Comparison of Erbium:YAG and Carbon Dioxide Lasers in Resurfacing of Facial Rhytides

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Objective: To compare the efficacy, adverse effects, and histological findings of erbium:YAG (Er:YAG) and carbon dioxide (CO₂) laser treatment in removing facial rhytides.

Design: An intervention study of 21 subjects with facial rhytides. All participants were followed up for 6 months. The end points of the study were wrinkle improvement and duration of adverse effects.

Setting: Academic referral center.

Subjects: Nineteen female and 2 male volunteers with skin type I to III and wrinkle class I to III participated in the study.

Intervention: In all subjects, 1 side of the face was treated with a CO₂ laser and other side with an Er:YAG laser. Skin biopsies were performed in 6 subjects before treatment and immediately, 1 day, 2 days, and 6 months after treatment. Observations were recorded by subjects, investigators, and a blinded panel of experts.

Main Outcome Measures: Improvement in wrinkles and severity and duration of adverse effects.

Results: The CO₂ laser–treated side had relatively better wrinkle improvement when evaluating all subjects (P<.03). However, in subjects receiving more than 5 passes of Er:YAG laser, improvement scores were not significantly different from those for 2 to 3 passes of CO₂ laser treatment. Posttreatment erythema was noted at 2 weeks in 14 subjects (67%) on the Er:YAG laser–treated side and 20 subjects (95%) on the CO₂ laser–treated side. The frequency of erythema was significantly less after Er:YAG laser treatment at 2 (P = .001) and 8 (P = .03) weeks. Hypopigmentation was seen in 1 Er:YAG-treated (5%) and 9 CO₂-treated (43%) sides (χ², P < .05). Histological evaluation showed residual thermal damage of up to 50 µm on the Er:YAG-treated side and up to 200 µm on the CO₂-treated side.

Conclusions: Erbium:YAG laser is safe and effective in removing facial rhytides. Subjects treated with Er:YAG laser recover more quickly from the procedure than those receiving CO₂ laser treatment.

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The clinical use of lasers in dermatologic disorders has increased significantly in past few years. The use of high-energy pulsed and scanning carbon dioxide (CO₂) lasers (10,600 nm) allows clinicians to remove rhytides and other effects of photodamage. These lasers typically restrict the laser-tissue interaction time to less than 1 millisecond (thermal relaxation time of the upper part of the skin interacting with the laser) so that thermal diffusion is limited during the laser pulse. The resulting band of residual thermally altered collagen normally measures less than about 150 µm.¹ One of the limitations of CO₂ laser resurfacing is the incidence of adverse effects, specifically prolonged erythema and dyschromias. Also, some physicians prefer to use general anesthesia or intravenous sedation for full-face resurfacing to achieve adequate pain relief. The degree of postoperative erythema and time for reepithelialization keeps most subjects at home for about 2 weeks. Many otherwise ideal candidates are unwilling or unable to take the time off to recover from the procedure.

The erbium:YAG (Er:YAG) laser (2940 nm) represents an opportunity to decrease the thermal damage observed with the CO₂ laser. This wavelength is strongly absorbed by water (absorption coefficient 12,000 vs 800 cm⁻¹ for CO₂) so that residual thermal damage has been shown to be less than about 50 µm vs the 80 to 150 µm typically observed after

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MULTIPLE PASSES OF PULSED CO₂ LASER EXPOSURE. Also, it has been shown that Er:YAG laser wounds reepithelialize earlier than CO₂ laser wounds.² Clinically, ablation threshold for Er:YAG laser has been found to be 1.5 to 1.7 J/cm² for pulses of about 100-microsecond duration.³⁻⁵

We performed a comparative clinical study of the 2 wavelengths in volunteer subjects, in a side-by-side manner. We examined the wounds grossly and microscopically and compared wrinkle improvement, erythema, edema, bleeding, and the incidence of dyschromia.

RESULTS

INTRAOPERATIVE QUALITATIVE OBSERVATIONS

The Er:YAG laser made a loud popping sound; the CO₂ laser made a more muted sound with each pulse. There was more airborne debris with the Er:YAG laser. There was very little gross contraction during Er:YAG irradiation; in contrast, after the first pass of the CO₂ laser, there was immediate visible skin contraction during the second and third passes. There was focal pinpoint bleeding associated with the Er:YAG laser, which increased with deeper treatment. After the first pass, there was less debris on the surface of the Er:YAG-treated sites. There was no need to wipe debris between subsequent passes using the Er:YAG laser.

ERYTHEMA

The protocol only documented presence or absence, and not the degree, of erythema. However, whenever erythema was present on both sides, it was noted to be

SUBJECTS, MATERIALS, AND METHODS

The study protocol was approved by the institutional review board of the Massachusetts General Hospital, Boston.

SUBJECT SELECTION

Subjects were recruited by advertising in a newspaper. Subjects were between the ages of 18 and 90 years. Subjects with any immunodeficiency or type IV to type VI skin, and pregnant women were excluded from the study. Twenty-one subjects with perioral or periorbital rhytides were enrolled in the study, of whom 19 were women. Twelve of these subjects had Fitzpatrick class II rhytides, 8 had class III rhytides, and 1 had class I rhytides. All subjects were informed verbally and in writing about the entire procedure, possible outcomes, and complications, and a written consent was obtained from each subject.

PREOPERATIVE TREATMENT

All subjects applied 0.05% tretinoin cream to the treatment area once daily for 3 weeks before treatment, and took oral clarithromycin, 250 mg twice daily, and acyclovir, 200 mg 5 times a day for 2 weeks, beginning 2 days prior to treatment.

ANESTHESIA

All subjects received local infiltration of the treatment area with 1% lidocaine with epinephrine (1:100,000). Regional infraorbital and mental nerve blocks were used in addition to local infiltration for perioral resurfacing. In addition, in some subjects, topical Emla cream (2.5% lidocaine and 2.5% prilocaine hydrochloride; Astra, Westborough, Mass) was applied 2 hours before surgery.

LASER PARAMETERS

A pulsed CO₂ laser (UltraPulse; Coherent Inc, Palo Alto, Calif) produced a 3-mm spot from a collimated handpiece. The Er:YAG laser (CB Erbium/2.94; Continuum Biomedical Inc, Dublin, Calif) produced a 5-mm spot. Both systems used an articulated arm. The CO₂ laser has a gaussian and the Er:YAG laser a flat-top beam profile. As Er:YAG laser did not have a scanner, no beam scanners were used on either side. The CO₂ and Er:YAG laser pulse durations were 800 and 300 microseconds, respectively. Fluences were 3.5 to 6.5 J/cm² with the CO₂ (250- to 450-mJ pulse energies). In general, 450 and 350 mJ per pulse were used for the first and subsequent passes in perioral sites, respectively, and 350 and 250 mJ for the periorbital sites. The Er:YAG-treated sites received fluences of 5 to 8 J/cm² (1-1.5 J per pulse). Fluences and number of passes on the Er:YAG side were increased after observing initial subjects during their follow-up visits, to provide a more symmetric appearance.

OPERATIVE PROCEDURE

Twelve perioral and 9 periorbital areas were treated. Two physicians (K.A.K. and V.R.) treated all the subjects, alternating the laser and the side of the face with each subject. One side of the face was treated with the CO₂ laser and the contralateral side was treated with the Er:YAG laser. The assignment of each laser on right or left side was randomized by alternating the Er:YAG and CO₂ lasers on each side.
greater on the CO₂ laser–treated side (Figure 1 and Figure 2). Erythema was noted at 2 weeks in 14 subjects (67%) on the Er:YAG-treated side and 20 subjects (95%) on the CO₂-treated side. At 2 months, 5 (24%) of Er:YAG laser– and 13 (62%) of CO₂ laser–treated sides had some degree of erythema. Two subjects (10%) still had mild erythema at 6 months on the CO₂-treated side; none had erythema 6 months after Er:YAG laser treatment.

POSTOPERATIVE CARE

A hydrogel dressing (2ND SKIN; Spenco Medical Corp, Waco, Tex) was applied to the treatment area. Subjects were instructed to change this dressing twice a day for 2 days followed by water and vinegar soaks (1 cup [0.24 L] of water and 1 tsp [5 mL] of white vinegar) 4 times a day. Treated areas were cleansed with a mild cleanser (Cetaphil, Galderma Laboratories Inc, Fort Worth, Tex) and kept moist by application of a thick ointment (Aquaphor, Beiersdorf Inc, Norwalk, Conn).

FOLLOW-UP

All subjects returned for evaluation at 1 week, 2 weeks, 2 months, and 6 months after the procedure. The follow-up visits were recorded by the same physicians who treated them. At each follow-up visit, photographs were taken and investigators recorded apparent improvement in wrinkles, presence or absence of erythema, infection, dyschromia, and scarring. These clinical evaluations were not blinded.

GRADING OF WRINKLE IMPROVEMENT

Wrinkle improvement was graded by the investigators and subjects, and a 3-member panel of dermatologists who were unaware of the laser type used for each side of the face. This panel reviewed all photographs taken before treatment and at each follow-up visit. Improvement was graded from score 1 to 5, where 1 indicated “poor” improvement; 2, “fair” improvement; 3, “good” improvement; 4, “excellent” improvement; and 5, “complete clearance” or 100% resolution of wrinkles. Using this method, a modal score was plotted for each side. The results were compared by the Wilcoxon signed rank test.

MICROSCOPIC ANALYSIS OF BIOPSY SPECIMENS

Biopsy specimens were procured in 6 consenting subjects. All had pretreatment biopsies performed on both sides. Two subjects had biopsies performed immediately after treatment; one, 1 day after; one, 2 days after; and two, 6 months after the treatment. Biopsy specimens were fixed in formalin and subsequently embedded in paraffin, upon which 3-µm sections were cut and stained with hematoxylin and eosin or Verhoeff van Gieson elastic tissue stain. The depth of tissue ablation could not be measured as there was no untreated skin in the same specimen. The depth of residual thermal injury to the dermis was determined. Histological features supportive of dermal connective tissue injury included eosinophilic homogenization of the dermis with variable infiltration by disintegrating leukocytes.
EDEMA (SWELLING)

Both sides always showed swelling immediately after the procedure. Swelling in the Er:YAG laser–treated sites tended to resolve earlier (Figure 5); however, a Fisher exact test showed no significant differences in incidence of edema for all time intervals (the smallest $P$ value was .12 for 1 week).

HYPERPIGMENTATION

The incidence of hyperpigmentation was similar on both sides, ie, 5 (24%) of Er:YAG-treated sides and 6 (29%) of CO2-treated sides. Resolution of hyperpigmentation was noted at the 6-month follow-up in all cases without any intervention.

HYPOPIGMENTATION OR LINE OF DEMARCATION

In 1 (5%) of Er:YAG laser– and 9 (43%) of CO2 laser–treated sides, there was a visible line of demarcation at the border between treated and nontreated skin, 6 months after treatment. These incidences of hypopigmentation were significantly different ($\chi^2$, $P<.05$).

INFECTION AND SCARRING

None of the subjects showed infection on either side, and none developed scarring on either side.

MICROSCOPIC EVALUATION

The extent of injury both qualitatively and quantitatively was assessed between sites treated with the Er:YAG laser and those treated with the CO2 laser. All biopsy specimens showed in common complete epidermal ablation. The depth of coagulative changes to the collagen and elastic fibers ranged from 50 to 200 $\mu$m in the CO2-treated specimens (average, 90 $\mu$m) compared with 30 to 50 $\mu$m (average, 45 $\mu$m) for specimens from Er:YAG-treated sites (Figure 6). Two of the CO2-treated sites showed brisk middermal perivascular lymphocytic infiltrates. The biopsy specimens of Er:YAG-treated sides were without significant inflammation.

With respect to the 6-month postoperative biopsy specimens, in 1 case, there was no fibroplasia present at the Er:YAG-treated site compared with a 200-$\mu$m-thick subepidermal fibrosing reaction at the CO2-treated site. In the second case, a similar subepidermal 75-$\mu$m-thick fibrotic band was present in the CO2-treated site, while the Er:YAG-treated site revealed a zone of fibroplasia of 475 $\mu$m, as shown in the Table and in Figure 7.

WRINKLE IMPROVEMENT

The results of modal scoring for wrinkle improvement by the blinded panel are shown in Figure 8. Investigators assessed the CO2 laser–treated side to have relatively better results when evaluating all the subjects. The aggregate scores (investigators, subjects, and panel’s combined data) showed a statistically significant difference between the 2 laser treatments when all subjects were considered in the calculations ($P<.03$), with CO2 laser showing greater improvement than the Er:YAG laser. However, when only the subjects with 5 or more passes of Er:YAG laser are included, the wrinkle improvement scores were not significantly different (Figure 9 and Figure 10).
Pulsed or scanned CO₂ lasers are presently a kind of criterion standard for laser skin resurfacing. Most of the initial studies were performed on patients with advanced photoaging and deep wrinkles. Recently, a number of normal-mode, flashlamp-pumped Er:YAG lasers have been developed for resurfacing.

Results of this study show that Er:YAG laser treatment, at similar fluence per pulse and number of passes as CO₂ laser treatment, produces more superficial ablation, promotes faster healing, and is less effective. Our results also show that by increasing the number of Er:YAG laser passes (≥5), the depth of injury can be increased to mimic the results of standard CO₂ laser resurfacing.

Like chemical peels and dermabrasion, laser resurfacing works by destroying the skin to a controlled depth. The fact that 3 radically different mechanisms—mechanical tissue removal (dermabrasion), chemical burn (peels), and thermal burn (laser)—can all yield excellent clinical results indicates that a wound healing process basically determines clinical outcome, rather than the precise method of tissue injury per se. One would therefore expect a strong correlation between the dura-
tion and extent of wound healing and clinical efficacy. This study supports that hypothesis. Indeed, it is reasonable to assume that any means of depth-controlled destruction could be used to treat photoaged skin. Differences in efficacy between application of different lasers should relate to factors affecting the wound healing response. Results from this study indicate that both efficacy and duration of wound healing are related to the total anatomic depth of necrosis, including residual thermal damage. Superficial injury, faster healing, and lower efficacy was observed with the Er:YAG laser by using fewer than 5 passes of laser treatment. We therefore suggest that the Er:YAG laser may be better suited for treating mild photodamage—with the caveat that a CO2 laser might do just as well when used in a manner to produce a similar depth of injury (eg, 1 or 2 low-fluence passes).

The mechanisms of tissue damage during laser resurfacing include removal by vaporization of a layer near the surface, thermal coagulation necrosis of cells in a residual layer, thermal denaturation of extracellular matrix proteins in a residual layer, and a deeper zone of sublethal thermal injury. In addition, some photomechanical damage may occur in the case of Er:YAG irradiation. In skin, water is the major absorber for both CO2 and Er:YAG laser wavelengths. At the 10.6-µm wavelength CO2 laser, $\mu_a$ (absorption coefficient) = 600 cm$^{-1}$ in skin, such that the CO2 laser optical energy is absorbed in a layer 15 to 20 µm thick. For the 2.9-µm wavelength Er:YAG laser, $\mu_a$ = 10 000 cm$^{-1}$, such that the optical energy is absorbed in a layer about 1 µm thick. The optical penetration depth sets a limit on the precision and depth of tissue injury. Thus, skin injury with an Er:YAG laser could conceivably be more precise and more superficial than with a CO2 laser, by more than an order of magnitude. However, this is not the case for the Er:YAG laser devices presently available, as explained below.

Heat conduction over a given distance takes time, and the concept of a “thermal relaxation time” for the optically heated layer is useful. Minimal depth of injury is obtained when the optical energy is delivered in less than the thermal relaxation time for the layer being directly heated, ie, the optical penetration depth. The thermal relaxation time in microseconds is approximately equal to the square of the layer thick-
ness in micrometers. When Er:YAG laser energy is delivered in a pulse less than about 1 microsecond, it is possible to remove and/or damage a tissue layer only a few micrometers thick, as shown in detail by Walsh et al.\textsuperscript{6} If CO\textsubscript{2} laser energy is delivered in a short pulse less than about 1 millisecond, it is possible to remove and/or damage a tissue layer only a few micrometers thick.

In general, when laser energy is delivered during a time longer than the thermal relaxation time for the optical penetration layer, the depth of damage increases due to heat conduction during the laser pulse. With pulse durations much greater than the thermal relaxation time, as is true for the Er:YAG laser used in this study, the depth of injury is much greater than the optical penetration depth. This was confirmed by our histological finding that Er:YAG laser thermal damage extended at least 30 µm below the ablation surface.

High-amplitude acoustic waves are probably caused during Er:YAG laser resurfacing. Whereas the CO\textsubscript{2} laser emits a smooth temporal pulse, relaxation oscillations in Er:YAG lasers cause a series of fluctuating "micropulses" during the 300-microsecond pulse width. It has been shown that these micropulses promote a more violent ablation process during Er:YAG laser tissue interaction. The sharp "snap" heard during Er:YAG laser resurfacing is consistent with tissue removal by micropulses. It is unknown what role, if any, photomechanical injury may play during Er:YAG laser resurfacing. We did not observe deep tissue injury, which has been described from excimer laser-induced photomechanical damage.\textsuperscript{7}

Another obvious consequence of residual thermal damage during laser resurfacing is immediate shrinkage due to denaturation of type I collagen. At approximately 60°C to 70°C, fibrillar type I collagen undergoes a helix-coil transition that forcefully shortens the fibers by about 30%. Collagen is oriented predominantly in the plane of the skin, such that when viewed from above, the skin appears to shrink (it also increases in thickness, which cannot be easily seen). This is not observed unless the dermis is involved. The role of collagen shrinkage in the efficacy of laser resurfacing is unknown, but frequently taken for granted. It seems so logical that obvious, immediate shrinkage of the skin would "tighten" the face, reducing wrinkles. However, denatured collagen is susceptible to rapid degradation by proteases, and is sloughed within days.\textsuperscript{8}

If collagen shrinkage was an absolute requirement for clinical improvement, chemical peels and dermabrasion simply would not work. To our knowledge, there is not yet convincing evidence that collagen shrinkage plays an important role in laser skin resurfacing.

In summary, results of this study show that both Er:YAG and pulsed CO\textsubscript{2} lasers are effective for treatment of photoaging, with important differences related to less residual thermal injury using the Er:YAG laser. The total anatomic depth of tissue necrosis, including residual thermal damage, is a primary determinant of both efficacy and healing time. With equal fluence and number of passes, the Er:YAG laser produces less residual thermal injury and hence less total depth of tissue necrosis—with faster healing and less effective treatment of deeper wrinkles. For the same reason, hemostasis is somewhat worse with Er:YAG laser. With a higher number of Er:YAG laser passes to achieve depth of tissue necrosis similar to conventional CO\textsubscript{2} laser resurfacing, efficacy was similar, with a trend toward faster healing. The Er:YAG laser appears to be better suited for treatment of mild photodamage, and patients with poor tolerance for post-treatment erythema. While deeper or multiple Er:YAG laser treatments may mimic standard CO\textsubscript{2} laser resurfacing, it is also likely that 1-pass, low-fluence CO\textsubscript{2} laser treatment will largely mimic Er:YAG laser results. We therefore suggest that the major variables in skin resurfacing are the patient and the physician.

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