

# A Comparative Study on the Usefulness of Fractional CO<sub>2</sub> and Fractional Er:YAG in Acne Scars: A Split-Face Trial

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## Abstract

**Background:** Acne is a dermatologic condition with a high burden in terms of psychosocial consequences as a result of scars remaining on the skin. Its effects are severe in adolescence and finding treatments with short therapy courses, superior results, and fewer adverse effects are of high importance.

**Materials and Methods:** We included 30 individuals with acne vulgaris scars in Al-Zahra academic training hospital from June 2018 to Jan 2019. Each individual received both fractional CO<sub>2</sub> and fractional Er:YAG lasers on right and left sides of the face, respectively. Three sessions of laser treatment were applied to each side with one-month intervals. Results were evaluated by patients according to subjective satisfaction and physicians' assessment and photo evaluation by two blinded dermatologists. Improvement was graded by a quartile grading scale: less than 25%: mild, 25% to 50%: moderate, 51% to 75%: good, and 76% to 100%: excellent response. Assessments were obtained at baseline and one month after the last visit.

**Results:** Based on subjective satisfaction ( $p < 0.05$ ) and physicians' assessment ( $p < 0.01$ ), fractional CO<sub>2</sub> laser was significantly more effective than Erbium:YAG laser. Also, Post-treatment side effects were mild and transient in both groups.

**Conclusion:** Laser therapies are common in the treatment of scars and each modality has special advantages and disadvantages. Choosing among them should be based on various criteria. Fractional CO<sub>2</sub> lasers have been revealed favorable results in most reports. Large comprehensive trials could help experts in choosing among alternatives for different subgroups.

**Keywords:** Acne vulgaris, clinical trial, CO<sub>2</sub> lasers, Er:YAG laser, scarring

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## INTRODUCTION

Acne is a common dermatological inflammatory disease experienced by up to 80% of people.<sup>[1]</sup> There are some factors involved in the appearance of acne including increased sebum production, altered keratinization, inflammation, and colonization with *Propionibacterium acnes* in hair follicles.<sup>[2]</sup> In some patients, severe inflammatory response leads to scarring which can affect the quality of life.<sup>[3]</sup> Scarring is linked with anxiety, lowered academic performance, poor self-esteem,

depression, and even suicide.<sup>[4,5]</sup> Post-acne scarring is problematic for both patients and physicians. Its prevalence is 14% in women and 11% in men.<sup>[6]</sup> Facial scarring affects about 20% of teenagers.<sup>[7]</sup>

The reason for acne scars appears to be a lack of collagen deposition in the healing course especially in cases with a late start of adequate treatment. This originates from the aberrant production and deposition of collagen around inflamed

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follicles, resulting in visibly depressed scars.<sup>[8]</sup> Acne scars can be classified into three groups: atrophic scar, hypertrophic scar, and keloid. Atrophic acne scar can be categorized into three sub-types: ice-pick scar, rolling scar, and boxcar scar according to their width, depth, and three-dimensional architectures.<sup>[8-10]</sup> Facial atrophic acne scarring can appear after any type of acne.<sup>[11]</sup>

High rates of prevalence along with the cosmetic and mental burden of acne scars have created a great interest in developing effective and short-course therapies with minimal adverse consequences. Clinical interventions aim to help patients manage their condition and alleviate the side effects of acne. In this regard, various types of treatments have been suggested in the literature including solo- and combined surgical and light-based approaches.<sup>[10-15]</sup> There are different modalities, such as soft tissue augmentation<sup>[12]</sup> deep chemical peels<sup>[13,14]</sup> surgical treatment,<sup>[15]</sup> dermabrasion,<sup>[16]</sup> microneedling,<sup>[17,18]</sup> platelet-rich plasma,<sup>[19,20]</sup> ablative and nonablative laser resurfacing<sup>[21]</sup> to help with acne scarring. Light-based therapies are increasingly used as an adjunct to medical treatments of dermatological disorders such as acne and acne scars. Lasers and radiofrequency are among options in the treatment of acne scars. The early laser-based therapies are effective in the treatment of a wide variety of dermatologic conditions, including acne scars.<sup>[22]</sup>

Ablative fractional resurfacing (AFR) systems, such as carbon dioxide (CO<sub>2</sub>) and erbium-doped yttrium aluminum garnet (Er:YAG) were developed in order to achieve more reliable clinical results. In these technologies, a microscopic treatment zones of total epidermal ablation with various amounts of dermal coagulation is made.<sup>[23-25]</sup> The CO<sub>2</sub> laser is a method that has been shown effective in this matter. In this method, a CO<sub>2</sub> laser with a wavelength of 10,600 nm is emitted. Water in the tissues absorbs the laser, and it can selectively elevate the temperature of the superficial skin. Here, the dermal collagen is heated in a controlled manner, and CO<sub>2</sub> laser can remove the collagen of the matrix that has been fragmented and induce the generation of new collagen, which in the end improves scar appearance. However, this approach is accompanied by some drawbacks like long recovery time, prolonged erythema, scars, hypopigmentation, and post-inflammatory hyperpigmentation, particularly in patients that have darker skin.<sup>[21]</sup> In 2003, another method called fractional thermolysis has been provided to overcome these complications. This technology is based on the principles of fractional thermolysis.<sup>[24]</sup> With these new lasers, the problematic issues with ablative (side effects) and nonablative (limited efficacy) lasers were solved.<sup>[26]</sup> Compared to the CO<sub>2</sub> laser, Er:YAG has some desired properties over the CO<sub>2</sub> laser in terms of the degree of thermal damage and decreased ablative efficiency.<sup>[27]</sup> A shorter healing period and fewer complications have made Er:YAG a competitor to CO<sub>2</sub> laser for acne scars.<sup>[12]</sup> Fractional Er:YAG laser provides a more controllable resurfacing and a rapid re-epithelization. However, the ablative fractional laser

still has extended postoperative recovery time and the risk of erythema or hyperpigmentation.<sup>[28,29]</sup>

Even though fractional Er:YAG and CO<sub>2</sub> has been widely used by cutaneous laser surgeons, there are still not sufficient studies to compare their efficacy and side effects. In this study, we aimed to compare the efficacy of two prominent therapies of fractional Er:YAG and fractional CO<sub>2</sub> in the treatment of acne vulgaris scars and assess the patient preference to continue the treatment courses.

## MATERIALS AND METHODS

This study included 30 individuals with acne scars referring to Al-Zahra hospital affiliated with the Isfahan University of Medical Sciences from June 2018 to Jan 2019. Following criteria were considered for inclusion of individuals in the study: having mild-to-moderate acne scar in both sides of the face, patients unwilling to use topical treatments and preferring laser therapies, no pregnancy or breastfeeding, receiving no systematic steroid-retinoid treatment in the last six months, no history of light sensitivity, no symptoms of inclination to forming keloid and hypertrophic scars, and signing informed consent. Individuals undergoing other therapies or with irregular visits were excluded from the study. All patients underwent a 10cc needle subcision on both sides of their faces. Finally, fractional Er:YAG Laser (Smart 2940D Plus, Deka, Calenzana, Italy, 2010) and fractional CO<sub>2</sub> Laser (Smarexide DOT, Advanced CO<sub>2</sub> Fractional technology, DEKA, Italy, 2009) were applied on the left and right side of patients' faces, respectively. Each patient on the left side of the face received laser treatment by a single operator. A 2940-nm Erbium: YAG laser with an average fluence of 12.5 mJ, spot size: 8 mm was applied. Treatments were performed 3 times with an interval of 4 weeks between each treatment. Similarly, each patient received treatment on the right side of the face by the same operator. A fractional CO<sub>2</sub> laser (10600 nm) with a pulse duration of 400 μs, Power 8 W, spacing 800 μm was used. In total, three treatments with four weeks intervals were administered. The severity of the disease was recorded for each patient by both patient and the physician by at the patient's entrance to the study. To evaluate how much the scars were improved, a grading system with quartile grading scale was used. Here, each patient and physician graded less than 25% improvement: mild, 25% to 50%: moderate, 51% to 75%: good, and 76% to 100%: excellent response. Patients were also asked to report any complications during the study period. Demographic information was collected using a questionnaire at the entrance of individuals to the study. In order to assess the severity of acne scarring, optical imaging system was done at baseline and after the third treatment session. Evaluation of the treated parts of the skin was conducted by comparing photographs of the areas based on patients' satisfaction and blinded.

To determine the minimum sample size, we considered the results of the previously published reports.<sup>[30]</sup> This led to a

minimum sample size of 22 individuals for a type I error of 0.01 and a power of 0.90. Descriptive statistics were reported as  $n$  (%) for categorical and mean  $\pm$  SD for continuous variables. The reductions in grades, from the initiation to after the last visit in the two therapies were compared using paired-samples  $t$ -test for both patients and physicians. Results with a  $P$  value  $<0.05$  were considered as a significant difference. All analyzes were performed using GraphPad Prism version 8.0.0 for Windows (GraphPad Software, San Diego, California, USA, www.graphpad.com).

## RESULTS

The final sample included 30 participants whose treatments sessions were done completely and followed afterwards for one month. On average patients were  $29.2 \pm 5.5$  years old. They asserted that after each session, they could observe clinical improvement of their scars. After evaluating the satisfaction surveys, it was observed that 23.3% (7 out of 30) of the patients in group Er:YAG laser evaluated their improvement less than 25%. Also, 66.6% (20 out of 30) rated for 25% to 50% of improvement and 10% (3 out of 30) 50% to 75% improvement. None of the patients in this group reported an excellent improvement (more than 75%). Although there were less patients with mild and moderate improvement in a group CO<sub>2</sub> laser, an increase was seen with satisfaction of more than 50% (from 10% in Er:YAG to 36.6% in the CO<sub>2</sub> group). Man-Whitney analysis demonstrated a notable higher improvement of scars in patients who received CO<sub>2</sub> laser treatments ( $p$ -value  $<0.05$ , Table 1). All in all, patients were more satisfied with the side on which CO<sub>2</sub> laser has been applied.

In the same way, two-blinded dermatologists evaluated the clinical improvement. Compared to Er:YAG laser, they rated a higher percentage of patients with good and excellent results after CO<sub>2</sub> laser (43.3%) compared to Er:YAG (6.7%). Their assessments confirmed that the fractional CO<sub>2</sub> is more efficient than Erbium:YAG, Man-Whitney test with a  $P$  value of 0.06 [Table 1].

No complication was reported during the therapy period. Two individuals had postinflammatory hyperpigmentation (PIH) on both sides of their faces for both treatments. There were no significant complications in either of the groups in follow-up. Nevertheless, 23 (92%) individuals preferred to continue the treatment course with CO<sub>2</sub> versus only 2 (8%) individuals preferring Er:YAG. Also, five patients were unwilling to

continue none of the therapies and one patient was unavailable in follow-up.

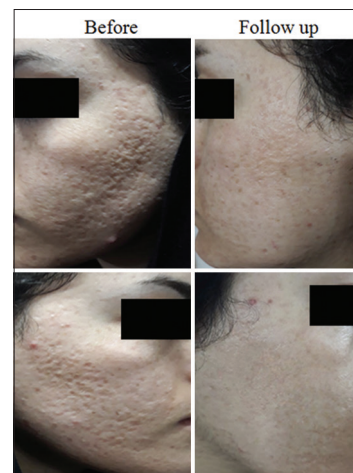
Figure 1 shows the two sides of the face of a patient before the treatment and at follow-up. It is observed that the results of CO<sub>2</sub> are more satisfying.

## DISCUSSION

Choosing among light-based therapies is a challenging issue in supplementation to other treatments of acne scars. Our findings suggest that fractional CO<sub>2</sub> outperformed fractional Er:YAG therapy from both physicians' and patients' views. Furthermore, the participants under study preferred to use fractional CO<sub>2</sub> rather than Er:YAG.

Acne scar is an important remnant of acne with long-lasting physical and psychological effects. This underscores the need for an efficient treatment for acne scars. Fibrosis band beneath the scars is the main cause of depression in acne scarring. Hence, subcision procedures are among the treatments for acne scars, especially deep scars. Other common modalities include dermabrasion, percutaneous collagen induction, punch excision, punch elevation, and chemical peeling. Non-invasive light-based alternatives are also common in the treatment of acne scars with desirable features and efficacy.

Fractional laser photothermolysis aims to reduce complications of laser modalities by restricting dermis injury to microscopic



**Figure 1:** Two sides of the face of a patient with acne scars treated with CO<sub>2</sub> (top row) and Er:YAG lasers (bottom row) before treatment and at follow-up

**Table 1: Patients and blinded investigators' evaluations of treatment**

	Laser	Response				P
		Mild * n (%)	Moderate n (%)	Good n (%)	Excellent n (%)	
Patients' evaluations	Erbium: Yag Laser	7 (23.3%)	20 (66.7%)	3 (10%)	0 (%)	< 0.05
	Fractional CO <sub>2</sub> Laser	3 (10%)	15 (50%)	11 (36.7%)	1 (3.3%)	
Blinded investigators	Erbium Yag Laser	9 (30%)	19 (63.3%)	2 (6.7%)	0 (%)	< 0.01
	Fractional CO <sub>2</sub> Laser	4 (13.3%)	13 (43.3%)	10 (33.3%)	3 (10%)	

zones with skip areas in between.<sup>[12]</sup> Fractional carbon dioxide (CO<sub>2</sub>) laser is among the early light-based modalities with acceptable results in various dermatological conditions including acne scars, with fewer post-treatment complications than CO<sub>2</sub> laser.<sup>[8,12]</sup> Fractional CO<sub>2</sub> has been used as a monotherapy and has shown to result in mild to significant improvements in almost 80% of acne scars with minimal side effects.<sup>[8,30,31]</sup> According to the available data, the use of CO<sub>2</sub> should be based on the characteristics of the scar, individualized plans, and the patient-side issues.<sup>[21]</sup>

Erbium YAG (Er:YAG) is another laser-based option in the treatment of various dermatological conditions such as vitiligo and acne.<sup>[32]</sup> Laser is used along with topical lotions to increase their efficacy. Er:YAG has shown to be effective in acne compared to other mechanical treatments.<sup>[33]</sup> Reinholz *et al.*<sup>[34]</sup> reported higher both objective and subjective efficacy and better smoothing for fractional CO<sub>2</sub> relative to Er:YAG laser.

Scientists have assessed the safety and efficacy of Fractional Er:YAG and CO<sub>2</sub> lasers for the treatment of atrophic scarring. In a study, 24 patients were evaluated for this purpose. After six months follow-up, 55% of CO<sub>2</sub> laser sites and 65% of Er:YAG laser sites were turned out to lead to an improvement of more than 50%. Improvement got better notably from 1- to 6-month follow-up ( $p < 0.001$ ). No major difference was observed comparing the two methods at 1- and 6-month follow-up. Here, clinical assessment has been done based on the lessening the scar volume.<sup>[30]</sup>

In another research, Manuskiatti *et al.*<sup>[24]</sup> evaluated the efficacy and safety of CO<sub>2</sub> ablative fractional resurfacing on atrophic acne scars in 13 Asian individuals. It was observed that 62% of patients reported at least 50% improvement. The most common side effect that was reported was mild post-inflammatory hyperpigmentation which was recovered in about five weeks on average.

Furthermore, Huang *et al.*<sup>[35]</sup> evaluated the therapeutic effect, safety, and risk of fractional resurfacing with ablative laser in the treatment of superficial scars. They studied 88 patients with of superficial scar. 66 of them with acne scar, 12 with burn scar, and 10 with other types of scars. They performed treatments with Er:YAG (2940 nm,  $\geq 3$  times), Ultra-pulse CO<sub>2</sub> (10600 nm,  $\geq 2$  times), or a combination of both lasers ( $\geq 3$  times). They stated a significant improvement in 80% of the patients and good improvement in 50%. It was reported one case with a persistent hyperpigmentation with CO<sub>2</sub> treatment. However, this side effect was improved later and no more complications were reported.

Meta-analysis of eight studies showed that the difference between the efficacy of fractional CO<sub>2</sub> and non-CO<sub>2</sub> lasers in the treatment of acne scars was not significant from neither physician nor patient viewpoint.<sup>[36]</sup> It is required to conduct more trials with standard settings and criteria to obtain comprehensive and credible data on comparison between laser modalities.

All laser-based modalities have shown to be effective in certain cases and the choice among them should be based on various parameters and factors. Both CO<sub>2</sub> and Er:YAG options are more appropriate for severe atrophic scars. Skin color is claimed to be a significant factor in the efficacy of these lasers whereas Er:YAG has fewer side effects in darker skins.<sup>[37]</sup> Here, the skin of participants was light skin and no significant complications were present in none of the groups.

It is claimed that non-ablative fractional lasers are better with comparable benefits to ablative lasers and interesting aspect of fewer adverse effects.<sup>[37]</sup> However, the reports are not fully consistent and some authors have reported superior results for ablative fractional CO<sub>2</sub> compared with non-ablative fractional Er:YAG laser.<sup>[22]</sup> Hence, these options could be applied and compared in future studies.

Our sample size was not big enough to perform post hoc tests in subgroups. Conducting larger studies could target the most suitable subgroups for each therapy and provide information on the participants' preferences among the treatments. We chose to use matched design to facilitate the conduct of the research. Using unmatched designs within larger samples could help obtain more practical and generalizable results. Combining lasers with topical treatments is common in practice.<sup>[12]</sup> It is suggested to compare various combined therapies of CO<sub>2</sub> and Er:YAG to determine the best choice in different conditions and subgroups.

## CONCLUSIONS

Laser therapies are common in treatment of scars and each modality has special advantages and disadvantages. Choosing among them should be based on various criteria. Fractional CO<sub>2</sub> lasers have been revealed favorable results in most reports. Large comprehensive trials could help experts in choosing among alternatives for different subgroups.

## DECLARATIONS

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### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

### Ethics approval and consent to participate

This study was approved by the ethical committee of Isfahan University of Medical Science (ethical approval ID: IR.MUI.MED.REC.1397.294). Written informed consent was obtained from participants before enrollment.

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### Conflicts of interest

There are no conflicts of interest.

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