

## Combined Effect of Fractional CO<sub>2</sub> Laser and Topical Application of Growth Factor Complex Solution on Old Facial Acne Scar

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### Abstract

<b>Background</b>	Acne is one of the most common skin conditions. Acne scars are usually leading to disfigurement and psychosocial problem.
<b>Objective</b>	To evaluate the efficacy and safety of carbon dioxide CO <sub>2</sub> fractional laser and to evaluate the efficacy and safety of growth factor solution when is used in constant with CO <sub>2</sub> fractional laser in the treatment of old severe acne scarring.
<b>Methods</b>	Twenty seven patients were divided in to three groups according to their ages and scarring ages. Group I & II were treated by CO <sub>2</sub> fractional laser only. Group III were treated by CO <sub>2</sub> fractional laser plus growth factor. A period of six-month follow-up was done after the last session. Responses to the treatment were graded on quartile grading scale.
<b>Results</b>	Near total improvement was observed in group I age (18-25 years), only (3) of them had marked improvement > 50% after 3 laser sessions. Group II, age (32-50 years), after 6 laser sessions (6) patient had (grade II) moderate improvement, (2) of them minimal improvement. Group III, age (32-45 years) after 6 laser sessions, two patients had (grade IV) > 75%, (5) of them (grade III) 51- 75% marked improvement.
<b>Conclusion</b>	Newly formed acne scarring in young patient responds and improved well to CO <sub>2</sub> fractional laser. Growth factor complex increased the improvement in old acne scarring.
<b>Keywords</b>	Acne, scars, fractional CO <sub>2</sub> , laser, growth factor complex solution

**List of abbreviation:** CO<sub>2</sub> = Carbon dioxide laser, AFR = Ablative fractional resurfacing, MTZ = Microscopic treatment zone, GF = growth factor, PIH = Hyperpigmentation, mm= millimeter, nm= nanometer, mj = Millijoule, ms = Millisecond, cm= Centimeter

### Introduction

Acne is one of the most common skin conditions <sup>(1)</sup>. Acne scars are usually leading to psychosocial distress due to disfigurement and social stigma problem <sup>(2-4)</sup>.

Scars originate in the site of tissue injury and may be atrophic or hypertrophic <sup>(5)</sup>. The wound healing process progresses through 3 stages as follow; inflammation, granulation tissue formation and matrix remodeling <sup>(6,7)</sup>. In matrix

remodeling, if the healing response is too exuberant, a raised nodule of fibrotic tissue forms hypertrophic scars, but if the response is inadequate, it will result in diminished deposition of collagen factors and formation of an atrophic scar <sup>(8)</sup>. In addition, genetic factors and the capacity to respond to trauma are the main factors that influence scar formation <sup>(9)</sup>. About 80-90% of people with acne scars have atrophic scars <sup>(5,10)</sup>. Atrophic scars are sub classified into: ice pick, boxcar, and rolling scars.

- Icepick scars are narrow (< 2 mm), deep, sharply emarginated epithelial tracts that extend vertically to deep dermis or

subcutaneous tissue (V-shape). They rarely respond to laser treatment<sup>(11,12)</sup>.

- Rolling scars are wider than (4-5 mm), (M-shaped), dermal tethering of the dermis to the subcuticular fat<sup>(5)</sup>.

- Boxcar scars maybe shallow (0.1 – 0.5 mm) or deep ( $\geq 0.5$  mm) and are most often (1.5 – 4.0 mm) in diameter (U- shape), shallow boxcar scars and most deep boxcar scars are amenable to fractional laser<sup>(13)</sup>.

Several modalities have been implicated to cure acne scarring including chemical peel, surgical excision, punch grafting, dermabrasion and tissue augmentation with a variety of dermal fillers, have been used to improve atrophic acne scars with varying degrees of success<sup>(3,14)</sup>.

Different types of laser, including the nonablative and ablative lasers are very useful in treating acne scars. Carbon dioxide laser and Erbium YAG laser are the most commonly used ablative lasers for the treatment of acne scars. These abrade the surface and help tighten the collagen fibers beneath<sup>(5)</sup>. All ablative lasers showed high risk of complications<sup>(5)</sup>, the high risk of complications following traditional CO<sub>2</sub> resurfacing has warranted the development of new treatment modalities<sup>(4,15)</sup>. This modality was the fractional photo thermolysis<sup>(16,17)</sup>. The use of ablative laser in a fractional mode was introduced in 2006<sup>(18)</sup>. Fractional laser is the delivery of energy in a manner sufficient to cause a thermal or ablated defect that extends into the dermis and is deeper than its width<sup>(4)</sup>. Ablative fractional resurfacing (AFR) creates microscopic treatment zone (MTZ) to stimulate a wound healing response<sup>(19,20)</sup>, with this technique the tissue surrounding each column is spared, ultimately resulting in rapid epidermal regeneration. This may offer increased efficacy and decreasing the complications associated with the traditional ablative resurfacing<sup>(4)</sup>.

This study was done to evaluate the efficacy and safety of CO<sub>2</sub> fractional laser in the treatment of patients with moderate to severe acne scars alone or in combination with

applying growth factor complex (solution contain multiple growth factor include epidermal and fibroblast growth factor).

## Methods

Twenty-seven patients (19 females and 8 males), age (18-50 years), Fitzpatrick skin type III and IV with mild, moderate to severe acne scarring were included in the study.

The study had done in Laser Medicine Clinic, Institute of Laser for Post-graduate Studies, University of Baghdad and Laser Medicine Clinic, University of Dijlah.

The patients treated with ablative CO<sub>2</sub> fractional laser of 10,600 nm wavelength the laser fluence had delivered with setting of energy (24.2-28.6 mJ) per-pulse, pulse width (1.1 ms), MTZ 90.26/cm<sup>2</sup>/pass, spot size 0.1 mm diameter, fluence 364.33 J/cm<sup>2</sup>, 4-5 pass as shown in (Table 1).

**Table 1: Treatment density**

Treatment Energy (mJ)	Treatment parameters (MTZ/cm <sup>2</sup> /pass)	Total density (MTZ/cm <sup>2</sup> )
$\geq 24$	$\geq 90$	$\geq 361$
$\geq 28$	$\geq 87$	$\geq 348$
$\geq 28$	$\geq 165$	$\geq 625$

Patients with the following criteria were excluded from the study: active infections, pregnancy, and smoking, those who had any procedures such as chemical peeling or dermabrasion done before and those on oral retinoid drugs within the past 10 months, and photosensitive patient.

Patient with history of herpes simplex virus infection prophylaxis antiviral treatment post laser procedures can give to minimize the incidence and adverse sequelae of these infections.

The patients divide in to three groups as in (Table 2)

- Group I: 12 patients with mild to moderate acne scarring, age (18-25 years), duration of acne scarring 12-18 months, (new acne scars).

- Group II: 8 patients with severe acne scarring, age (32-50 years), duration of acne scarring > 6 years, (old acne scars).
- Group III: 7 patients with severe acne scarring, age (32-45 years), duration of acne scarring > 6 years, (old acne scars).

**Table 2: Groups of patients included in the study**

Patient	Age (yr)	No. of patient	Duration of acne scars
Group I	18-20	12	12-18 months mild to moderate acne scars
Group II	32-50	8	> 6 years old acne scars
Group III	32-45	7	> 6 years old acne scars

Preparation the patients to laser sessions should be done; at first, the acne is cleared before treating scarring, sunscreen cream was advised at the start of therapy and continued throughout the duration of the treatment. Topical anesthesia with Emla (eutectic mixture of lidocaine and prilocaine), 1 hour with occlusive dressing prior to laser irradiation was applied. After an hour of application, the anesthetic cream was gently removed. The face washes thoroughly and let the skin dry before treatment, covers the patient eyes with non-reflecting protective goggle. Immediately after laser session, only Group III patient have growth factor complex solution (which contain two type of growth factor Epidermal + Fibroblast GF, concentration of 1 ml per liter; pure concentration of 1 mg per liter. FDA-registered manufacture, USA) Put on their face. The others groups put only a thick layer of sun

block. Cold compressor used to reduce discomfort or burning sensation. They were also instructed to limit sun exposure. Moisturizing cream used at night, used sterile water when wash the faces.

Photographic documentation was used before and after each treatment session. We compared improvement rate of scars after every sessions at 3-4 weeks interval then adverse effects and recovery times were recorded in each session and visit.

Improvement in acne scars was recorded on a specially devised pro forma with a quartile grading scale as shown in (Table 3).

**Table 3: Scale of clinical improvement**

Grade	% of improvement
1	< 25% minimal improvement
2	26-50% moderate improvement
3	51-75% marked improvement
4	> 75% near total improvement

### Results

On completion of study, (27) patients were available for evaluation. All of them had improvement in their acne scarring, especially Group I (Fig. 1, Fig. 2) who had new acne scarring treated more easily, and after (2-3) session (9) patient showed grade IV (near total improvement), and only three of them showed grad III (51-75% marked improvement), (Table 4).

Group II (Fig. 3, Fig. 4); (8) patients with severe old acne scarring treated by CO<sub>2</sub> fractional laser after six session, (6) patient showed grade II (26-50% moderate improvement), and only (2) patients showed grade I (<25% minimal improvement).



**Fig. 1. Group 1: Prelaser (left) and post laser (right) as three session with (grade IV) >75% improvement.**



**Fig. 2. Group 1: Prelaser (left) and post laser (right) as three session with (grade III) >50% improvement**



**Fig. 3. Group II: prelaser (left) and post laser (right) as six laser sessions with (grade II) moderate improvement**

**Table 4: The improvement in acne scar in three groups of patients**

Patients	Age	No. of patient	Treatment	No. of sessions	Improvement
Group I	18-20	12	CO <sub>2</sub> fractional laser	2-3	(9 patient) > 75% grade 4 (3 patient) 51-75% grade 3
Group II	32-50	8	CO <sub>2</sub> fractional laser	6	(6 patient) 26-50% grade 2 (2 patient) <25% grade 1
Group III	32-45	7	CO <sub>2</sub> fractional laser + growth factor	6	(2 patient) > 75% grade 4 (5 patient) 51-75% grade 3



**Fig. 4. Group II: Prelaser (left) and post laser (right) as six laser session with (grade I) minimal improvement**

Group III (Fig. 5, Fig. 6); patient with severe old acne scarring treated by fractional CO<sub>2</sub> laser plus applying growth factor complex after six laser session (2) of them showed grad IV (>75%

near total improvement), and (5) of them showed grad III 51-75% marked improvement). Growth factor complex enhance the Results in this group, as showing in (Table 5).



**Fig. 5. Group III: Prelaser (left) and post laser (right) as six laser session with (grad IV) >75% near total improvement**

**Table 5: Comparisons between two groups of patients had old severe acne scars**

<b>Group II</b>	<b>Group III</b>
Treated by CO <sub>2</sub> fractional laser	Treated by CO <sub>2</sub> fractional laser + growth factor complex
Down time (redness swelling erythema and edema) seven days	Down time (redness swelling erythema and edema) 2-3 days
Improvement in skin texture and firmness	More Improvement in skin texture and firmness
Improvement in acne scars (5 patient) 26-50%, (2 patient) 1-25%	Improvement in acne scars (2 patient) > 75% (5 patient) 50-75%
No of session 6	No of session 6

**Fig. 6. Group III: Prelaser (left) and post laser (right) as six laser session with (grade III) marked improvement**

All subjects reported that any discomfort associated with procedure was only during active intervention and resolved immediately as post procedure. Except the patients with

growth factor complex explain burning sensation resolve after 1 hr.

Swelling and mild to moderate erythema resolved after seven day except in patient with growth factor complex resolved after 2-3 days. Prolonged erythema seen in one patient (group II), incidence (3.5%), three-month duration, and this patient had previous history of rosacea, treated by metronidazole gel and responded to treatment after two months. Post inflammatory hyperpigmentation (PIH) was seen in two patient, incidence (7%), one of them (group I) with skin type IV, had previous history of (PIH). Second patient (group II) skin

type IV have multiple laser session, and both of them treated by topical hydroquinone preparations.

A bronzed or tanned appearance seen in one patient (group I), incidence (3.5%) that was evident at six months follows up visit. This may be due to sun exposure without used sunscreen; this patient was treated by sun block and vitamin C cream.

There were no incidences of infections, scarring, hypopigmentation, or other serious complications (Table 6).

**Table 6: The complication seen in three groups of patients**

Patients	Transient erythema and edema	Prolonged erythema (3 months) duration	Hyper-pigmentation	Hypo-pigmentation	A bronzed or tanned appearance	Burning sensation	Scarring formation	Infection
Group I	All patients	-ve	One patient	-ve	One patient	-ve	-ve	-ve
Group II	All patients	One patient	One patient	-ve	-ve	-ve	-ve	-ve
Group III	All patients	-ve	-ve	-ve	-ve	All patients	-ve	-ve

**Discussion**

Fractional ablative laser therapy is a relatively new therapeutic modality which will likely be widely used because of its efficacy and limited side-effect profile<sup>(21,22)</sup>.

Acne scarring is a complex problem that is not amenable to a simple, definitive solution. A combination of several treatment procedures over multiple treatment session may be appropriate<sup>(10,23-25)</sup>. In this study, (group I), which involved young s had newly formed acne scars treated by CO<sub>2</sub> fractional laser, nine of them reached near total (grade IV), after 2-3 laser sessions. This may be due to young age patients, because aging and ultra violet exposure lead to reduction of procollagen synthesis, increase of collagen degradation in dermal extra cellular matrix, increase in irregular elastin deposition<sup>(26)</sup>, and rendered the old acne scar more deep resistance to laser treatment<sup>(27)</sup>.

It has been seen in this study that the acne scarring gave a good result when was treated as soon as possible by fractional CO<sub>2</sub> laser.

Because the CO<sub>2</sub> lasers have a double effect: they promote the wound healing process and arouse on amplified production of myofibroblasts and matrix proteins such as hyaluronic acid<sup>(28)</sup>.

The other two groups have old severe acne scarring, (Group II), (8) Patients treated by fractional CO<sub>2</sub> laser; only (6) of them showed (grade II) (26-50% improvement). While group III (7) patients who was treated by CO<sub>2</sub> fractional laser plus applying growth factor complex solution on their acne scarring showed more improvement, (5) patients had (51-75%) improvement (grade III), and (2) of them had more than 70% improvement (grade IV).

This may be due to the effect of growth factors which stimulate the migration and proliferation of fibroblasts<sup>(29)</sup>, it was also regulating fibroblasts in treated skin, thereby resulting in neo collagenesis<sup>(30,31)</sup>.

This study also revealed that there was a synergistic effect of growth factor with CO<sub>2</sub> fractional laser because the second one creates

micropunctures in to stratum corneum and dermis before topical application of growth factor complex, with the assumption that reduced barrier will result in greater efficacy of growth factor<sup>(26)</sup>.

The complication in this study was very few, may be because the study was done in winter follow up the patient in summer, so that the Hyperpigmentation (PIH) seen in two patients only. Both of them skin (type IV) dark skin<sup>(32,33)</sup>, with history of neglect used sun Block, Both of them treated by topical hydroquinone preparations.

Erythema of longer duration it was found in one patient (group II), may be due to increase number of laser passes performed<sup>(34,35)</sup>, and increase number of laser session.

One patient (group I) experienced a bronzed or tanned appearance that was evident at the 6 months follow-up visits. May be due to secondary desiccation and/or optical changes in portions of the epidermis and dermis, along with the underlying erythema and wound healing response<sup>(4)</sup>.

Lastly, all participants felt an ascending improvement rate during and after the course of treatment. Also we see significant improvement rate in skin texture and increase firmness after treatment in all patient especially patient with growth factor.

This study concluded that treatment of moderate to severe facial acne scarring by CO<sub>2</sub> fractional laser provides a safe and effective treatment with minimum complication. Additionally, treatment of acne scars in the early stages by CO<sub>2</sub> fractional laser, gives the best results than late treatment.

Also this study concluded that concomitant use of CO<sub>2</sub> fractional laser with growth factor complex solution for the treatment of old severe acne scars give the best results, with minimal down time and no complication.

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### Author contribution

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### Conflict of interest

There was no conflict of interest.

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### References

1. Gerald O' Daniel T. Multimodal management of atrophic acne scarring in the aging face. *J aesthetic plastic surgery*. 2011; 35(6): 1143-50.
2. Woo SH, Park JH, Kye YC. Resurfacing of different types of facial acne scar with short-pulsed, variable-pulsed, and dual-mode Er:YAG laser. *Dermatol Surg*. 2004; 30: 488-93.
3. Grevelink JM, White VR. Concurrent use of laser skin resurfacing and punch excision in the treatment of facial acne scarring. *Dermatol Surg*. 1998; 24: 527-30.
4. Walgrave SE, Ortiz AE, MacFalls HT, et al. Evaluation of a novel fractional resurfacing device for treatment of acne scarring. *Lasers Surg Med*. 2009; 41: 122-7.
5. Fabbrocini G, Annunziata MC, D'Arco V, et al. Acne scars: pathogenesis, classification and treatment. *Dermatol Res Pract*. 2010; 2010: 893080. doi: 10.1155/2010/893080
6. Wolfram D, Tzankov A, Püzl P, et al. Hypertrophic scars and keloids - a review of their pathophysiology, risk factors, and therapeutic management. *Dermatol Surg*. 2009; 35(2): 171-81.
7. Cowin AJ, Brosnan MP, Holmes TM, et al. Endogenous inflammatory response to dermal wound healing in the fetal and adult mouse. *Developmental Dynamics*. 1998; 212(3): 385-93.
8. Chivot M, Pawin H, Beylot C, et al. Acne scars: epidemiology, physiopathology, clinical features and treatment. *Annales de Dermatologie et de Venereologie*. 2006; 133(10): 813-24.
9. English RS, Shenefelt PD. Keloids and hypertrophic scars. *Dermatologic Surgery*. 1999; 25(8): 631-8.
10. Goodman G. Post acne scarring: a review. *J Cosmetic Laser Ther*. 2003; 5: 77-95.
11. Goodman GJ. Post-acne scarring: A review of its pathophysiology and treatment. *Dermatol Surg*. 2000; 26: 857-71.
12. Goodman GJ. Treatment of acne scarring in Ethnic Skin. In: Alam M, Bhatia AC, Kundlu RV, et al. (eds.)

- editors. *Cosmetic Dermatology for Skin of Colour*. 3<sup>rd</sup> ed. New Delhi: Tata McGraw; 2009. p. 136-54.
13. Sardana K, Garg VK, Arora P, et al. Histological validity and clinical evidence for use of fractional lasers for acne scars. *J Cutan Aesthet Surg*. 2012; 5(2): 75-90.
  14. Jacob CI, Dover JS, Kaminer MS. Acne scarring: a classification system and review of treatment options. *J Am Acad Dermatol* 2001; 45: 109-17.
  15. Chapas AM, Brightman L, Sukal S, et al. Successful treatment of acneiform scarring with CO<sub>2</sub> ablative fractional resurfacing. *Lasers Surg Med*. 2008; 40(6): 381-6.
  16. Tanzi EL, Wanitphakdeedecha R, Alster TS. Fraxel laser indications and long-term follow-up. *Aesthet Surg J*. 2008; 28: 675-8.
  17. Narurkar VA. Nonablative fractional laser resurfacing. *Dermatol Clin*. 2009; 27: 473-8.
  18. Daniel A. Cassuto, MD; Neil S. et al. An innovative device for fractional CO<sub>2</sub> laser resurfacing: a preliminary clinical study. *Am J Cosmetic Surg*. 2008; 25(2): 97-102.
  19. Laubach HJ, Tannous Z, Anderson RR, et al. Skin responses to fractional photothermolysis. *Lasers Surg Med* 2006; 38: 142-9.
  20. Manstein D, Herron GS, Sink RK, et al. Fractional photothermolysis: A new concept for cutaneous remodeling using microscopic patterns of thermal injury. *Lasers Surg Med*. 2004; 34: 426-38.
  21. Waibel J, Beer K, Narurkar V, et al. Preliminary observations on fractional ablative resurfacing devices: clinical impressions. *J Drugs Dermatol*. 2009; 8(5): 481-5.
  22. Hantash BM, Bedi VP, Kapadia B, et al. In vivo histological evaluation of a novel ablative fractional resurfacing device. *Lasers Surg Med*. 2007; 39(2): 96-107.
  23. Kang WH, Kim YJ, Pyo WS, et al. Atrophic acne scar treatment using triple combination therapy: dot peeling, subcision and fractional laser. *J Cosmet Laser Ther*. 2009; 11(4): 212-5.
  24. Sadove R. Injectable poly-L-lactic acid: a novel sculpting agent for the treatment of dermal fat atrophy after severe acne. *Aesthetic Plast Surg*. 2009; 33: 113-6.
  25. Alam M, Dover JS. Treatment of acne scarring. *Skin therapy letter*. 2006; 11(9): 7-9.
  26. Draelos ZD. *Cosmeceutical Myths*. In: Draelos ZD, Dover JS, Alam M. *Procedures in cosmetic dermatology*. 3<sup>rd</sup> ed. USA: Elsevier Health Sciences; 2014. p. 134-8.
  27. Goodman GJ, Baron JA. The management of post-acne scarring. *Dermatol Surg*. 2007; 33: 1175-88.
  28. Smith KJ, Skelton HG, Graham JS, et al. Increased smooth muscle actin, factor XIIIa, and vimentin-positive cells in the papillary dermis of carbon dioxide laser-debrided porcine skin. *Dermatologic Surgery*. 1997; 23(10): 891-5.
  29. Stadelmann WK, Digenis AG, Tobin GR. Physiology and healing dynamics of chronic cutaneous wounds. *Am J Surg*. 1998; 176(2A): 26S-38S.
  30. Fitzpatrick RE, Rostan EF. Reversal of photodamage with topical growth factors. *J Cosmetic Laser Ther*. 2003; 5: 25-34.
  31. Lillian B Nanney. Epidermal and dermal effects of epidermal growth factor during wound repair. *J Invest Dermatol*. 1990; 94, 624-9.
  32. Sriprachya-anunt S, Fitzpatrick RE, Goldman MP, et al. Infections complicating pulsed carbon dioxide laser resurfacing for photo-aged facial skin. *Dermatol Surg* 1997; 23: 527-36.
  33. Alster TS. Commentary on increased smooth muscle actin, factor XIII a, and vimentin positive cells in the papillary dermis of carbon dioxide laser-debrided porcine skin. *Dermatol Surg*. 1998; 24: 155.
  34. Nanni CA, Alster TS. Complications of carbon dioxide laser resurfacing: an evaluation of 500 patients. *Dermatol Surg*. 1998; 24: 315-20.
  35. Alster TS. Cutaneous resurfacing with CO<sub>2</sub> and erbium: YAG lasers: preoperative, intraoperative, and postoperative considerations. *Plast Reconstr Surg*. 1999; 103: 619-32.

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