Ablative Fractional Lasers (CO2 and Er:YAG): A Randomized Controlled Double-Blind Split-Face Trial of the Treatment of Peri-Orbital Rhytides

Syrus Karsai, MD,1 Agnieszka Czarnecka, MD,1 Michael Jünger, MD, PhD,2 and Christian Raulin, MD, PhD1,3*
1Laserklinik Karlsruhe, Kaiserstr. 104, D-76133 Karlsruhe, Germany
2Department of Dermatology, University of Greifswald, Ferdinand-Sauerbruch-Strasse, D-17475 Greifswald, Germany
3Department of Dermatology, University of Heidelberg, Voßstr. 2, D-69115 Heidelberg, Germany

Background and Objective: Ablative fractional lasers were introduced for treating facial rhytides in an attempt to achieve results comparable to traditional ablative resurfacing but with fewer side effects. However, there is conflicting evidence on how well this goal has generally been achieved as well as on the comparative value of fractional CO2 and Er:YAG lasers. The present study compares these modalities in a randomized controlled double-blind split-face study design.

Study Design/Materials and Methods: Twenty-eight patients were enrolled and completed the entire study. Patients were randomly assigned to receive a single treatment on each side of the peri-orbital region, one with a fractional CO2 and one with a fractional Er:YAG laser. The evaluation included the profilometric measurement of wrinkle depth, the Fitzpatrick wrinkle score (both before and 3 months after treatment) as well as the assessment of side effects and patient satisfaction (1, 3, 6 days and 3 months after treatment).

Results: Both modalities showed a roughly equivalent effect. Wrinkle depth and Fitzpatrick score were reduced by approximately 20% and 10%, respectively, with no appreciable difference between lasers. Side effects and discomfort were slightly more pronounced after Er:YAG treatment in the first few days, but in the later course there were more complaints following CO2 laser treatment. Patient satisfaction was fair and the majority of patients would have undergone the treatment again without a clear preference for either method.

Conclusions: According to the present study, a single ablative fractional treatment session has an appreciable yet limited effect on peri-orbital rhytides. When fractional CO2 and Er:YAG lasers are used in such a manner that there are comparable post-operative healing periods, comparable cosmetic improvement occurs. Multiple sessions may be required for full effect, which cancels out the proposed advantage of fractional methods, that is, fewer side effects and less down time. Lasers Surg. Med. 42:160–167, 2010. © 2009 Wiley-Liss, Inc.

Key words: skin aging; laser surgery; fractional photothermolysis; comparative study

INTRODUCTION

The procedural volume of laser treatment of skin aging (rhytides, telangiectasias, and pigmentation) has substantially increased during the past decade: Tierney and Hanke [1] estimated a 330% increase of non-ablative skin rejuvenation procedures and a 66% increase of ablative ones in the USA between 2001 and 2007. These data clearly show a trend towards more tolerable non-invasive methods; however, compared to skin resurfacing, non-ablative laser devices have so far failed to achieve equivalent effects. Furthermore, controversy persists regarding the optimal laser treatment of rhytides.

Carbon dioxide (CO2) and erbium:yttrium–aluminum–garnet (Er:YAG) laser ablation are accepted and widely employed methods of skin rejuvenation [2]. In contrast to CO2 lasers (10,600 nm), the Er:YAG laser has a technical benefit because its wavelength of 2,940 nm is much closer to an absorption maximum of water (3,000 nm) [3–5], thus allowing for high precision yet superficial skin ablation. With the selection of appropriate parameters, however, the biophysics of CO2 and Er:YAG laser–tissue interaction creates similar injuries and cosmetic results [4–7]. Conceivably, the shortcomings of both methods are very similar: while they produce clinically efficacious results, the intensity and depth of the thermal injury may require anesthesia and result in unwanted effects such as hypo- or hyperpigmentation, prolonged wound healing and even scarring [1,6,8,9]. Extended downtime and long lasting side effects are obvious drawbacks for patients undergoing these procedures. On the other hand, the effect of
non-ablative methods is generally only moderate and typically requires 5–6 treatment sessions to be accomplished [10].

Fractional methods have the potential to provide great efficacy in treating rhytides while minimizing downtime and side effects [11]. The findings about ablative fractional photothermolysis of rhytides that have been published so far are encouraging, but they are inconsistent in detail as far as study design and the respective efficacy of different laser modalities are concerned. Whereas several studies claim encouraging results of erbium lasers (e.g., [12–14]), the same holds true for fractional CO2 ablation [15–17]. There is very little evidence on the comparative safety and efficacy of both methods, but the limited scope of the literature to date suggests a roughly equivalent status [18], just as it does for non-fractional applications [4–7]. However, claims that the fractional CO2 laser is superior to fractional Er:YAG [19] call for evidence-based scrutiny, as do the extremely encouraging results of fractional erbium lasers [14,20]. No systematic comparative studies of both fractional modalities have been published, according to a recent MEDLINE research. Furthermore, data that have been generated with traditional ablative lasers cannot necessarily be attributed to ablative fractional devices due to different laser–tissue interactions.

The issue of comparative effectiveness and safety is of major relevance in the clinical setting where economical considerations play a considerable role for both patient and surgeon. Since devices for fractional Er:YAG therapy might be more economical than those for fractional CO2 laser treatment—both in terms of equipment acquisition (US $60,000–70,000 vs. US $120,000–150,000 for the devices used in the present study) and maintenance, Er:YAG would be an attractive option, assuming the results are comparable. This study therefore attempts to compare both methods in terms of:

- the effect of a single treatment session on the Fitzpatrick wrinkle score and the profilometric wrinkle depth;
- side effects and tolerability;
- patient satisfaction.

MATERIALS AND METHODS

Study Design

The study was performed as a randomized controlled double-blind trial in a split-face design. Based on the results of previous studies [7,21], the sample size was calculated with the statistical sign test [22] using the following parameters: probability of first-order error \( \alpha = 0.05 \), probability of second-order error \( \beta = 0.20 \), expected percentage of improvement according to the Fitzpatrick wrinkle score \( 23 = 30–60\% \), likelihood of a significant difference \( \delta = 0.75–0.86 \). Depending on the scope of these parameters, the required sample size for a split-face design was 25–30 patients. The randomization table was generated by an external statistician not otherwise involved in the study after the sample size calculation.

Patients

Patients were recruited for the trial between August and October 2008 in a private practice for cosmetic laser surgery. To be eligible for enrollment, patients of either sex had to be between 40 and 55 years of age with mild to moderate peri-orbital rhytides ("crow's feet") at rest (Class II according to Fitzpatrick [23]; see Table 1).

Exclusion criteria included: (1) unrealistic expectations; (2) inability to meet follow-up criteria; (3) Fitzpatrick skin phototype > III [24]; (4) coagulation disorders or anti-coagulant treatment; (5) allergy to lidocaine or tetracaine; (6) oral isotretinoin within the last 6 months; (7) any active skin disease within the treatment area (e.g., cancer or autoimmune disease); (8) synthetic implants in the treatment area; (9) facial cosmetic procedures affecting the treatment area (e.g., blepharoplasty, botulinum toxin, dermabrasion, chemical peeling, laser surgery, or face-lift) within the last 6 months; (10) photosensitizing medications (e.g., tetracycline or gold); (11) history of keloid formation; (12) pregnancy.

Informed consent (oral and written) was obtained from all patients. The study met Good Clinical Practice criteria and the principles of the Declaration of Helsinki. The protocol was approved by the Institution’s Human Research Review Committee and registered with Clinical-Trials.gov (identifier: NCT00990431).

Overall, 45 patients were considered during the study period, 33 of which met the study criteria. Two patients were enrolled but dropped out prior to the study due to disease, and three withdrew their consent because of the anticipated downtime. The 28 remaining patients were predominantly female \( n = 26; 92.9\% \) and on average 46.1 ± 4.0 years of age.

### Table 1. Fitzpatrick Wrinkle Score and Its Application in the Study*

<table>
<thead>
<tr>
<th>Class</th>
<th>Wrinkling</th>
<th>Score</th>
<th>Degree of elastosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Fine wrinkles</td>
<td>1–3</td>
<td>Mild (fine textural changes with minimal skin lines)</td>
</tr>
<tr>
<td>II</td>
<td>Fine to moderate depth wrinkles, moderate number of lines</td>
<td>4–6</td>
<td>Moderate (distinct elastosis with yellow discoloration of individual papules)</td>
</tr>
<tr>
<td>III</td>
<td>Fine to deep wrinkles, numerous lines (with or without redundant skin folds)</td>
<td>7–9</td>
<td>Severe (marked confluent elastosis with thickened, multipapular and yellowed skin)</td>
</tr>
</tbody>
</table>

*The score is based on depth first and foremost and then takes into account the number of lines. All investigators were instructed to take the deepest wrinkle as the basis for their scoring.
Treatment

Technical data. Treatment parameters were chosen according to the manufacturers’ recommendation, the published evidence (e.g., [15,18]) and an estimated downtime of 4–5 days for both methods. Both procedures were limited to a single treatment session.

The Er:YAG laser used in this study has a fractional handpiece (MCL 30 Dermablate, Asclepion Laser Technologies GmbH, Jena, Germany). By means of a microlens array the laser beam is divided into 13/13 small spots with 250 μm diameter each, spread over an area of 13 × 13 mm². A coverage of 5% of the skin is achieved with a single pass. The pulse duration is 400 μseconds. In this trial, we performed four passes (resulting in coverage of 20% of the treated skin) with a total fluence of 60 J/cm² and six stacked pulses to optimize thermal exposure [25].

The CO2 laser (Fraxel Re:pair, Solta Medical, Inc., Hayward, CA) employs disposable tips with a diameter of 7 and 15 mm, the smaller being used for the peri-orbital region. The laser beam is delivered through multiple reflective and refractive elements; it is focused to a spot size of approximately 120 μm in diameter at incidence to the skin to deposit an array of laser beams across the surface. Pulse energy varies from 5 to 70 mJ and density from 5% to 70%. The pulse duration is 10 milliseconds. In the present trial, patients received two passes (resulting in coverage of 20% of the treated skin) with a total density of 20%. The skin coverage is slightly below the manufacturer’s recommendation (of up to 40%) due to the following considerations:

- We employed pinpoint bleeding and a slight serosanguinous exudate as established and well-accepted clinical end points for ablative resurfacing.
- Ablative fractional resurfacing is far from being free of side effects. Serious side effects have been reported [26,27] and the manifest risk of scarring demands great caution when ablative fractional resurfacing is applied to delicate regions such as the peri-orbital area or the neck [28].

Treatment protocol. Four weeks prior to the treatment, patients were advised to avoid direct UV light exposure and to apply sun-blocking lotions on a daily basis regardless of the weather. Immediately before starting the procedure, any creams and cosmetic residues were meticulously removed with saline solution. On the side of the face that was designated for CO2 laser treatment, a topical anesthetic gel (23% lidocaine and 7% tetracaine in LipoThene 133™, LipoThene, Inc., Pacific Grove, CA) was applied and left for 30 minutes; the contralateral (Er:YAG) side received no anesthetic. The differential application of the topical anesthetic in this study corresponds to the daily routine where sites treated with the short-pulsed Er:YAG laser are generally not numbed.

The patients were advised to keep their eyes closed, and the eyes were covered with a moist gauze held in place by an assistant during the entire procedure.

The fractional lasers were applied without overlapping or gaps between laser pulses. The hand-piece and thus the pattern were rotated by an angle of 45’ (Er:YAG) and 90’ (CO2), respectively, between consecutive passes to avoid meeting single spots.

At the end of the treatment, the CO2-treated area showed pinpoint bleeding and a slight serosanguinous exudate, whereas the Er:YAG-laser treated site had delicate crusts. Vaseline was applied to the treatment areas immediately after the procedure. Patients were instructed to gently cleanse the peri-orbital region three times a day with cold black tea and to re-apply Vaseline as needed (to maintain moisture) until complete shedding of crusts and scales. Also, they were advised to stay away from direct sun exposure.

<table>
<thead>
<tr>
<th>Time</th>
<th>Fitzpatrick wrinkle score</th>
<th>Profilometry</th>
<th>Side effects</th>
<th>Patient satisfaction questionnaire</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before treatment</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>1 day after treatment</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>3 days after treatment</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>6 days after treatment</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>3 months after treatment</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>

TABLE 2. Patient Evaluation

<table>
<thead>
<tr>
<th>Time</th>
<th>CO2</th>
<th>Er:YAG</th>
<th>Neither</th>
<th>CO2</th>
<th>Er:YAG</th>
<th>Both</th>
<th>Neither</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 day after treatment</td>
<td>13 (46.4%)</td>
<td>14 (50.0%)</td>
<td>1 (3.6%)</td>
<td>14 (50.0%)</td>
<td>6 (21.4%)</td>
<td>4 (14.3%)</td>
<td>4 (14.3%)</td>
</tr>
<tr>
<td>3 days after treatment</td>
<td>11 (39.3%)</td>
<td>13 (46.4%)</td>
<td>4 (14.3%)</td>
<td>13 (46.4%)</td>
<td>6 (21.4%)</td>
<td>5 (17.9%)</td>
<td>4 (14.3%)</td>
</tr>
<tr>
<td>6 days after treatment</td>
<td>15 (53.6%)</td>
<td>11 (39.3%)</td>
<td>2 (7.1%)</td>
<td>10 (35.7%)</td>
<td>10 (35.7%)</td>
<td>6 (21.4%)</td>
<td>2 (7.1%)</td>
</tr>
<tr>
<td>3 months after treatment</td>
<td>17 (60.7%)</td>
<td>9 (32.1%)</td>
<td>2 (7.1%)</td>
<td>8 (28.6%)</td>
<td>13 (46.4%)</td>
<td>5 (17.9%)</td>
<td>2 (7.1%)</td>
</tr>
</tbody>
</table>

TABLE 3. Patient Satisfaction

<table>
<thead>
<tr>
<th>Time</th>
<th>Which of the sides caused more discomfort?</th>
<th>Which of the sides would you undergo again or recommend to others?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CO2</td>
<td>Er:YAG</td>
</tr>
<tr>
<td>1 day after treatment</td>
<td>13 (46.4%)</td>
<td>14 (50.0%)</td>
</tr>
<tr>
<td>3 days after treatment</td>
<td>11 (39.3%)</td>
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<td>17 (60.7%)</td>
<td>9 (32.1%)</td>
</tr>
</tbody>
</table>
exposure and to refrain from picking and rubbing the skin. Prior to follow-up examinations, patients were explicitly asked to avoid any skin-care products since the skin’s moisture content might have influenced the assessment of possible side effects and wrinkle depth.

**Evaluation**

Patients were assessed according to Table 2.

The first primary end point was the objective wrinkle depth (in mm). The wrinkle profile recording was performed by using the optical 3D in vivo measurement system PRIMOS (Phaseshift Rapid In vivo Measurement Of Skin) (GFMesstechnik GmbH, Teltow, Germany). The system is based on the digital fringe projection technique as described by Jaspers et al. [29], and has been validated for rhytide assessment in several clinical studies [30–32]. Briefly, a parallel stripe pattern is projected onto the skin surface by using micro-mirrors and recorded by a CCD camera. The 3D effect is achieved by the minute elevation differences on the skin surface, which deflect the parallel projection stripes. The measurements of these deflections provide qualitative and quantitative data of the skin profile and therefore allow the assessment of the effect of laser skin resurfacing [30]. The PRIMOS measurement was performed with a facial camera mount (Canfield Scientific, Inc., Fairfield, NJ) that was left in place for the photographic documentation. To ensure reproducibility between the images, the baseline image was recalled at half intensity and the subject’s head position was adjusted until it was directly aligned with the baseline image prior to image capture.

Photographs were taken with a Canon Digital Camera (EOS 350D with Macro Lens EF-S 60 mm f/2.8 USM, Canon, Inc., Tokyo, Japan) equipped with a lens mounted ring flash (Macro Ring Lite MR-14EX, Canon, Inc.). Standardized views (frontal and 45° oblique) with a defined distance between the camera and skin were used, and the same laboratory processed all photographs. Photographs were assessed according to the Fitzpatrick wrinkle score [23] by a panel of three dermatologists familiar with laser resurfacing but not involved in the study. Photos were evaluated in a blinded fashion, that is, the photographs were mixed intra-individually and the examiners were unaware of whether the photographs were pre-operative or post-operative. The Fitzpatrick score had been validated in previous studies and has shown good inter- and intra-observer reproducibility [33,34]; hence it was chosen as the second primary end point.

Patient satisfaction as the secondary end point was assessed using two simple questions:

- “Which of the sides caused more discomfort?”
- “Which of the sides would you undergo again or recommend to others?”

All undesired effects of the procedures were rated on site by a physician assistant not otherwise involved in the study on a 10-point visual analogue scale 1, 3, and 6 days as well as 3 months after treatment.

**Statistical Data Evaluation**

All data were analyzed using the Statistical Package for Social Sciences (SPSS/PC+) program (Version 12.0 for Windows), employing the Wilcoxon signed rank test and McNemar test. The average value was used for the analysis of the continuous variables.

The significance level was set to $P<0.05$. Descriptive statistics were also calculated (mean, standard deviation, median, minimum, maximum, numbers, percentage rates).

**RESULTS**

**Fitzpatrick Wrinkle Score**

Overall, both modalities yielded a significant, albeit only moderate, reduction of the Fitzpatrick score (Fig. 1). The difference between sides was not significant before ($P = 0.081$) and after treatment ($P = 0.53$).

64.3% of the sides treated with the CO$_2$ laser and 57.1% of those treated with the Er:YAG laser were rated as “improved.” Figure 2 shows an example of a patient with a considerable reduction in rhytides on both sides.

**Profilometry**

The wrinkle depth was significantly reduced by both modalities (from $1.97 \pm 2.05$ mm to $1.64 \pm 2.04$ mm on the CO$_2$ side and from $1.97 \pm 1.29$ mm to $1.63 \pm 1.20$ mm on the Er:YAG side), and the relative reduction was somewhat more marked than the values on the Fitzpatrick score (Fig. 3). CO$_2$ laser treatment was again slightly more efficient, but the differences were statistically not significant and not perceivable. An improvement was considered in 88.9% (CO$_2$) and 82.1% (Er:YAG) of treated sides, respectively.

**Side Effects**

Both modalities resulted in marked pinpoint bleeding (CO$_2$) or crust formation (Er:YAG), respectively.

The intensity of the concomitant and side effects over the course of follow-up is displayed in Table 4. Early after treatment, complaints were substantially more marked on
the side treated with the Er:YAG laser with the notable exception of bleeding which occurred more frequently after CO2 laser treatment.

Six days after treatment, erythema and swelling were more persistent in the sides treated with the CO2 laser, and after 3 months there was a more marked hyperpigmentation on the same sides.

Patient Satisfaction

The patients’ rating of both methods showed no appreciable or statistically significant difference (Table 3). There was a certain preference for the CO2 laser early on during follow-up, more or less correlating to the occurrence of side effects, although later it reversed.

DISCUSSION

Non-ablative fractional methods have been reported to be effective and to have limited side effects [35], but they failed to achieve results comparable to those of conventional ablative techniques, which finally led to the development of ablative fractional devices [16,19]. In contrast to some claims in the literature [19], the present study failed to demonstrate appreciable differences between both methods in treating peri-orbital rhytides in a meticulously chosen experimental setting with randomized, blind allocation of treatment sites in a split-face design. Correspondingly, this confirms previous comparative reports about non-fractional skin resurfacing [4–7]. Basically, the efficacy of both methods was roughly equal, and whereas the discomfort was somewhat more pronounced after Er:YAG treatment during the first days (with the notable exception of bleeding), CO2 treatment was perceived as more unpleasant in the later course of follow-up. The majority of patients rated both methods as equally disturbing, and a majority would undergo the treatment again without a clear preference for either modality.

Like chemical peels and dermabrasion, laser resurfacing works by injuring the skin to a controlled depth. The question arises as to what extent this ablation has to take place for effective rhytide reduction. Indeed, a major technical precaution for successful resurfacing is an ablation of the layers of the dermis that are mainly affected by photodamage. Since UV light is the causative agent, it is obvious that the more superficial strata of the dermis should be mainly altered, and histological findings confirm this assumption [36,37].

With energy settings in the same order of magnitude as in the present study, the penetration depth of CO2 lasers is 400–450 μm [16] and the one of Er:YAG lasers is 150–200 μm [18]. According to an histological study by Gonzalez-Ulloa et al. [38], the penetration depth of Er:YAG lasers is sufficient to reach the papillary dermis in every facial region except the forehead, where the epidermis is 202 μm thick. Especially in the peri-orbital region, the epidermis is delicate with a thickness of only 130 μm, rendering the dermis easily accessible by Er:YAG laser light.

For the CO2 laser, some of the laser-induced heat is diffused into the surrounding tissue due to the relatively long pulse duration (10 milliseconds), which is higher than the thermal relaxation time of water (1 milliseconds). The greater degree of thermal exposure in turn yields a more “aggressive” treatment leading to collagen shrinking. This seems beneficial in regions of the face where severe elastosis is the prevailing reason for rhytide formation (e.g., the upper lip) and with higher epidermis thickness, but less so in the peri-orbital region. Moreover, stacking of repetitive Er:YAG laser pulses has been demonstrated to cause deep collagen denaturation and remodeling on human lid skin despite the limited thermal exposure [39].

The literature to date fails to convincingly demonstrate the superiority of either method. Whereas Waibel et al. [19] consider fractional CO2 laser treatment superior to fractional Er:YAG, this conclusion is based on a limited number of patients and was therefore declared preliminary by the authors themselves. Bodendorf et al. [18] found no difference between both modalities based on the published material and their own experience; this conclusion is in complete agreement with our own results.

![Figure 2](image_url)  
**Fig. 2.** Top left: Pre-operative appearance (the black line demarcates the treatment area); top right: 3 months post-operatively (CO2). Bottom left: Pre-operative appearance; bottom right: 3 months post-operatively (Er:YAG). Marked reduction in rhytides on both sides. [Figure can be viewed in color online via www.interscience.wiley.com.]

![Figure 3](image_url)  
**Fig. 3.** Mean reduction of profilometrically measured wrinkle depth 3 months after treatment in comparison to pre-treatment values.
TABLE 4. Concomitant and Side Effects

<table>
<thead>
<tr>
<th>Symptom</th>
<th>CO₂</th>
<th>Er:YAG</th>
<th>CO₂</th>
<th>Er:YAG</th>
<th>CO₂</th>
<th>Er:YAG</th>
<th>CO₂</th>
<th>Er:YAG</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 day</td>
<td>3 days</td>
<td>6 days</td>
<td>3 months</td>
<td>1 day</td>
<td>3 days</td>
<td>6 days</td>
<td>3 months</td>
</tr>
<tr>
<td>Pain</td>
<td>2.1 ± 2.1</td>
<td>2.9 ± 2.5**</td>
<td>0.3 ± 0.8</td>
<td>0.4 ± 0.9</td>
<td>0.04 ± 0.2</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Burning, itching</td>
<td>2.0 ± 2.5</td>
<td>2.8 ± 2.7**</td>
<td>0.5 ± 0.9</td>
<td>1.4 ± 1.6*</td>
<td>0.4 ± 0.8</td>
<td>0.3 ± 0.4</td>
<td>0.2 ± 0.9</td>
<td>—</td>
</tr>
<tr>
<td>Erythema</td>
<td>6.6 ± 2.1</td>
<td>6.2 ± 2.4</td>
<td>3.6 ± 1.5</td>
<td>3.6 ± 1.2</td>
<td>2.5 ± 1.2**</td>
<td>1.2 ± 1.2</td>
<td>0.1 ± 0.6</td>
<td>0.04 ± 0.2</td>
</tr>
<tr>
<td>Swelling</td>
<td>6.9 ± 2.3</td>
<td>6.0 ± 3.2</td>
<td>2.2 ± 1.9</td>
<td>2.0 ± 1.9</td>
<td>0.6 ± 1.0*</td>
<td>0.3 ± 1.0</td>
<td>0.3 ± 1.0</td>
<td>0.1 ± 0.6</td>
</tr>
<tr>
<td>Blistering</td>
<td>0.3 ± 0.8</td>
<td>0.9 ± 2.5</td>
<td>0.04 ± 0.2</td>
<td>0.1 ± 0.8</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Secretion</td>
<td>0.7 ± 1.4</td>
<td>2.2 ± 3.2**</td>
<td>0.1 ± 0.3</td>
<td>0.4 ± 1.0*</td>
<td>0.04 ± 0.2</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Bleeding</td>
<td>3.6 ± 2.9***</td>
<td>0.6 ± 1.8</td>
<td>0.1 ± 0.6</td>
<td>0.1 ± 0.6</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Crusting</td>
<td>4.1 ± 2.6</td>
<td>3.4 ± 3.2</td>
<td>2.0 ± 1.9</td>
<td>2.1 ± 2.0</td>
<td>0.1 ± 0.4</td>
<td>0.04 ± 0.2</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Hypopigmentation</td>
<td>—</td>
<td>—</td>
<td>0.1 ± 0.4</td>
<td>0.04 ± 0.2</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
<td>—</td>
<td>—</td>
<td>0.1 ± 0.4</td>
<td>0.1 ± 0.6</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Scars</td>
<td>—</td>
<td>—</td>
<td>0.1 ± 0.4</td>
<td>0.1 ± 0.4</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Atrophy</td>
<td>—</td>
<td>—</td>
<td>0.1 ± 0.4</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Sum</td>
<td>27.3 ± 10.2</td>
<td>26.0 ± 15.1</td>
<td>9.3 ± 4.9</td>
<td>10.6 ± 8.4</td>
<td>3.9 ± 1.9***</td>
<td>1.8 ± 1.6</td>
<td>2.2 ± 2.9**</td>
<td>0.3 ± 0.7</td>
</tr>
</tbody>
</table>

Gray background: significant difference between groups (significantly higher values marked with *P < 0.05, **P < 0.01, ***P < 0.001).

As for ablative fractional methods in general, the efficacy of various laser modalities for rhytide reduction has been demonstrated (e.g., [2,5,12,13,15,17,18]) but the effect of a single treatment session may not be comparable to conventional ablative methods. There is published material opposing this statement; for instance, Trelles et al. [14] published very encouraging results about a single treatment with a fractional Er:YAG laser, albeit in a very inhomogeneous sample in terms of treated region and treatment parameters. Another major shortcoming is illustrated in Figure 3 of the article under discussion: The photographs showing the pre- and post-treatment findings are different both in dimension (distance from camera to skin) and lighting, making it virtually impossible to objectively assess the degree of improvement [40]. Moreover, at the time the photograph was taken, there was obviously still a substantial edema present. We therefore suggest that photographic evaluation take place no less than 12 weeks after treatment (as in the present study).

Furthermore, histological specimens are often included in clinical studies to confirm the clinical effects of laser treatment. Indeed, histological examination of specimens is very valuable in basic research on laser effects (e.g., [16]); in a clinical longitudinal study setting where tissue is sampled several times during follow-up (e.g., [41]), its utility is limited because by definition a given specimen can only be obtained and examined once, and adjacent tissue is not necessarily comparable.

The present trial has shown that the dilemma of efficacy versus tolerability in laser therapy of facial rhytides is far from being resolved. Whereas side effects were easily identifiable, and treatment specifications were chosen according to the best available evidence and established local end points (such as pinpoint bleeding in CO₂-treated sites), the treatment result was overall satisfactory, albeit rather moderate. From a practical and therapeutic point of view, the surgeon would have suggested one or more follow-up sessions in most cases, which puts the lower down time in comparison to non-fractional laser ablation in perspective. Just as for the non-ablative modalities [42], the ostensible advantage of fractional methods seems to diminish substantially when results are analyzed meticulously.

As a final note, we should like to enumerate a number of methodological requirements for future studies:

- Patient satisfaction has been included in only very few studies on fractional resurfacing so far [2], but should be a mandatory part of the evaluation.
- Reproducibility and consistency of evaluation conditions (photography, scoring) and methods are paramount [40].
- Randomized split-face comparison to one of three modalities (sham treatment, non-fractional laser or a different fractional modality) is likely to enhance the evidence of the results.

A lack—or thorough documentation—of manufacturer affiliations will be helpful in assessing the meaningfulness of trials.

CONCLUSIONS

According to the present study, a single ablative fractional laser session has an appreciable yet limited effect on peri-orbital rhytides. When fractional CO₂ and Er:YAG lasers are used in such a manner that there are comparable post-operative healing periods, comparable cosmetic improvement occurs.

The limited success suggests that more than one treatment cycle is required to achieve sustainable patient
REFERENCES


