 3.3% | 26.7% |

In this study, the Antera skin image analysis system was used to measure and compare the changes in the depth of the scars after both treatment modalities. This work is the first to use a skin image analysis system for objective assessment of results. The image analysis system developed by Antera is a digital quantitative system that overcomes the problem of inter-observer variability that resulted from the visual assessment of digital images in previous studies. Both treatment modalities showed a significant improvement in the sear and texture of the skin. However, the combined use of FCL and PRP was superior to the use of FCL alone in treatment of acne scars. Objective assessment of scar depth reduction in microns revealed that 26.7% and 3.3% of patients showed excellent scar depth improvement of more than 20 microns in the FCL and FCL and PRP treated sides, respectively.

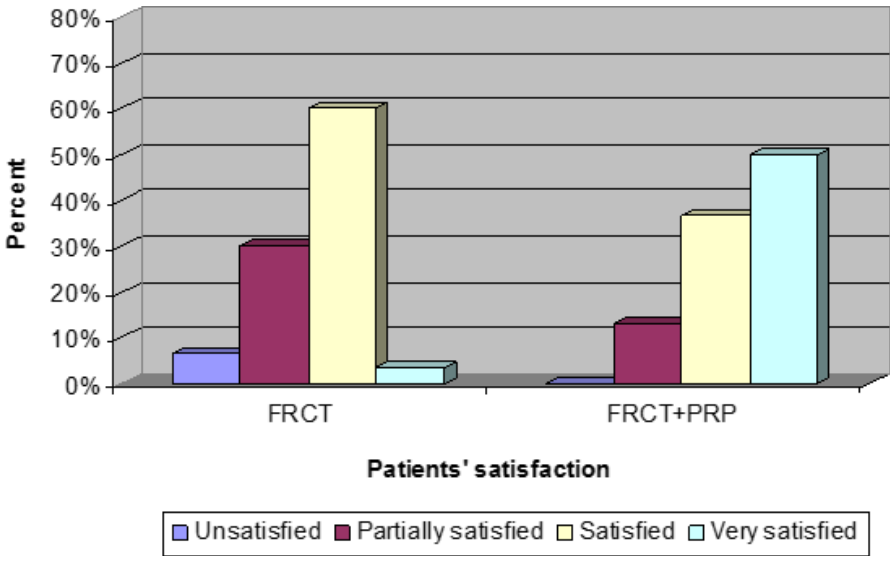


**FIGURE 5** Patient satisfaction regarding each treatment modality

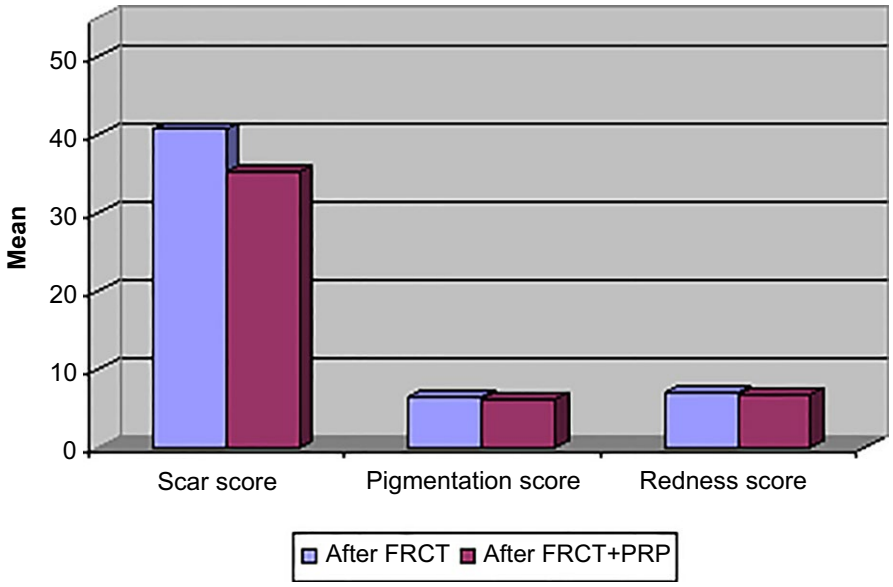


**FIGURE 6** Description of patient satisfaction after treatment for each treated side

In accordance with our work, Lee et al compared both treatment modalities in a split-face pilot trial involving 14 Korean patients. They recorded significant clinical improvement on the side treated with FCL and PRP compared to the side treated with FCL only.[12] They also reported faster improvement in erythema, edema, and crusting on the side that received the combined treatment.[12]

Similarly, the combined FCL and PRP treatment showed superiority over FCL monotherapy in the work done by Gawdat et al.[13]

Although the FCL proved its efficacy in treating acne scars, the probability of hyperpigmentation in dark skin types stands as an obstacle.[16] That is why a relatively low fluence was used in the studies that were performed in Middle East. This approach, in turn, required more laser sessions to achieve clinical improvement. In the current study, 70% of the patients were of dark skin types. Nevertheless, none of our patients experienced hyperpigmentation. Evaluation of both treatment modalities was done after 3 months. However, in a study that involved the same type of patients, Gawdat et al[13] reported hyperpigmentation in 13.3% of the patients who received FCL therapy only.

The type of scar played an important role in the degree of improvement. In our work, ice pick scars in a linear regression model served as an independent variable predicting the grade of improvement in the Goodman score. This is a predictive value for cases treated with FCL. In this work, the best improvement happened in rolling and ice pick scars and the least improvement was found in boxcar scars. In contrast, Majid et al[7] found that rolling and superficial boxcar scars responded better than pitted scars.

## 7 | CONCLUSION

The use of FCL combined with PRP treatment could function synergistically to improve acne scars and reduce side effects.

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**APPENDIX 1**

## GOODMAN QUANTITATIVE GLOBAL ACNE SCARRING GRADING SYSTEM

Grading typeNumber of lesions (1-10)Number of lesions (11-20)Number of lesions (>20)Mild scarring (1 point each)
Macular erythematous, pigmented, mildly atrophic, dish-like1 point2 points3 pointsModerate scarring (2 points each) moderately atrophic, dish-like, punched out with shallow bases, small scar (<5 mm), deep, broad atrophic area2 points4 points6 pointsSevere scarring (3 points each)
Punched out with deep but normal bases, small scars (<5 mm)
Punched out with deep but abnormal bases, small scars (<5 mm)
Linear or troughed dermal scarring,
deep, broad atrophic areas3 points6 points9 pointsHyperplasticPapular scars2 points4 points6 points
Area > 20 cm
18 pointsKeloidal/hypertrophic scarsArea < 5 mm -
6 pointsArea 5-20 $cm^2$ -
12 pointsArea > 20 cm -
18 points