Comparison of Four Carbon Dioxide Resurfacing Lasers
A CLINICAL AND HISTOPATHOLOGIC EVALUATION

TINA S. ALSTER, MD, CHRISTOPHER A. NANNI, MD, AND CARMEN M. WILLIAMS, MD
Washington Institute of Dermatologic Laser Surgery, Washington, DC

BACKGROUND. Several high-energy, pulsed and scanned carbon dioxide (CO\textsubscript{2}) lasers are currently available for cutaneous resurfacing. Although each laser system adheres to the same basic principles of selective photothermolysis, there are significant differences between lasers with respect to tissue dwell time, energy output, and laser beam profile. These differences may result in variable clinical and histologic tissue effects.

OBJECTIVE. The purpose of this study was to examine the in vivo clinical and histopathologic effects of four different high-energy, pulsed or scanned CO\textsubscript{2} resurfacing lasers.

METHODS. A prospective study using four different CO\textsubscript{2} resurfacing lasers (Coherent UltraPulse, Tissue Technologies TruPulse, Sharplan FeatherTouch, and Luxar NovaPulse) was performed. Each of seven patients was divided into four quadrants. Each quadrant was randomly assigned to receive treatment with one of four CO\textsubscript{2} lasers. Skin biopsies were obtained intraoperatively from each quadrant, after each of three laser passes, and at 1 and 3 months postoperatively. Blinded clinical assessments of each laser quadrant were made at 1, 3, and 6 months postoperatively by three physicians. Degree of lesional improvement as well as erythema severity, re-epithelialization rates, and presence of side effects were recorded. Blinded histologic examination of laser-treated quadrants was performed to determine the amount of tissue ablation, residual thermal damage, inflammation, and new collagen synthesis.

RESULTS. The four CO\textsubscript{2} lasers produced equivalent clinical improvement of rhytides and scars. Re-epithelialization occurred in all laser quadrants by day 7. Postoperative erythema was most intense in the quadrants treated by UltraPulse and NovaPulse; however, overall duration of erythema was equivalent for all four laser systems (3 months). Postinflammatory hyperpigmentation was the most frequently encountered side effect and occurred with equal frequency in each quadrant. No scarring, hypopigmentation, or infections were observed. After one laser pass, histologic examination revealed partial ablation of the epidermis with the TruPulse laser and complete epidermal ablation using the UltraPulse, NovaPulse, and FeatherTouch laser systems. The greatest degree of residual thermal damage was seen after FeatherTouch and NovaPulse laser irradiation. New collagen formation was greatest in the UltraPulse and FeatherTouch laser-irradiated quadrants.

CONCLUSIONS. Equivalent clinical results were observed using the FeatherTouch, NovaPulse, TruPulse, and UltraPulse CO\textsubscript{2} lasers. While postoperative erythema intensity differed between laser systems, total duration of erythema was equivalent for all four laser systems produced equivalent clinical improvement of rhytides and scars. Re-epithelialization occurred in all laser quadrants by day 7. Postoperative erythema was most intense in the quadrants treated by UltraPulse and NovaPulse; however, overall duration of erythema was equivalent for all four laser systems (3 months). Postinflammatory hyperpigmentation was the most frequently encountered side effect and occurred with equal frequency in each quadrant. No scarring, hypopigmentation, or infections were observed. After one laser pass, histologic examination revealed partial ablation of the epidermis with the TruPulse laser and complete epidermal ablation using the UltraPulse, NovaPulse, and FeatherTouch laser systems. The greatest degree of residual thermal damage was seen after FeatherTouch and NovaPulse laser irradiation. New collagen formation was greatest in the UltraPulse and FeatherTouch laser-irradiated quadrants. Equivalent clinical results were observed using the FeatherTouch, NovaPulse, TruPulse, and UltraPulse CO\textsubscript{2} lasers. While postoperative erythema intensity differed between laser systems, total duration of erythema was equivalent for all four laser systems.

CUTANEOUS CARBON DIOXIDE (CO\textsubscript{2}) laser resurfacing is a safe and effective procedure for the reduction of facial rhytides and atrophic scars, as well as for the treatment of a variety of epidermal and dermal lesions.\textsuperscript{1-8} The introduction of high-energy, pulsed and scanned CO\textsubscript{2} systems has permitted laser surgeons to ablate epidermal and dermal tissue with minimal risk of scarring.\textsuperscript{8,9,10} Older CO\textsubscript{2} technology using continuous wave and superpulsed delivery systems were efficient at ablating tissue, but they also created char and a significant degree of residual thermal damage that resulted in skin-texture changes or scar formation.\textsuperscript{11-14} Using the principles of selective photothermolysis,\textsuperscript{15} the new generation of CO\textsubscript{2} lasers limit residual thermal injury in the skin by producing high-energy laser light with tissue dwell times shorter than the thermal relaxation time of the epidermis (estimated to be approximately 1 millisecond for CO\textsubscript{2} in 70% water-containing tissue). These new CO\textsubscript{2} laser systems are not identical, however, producing different beam profiles as a result of their differing technologies.\textsuperscript{16-20}

In order to limit CO\textsubscript{2} laser-tissue dwell times, two unique technologies have been developed: pulsed and scanned laser systems. High-energy, pulsed CO\textsubscript{2} lasers (eg, Coherent UltraPulse, Tissue Technologies TruPulse) use radio frequency (RF)-excited waves to produce single pulses of high energies with short pulse durations. The UltraPulse system can deliver fluences of up to 7 J/cm\textsuperscript{2} with pulse widths shorter than 1 ms, whereas the TruPulse laser can produce peak powers of up to 10,000 watts at pulse durations of approximately 90 μsec. Scanned laser systems (eg, Sharplan FeatherTouch) operate by generating a continuous beam of CO\textsubscript{2} laser energy that moves rapidly across an area of skin with the aid of a computerized scanning device. The scanned beam effectively limits the tissue dwell time to 0.3 msec (shorter than the epidermal thermal relaxation time) thereby preventing the continuous wave laser from causing excessive tissue heating. The NovaPulse CO\textsubscript{2} laser
utilizes superpulsed technology, but unlike the original superpulsed systems, it can deliver a fluence of approxi-
mately 7 J/cm² by moving a small spot size rapidly
through a computer pattern generator.

These four different laser systems offer physicians a
variety of treatment options to safely and effectively re-
surface skin with their unique ability to deliver high-
energy laser light using brief tissue dwell times. How-
ever, direct clinical and histologic side-by-side compa-
rison of these systems to compare safety profiles, clinical
efficacy, and tissue effects have not been conducted in
humans. Manufacturer claims and aggressive advertis-
ing campaigns have raised valid concerns over the pos-
sible differences that may exist between CO₂ lasers sys-
tems. This study was designed in an attempt to examine
both the clinical and histopathologic effects of four dif-
ferent CO₂ resurfacing lasers in vivo.

Materials and Methods

Seven patients (1 male, 6 female, age range 29–67, mean 46
years, skin types I–II) with symmetric mild to moderate facial
photodamage or atrophic scars were enrolled in this study af-
after informed consent had been obtained. Patients were not
permitted to use hydroquinone nor retinoic, glycolic, azelaic,
or glycolic acid preparations within 6 months of study entry.

Patients received prophylaxis for herpes simplex infection
with a 10-day course of acyclovir (Zovirax, Glaxo Wellcome,
Research Triangle Park, NC) 400 mg orally TID beginning
24 hours prior to surgery. Antibiotic prophylaxis with 500
mg of azithromycin (Zithromax, Pfizer Labs, New York, NY)
was given to all patients for the first day and 250 mg daily
thereafter for 4 days. In addition, 1 g of intravenous cefazolin
(Ancef, SmithKline Beecham, Pittsburgh, PA) was adminis-
tered to patients intraoperatively.

The cheeks of each patient were bisected by drawing a
horizontal imaginary line from the tragus to the nasolabial
fold such that a total of 4 quadrants were effectively cre-
ated. Cheek quadrants in every patient were randomly as-
signed to be treated by one of four carbon dioxide lasers:
FeatherTouch (Sharplan/ESC Laser Inc, Allendale, NJ),
NovaPulse (Luxar Corp., Portland, OR), TruPulse (Tissue
Technologies, Palo Alto, CA), UltraPulse (Coherent Laser
Corp., Palo Alto, CA), such that treatment quadrants dif-
fered between patients. All of the laser procedures were per-
formed by a single laser operator (TSA) using clinically
equivalent parameters typically used for cutaneous laser re-
surfacing (energy density = 5.0 J/cm²). Light intravenous se-
dation was administered by a nurse anesthetist using appropi-
ate titrations of midazolam (Versed, Roche Laboratories,
NJ), propofol (Diprivan, Stuart Pharmaceuticals, Wilming-
ton, DE) and fentanyl citrate (Sublimaze, Akorn, Inc., Abita
Springs, LA). Laser operating protocol consisted of the deliv-
er of non-overlapping spots or scans over each quadrant us-
ing the randomly assigned laser system. Cheek quadrants
treated with the UltraPulse laser were ablated using the 8 mm
square computer pattern generator (CPG) scan at settings of
300 mJ, 60 W power, and a density of 6. The TruPulse sys-
tem was used at 500 mJ with a 3-mm scan spot and a power
of 68,600 W/cm² at 8 Hz. The NovaPulse laser was set to
420 mJ and 7 W using a 12.2 × 8 mm computer-generated
pattern at a density of +3. The FeatherTouch system was
operated using 36 W, a 10 mm square spot, and 0.24 sec on
time and 0.48 sec off time. Partially desiccated tissue was
manually removed with saline-soaked gauze after each laser
pass. A 3 mm skin punch biopsy was obtained in the lased
preauricular region of each quadrant following 1, 2, and 3
passes with each laser system for a total of 12 intraoperative
biopsies per patient, and the resultant tissue defects were
closed with 5-0 nylon sutures.

Patients used an “open technique” postoperatively that in-
cluded frequent topical applications of Catrix-10 ointment
(Donnell Inc., New York, NY), petrolatum (Vaseline), or
Aquaphor ointment (Beisdorf Inc., Norwalk, CT). Ice water
soaks and compresses every 1–2 hours were recommended
for the first 48–72 hours during waking hours. On the fourth
postoperative day, patients were evaluated and received a
cleansing treatment consisting of gentle facial steaming, dilute
hydrogen peroxide debridement, and Catrix-10 ointment ap-
tication. These facial treatments continued on a daily basis
for one week. After re-epithelialization (postoperative days
7–10), patients applied a cream-based emollient (Hydrotone,
ICN Pharmaceuticals, Costa Mesa, CA) twice daily and were
instructed to avoid sun exposure.

Clinical evaluations were conducted with photographic
documentation 3, 5, 7, 10, 30, 90, and 180 days postopera-
tively. Three physicians blinded to the study protocol inde-
pendently rated the degree of re-epithelialization based upon
the presence of crusting, oozing, and the gross appearance of
intact epidermis using a numeric scale (0 = none, 1 = mini-
mal, 2 = partial, 3 = complete). The degree of erythema was
also rated on a similar scale (0 = none, 1 = mild, 2 = moder-
ate, 3 = severe). Lastly, reduction in rhytides and scars were
assessed using the following numeric scale: 0 = <25%, 1 =
25%–50%, 2 = 50%–75%, 3 = >75%. Any adverse reac-
tions or complications at each postoperative visit were re-
corded.

Blinded histopathologic evaluation of tissue biopsies pre-
served in 10% formalin, paraffin embedded, and processed
with hematoxylin and eosin was conducted by a board-certif-
tified dermatopathologist using standard light microscopy
and an ocular measuring device (micrometer). Intraopera-
tive specimens obtained after one, two, and three passes
with each laser system were evaluated for depth of tissue ab-
lation and relative presence or absence of the epidermis. The
depth of residual thermal damage was determined by mea-
suring the zone of amorphous, eosinophilic collagen that re-
ained after resurfacing. Skin biopsies obtained one and
three months after laser resurfacing were examined for de-
gree of inflammation and new collagen formation. The in-
flammatory infiltrate observed at low-power magnification
was rated as mild, moderate, or dense, and inflammatory
cell types were recorded. The degree of new collagen forma-
tion in each biopsy specimen was evaluated based upon an average of 5 measurements made from the tip of several dermal papillae to the depth of eosinophilic collagen bundles arranged in a compact parallel fashion.

**Results**

**Clinical Results**

All laser-treated cheek quadrants displayed similar intraoperative tissue reactions. Laser-irradiated skin appeared pale yellow in color upon laser impact, and a nonbleeding pink base was exposed after wiping the skin with saline-soaked gauze. A similar degree of intraoperative tissue shrinkage was evident with all laser systems, as grossly determined by caliper measurements before and after laser irradiation in the mid-cheek regions.

Clinical re-epithelialization was complete in all laser quadrants by one week postoperatively (Figure 1). Post-laser erythema was less intense in all patients within the quadrants treated by FeatherTouch and TruPulse; however, total duration of erythema was the same for all treated sites (Figures 2 and 3). All lased quadrants resulted in similar improvement of wrinkles and atrophic scars at 30, 90, and 180 days postoperatively (Figures 4 and 5).
Histologic Results

One pass with the TruPulse laser resulted in incomplete epidermal ablation, whereas the FeatherTouch, NovaPulse, and UltraPulse lasers achieved ablation of the entire epidermis after a single pass. Three passes resulted in ablation down to the upper reticular dermis with all four lasers (Figure 6). Residual thermal damage was minimal in all laser quadrants, with the greatest degree of thermal damage evident in tissue treated with the FeatherTouch and NovaPulse systems (Figure 7).

Dermal inflammation was most prominent at 1 month, with the infiltrate composed predominantly of lymphocytes and scattered polymorphonuclear cells. The UltraPulse and NovaPulse lasers displayed the greatest degree of inflammation at all follow-up points.

Minimal inflammation was evident by the third postoperative month. New collagen formation in the upper dermis was observed in all postoperative biopsy samples. The zone of new collagen was greatest in the quad-
Discussion

Cutaneous laser resurfacing with high-energy pulsed or scanned CO₂ lasers has become a safe and effective method for tissue ablation. The current success of laser resurfacing is attributed to several important factors, including laser engineering based upon the principles of selective photothermolysis and recent technological advances.

The UltraPulse system was the first pulsed CO₂ laser able to achieve high peak powers with a short pulse duration (30–100 μsec). The FeatherTouch and NovaPulse systems also deliver high energies with limited tissue dwell times, but do so through the use of scanners (FeatherTouch) or computer pattern generators (NovaPulse) that quickly move small spots of continuous wave or superpulsed beams across the skin surface. The same general concept of producing high energies with a pulse duration shorter than the epidermal thermal relaxation time has thus been accomplished by these different laser systems; however, the clinical and histologic effects from each have been reported to vary. Although claims have been asserted that each laser has specific advantages and disadvantages, these differences have not been previously examined in a controlled in vivo experiment.

The results of this study demonstrate that all four lasers produced similar clinical intraoperative results using equivalent laser parameters. Gross clinical inspection of tissue upon laser impact and after removing partially-desiccated tissue with saline-soaked gauze was similar, as was the depth of tissue ablation. Even intraoperative tissue shrinkage (skin contraction) appeared remarkably similar, despite the fact that shrinkage is associated with thermal diffusion to the underlying collagen and connective tissue components (and the laser systems were shown to vary histologically in their degrees of residual thermal damage).

Postoperative evaluations of re-epithelialization in all laser-treated quadrants were equivalent as assessed by visual inspection. Although oozing and serous discharge were more prominent in the sites treated by UltraPulse and NovaPulse, all quadrants ultimately healed by the seventh postoperative day.

The degree of postoperative erythema was the most striking clinical difference between laser groups. Patients spontaneously noted distinct differences in erythema intensity between quadrants. The quadrants treated by TruPulse and FeatherTouch were much less erythematous than the UltraPulse and NovaPulse quadrants in the first postoperative month in all patients. Although the UltraPulse and NovaPulse systems produced more intense postoperative edema initially, all laser-treated quadrants showed equal duration of erythema. Evaluations of clinical improvement of rhytides and scars was also equivalent in all laser quadrants.

Histologic analysis revealed that one pass with the UltraPulse and NovaPulse lasers at one and three months postoperatively (Figure 8).

<table>
<thead>
<tr>
<th>FeatherTouch</th>
<th>NovaPulse</th>
<th>TruPulse</th>
<th>UltraPulse</th>
</tr>
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<tbody>
<tr>
<td>30 days</td>
<td>0.024 ± .081</td>
<td>0.020 ± 0.12</td>
<td>0.080 ± 0.067</td>
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<tr>
<td></td>
<td>(.01 to .06)</td>
<td>(.01 to .04)</td>
<td>(.05 to .20)</td>
</tr>
<tr>
<td>90 days</td>
<td>0.022 ± .008</td>
<td>0.033 ± .011</td>
<td>0.114 ± .057</td>
</tr>
<tr>
<td></td>
<td>(.01 to .03)</td>
<td>(.02 to .04)</td>
<td>(.05 to .17)</td>
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rants treated with the UltraPulse and TruPulse lasers at one and three months postoperatively (Figure 8).
ferences observed between quadrants were minor but consistent between study subjects. In general, the pulsed laser systems (UltraPulse and TruPulse) produced the least overall thermal damage, while the superpulsed NovaPulse system and scanned FeatherTouch laser produced slightly more residual damage.

At one month, all lased sites exhibited complete epidermal regrowth and a significant degree of inflammation. The same lasers that clinically produced the greatest degree of erythema and serous discharge, namely the UltraPulse and NovaPulse systems, also had the greatest degree of inflammation on histologic examination. Measurements of the average depth of new collagen formation at 30 and 90 days postoperatively revealed more new collagen in the upper dermis after the use of the pulsed CO\textsubscript{2} systems (UltraPulse and TruPulse) as compared to the scanned systems (FeatherTouch and NovaPulse).

Our findings conflict with the concept that new collagen formation correlates directly with the depth of ablation, degree of residual thermal damage, and duration and degree of erythema. The randomness of these results may reflect the small study population or may indicate faulty premises in terms of collagen remodeling. In fact, Burkhardt and Maw\textsuperscript{21} have shown that more than 3 laser passes using a CO\textsubscript{2} laser do not necessarily lead to improved clinical and histologic results. Despite best efforts to determine the degree of neocollagenesis through histologic evaluation, measurements from such evaluations remain highly variable. Thus, placing so much emphasis on the results obtained in this limited study may be unfounded.

In conclusion, the results of this study suggest that cutaneous laser resurfacing using any of the high-energy, pulsed or scanned CO\textsubscript{2} laser systems (FeatherTouch, NovaPulse, TruPulse, UltraPulse) produce equivalent clinical outcomes when operated using the treatment parameters and techniques outlined. Although differences in clinical and histologic data were found, the overall clinical results were not significantly different. The pulsed CO\textsubscript{2} laser systems (TruPulse and UltraPulse) resulted in less thermal necrosis in the dermis with greater subsequent collagen formation. The laser with the shortest pulse duration (TruPulse) produced the least tissue ablation per pass and the least intense postoperative erythema. The FeatherTouch scanned system and the NovaPulse superpulsed laser resulted in the greatest degree of residual thermal damage and the least amount of new collagen formation.

While each of these laser systems differs technologically—with varying energies, spot sizes, and delivery systems—equivalent clinical laser-tissue interactions were observed when similar laser parameters and intraoperative tissue endpoints were the goal. It is difficult to generalize the results of this study due to the small sample size. The fact that clinical and histologic differences between laser systems were not seen may be due to the lack of statistical power to demonstrate subtle differences. However, the merits of such a controlled, in vivo analysis are clear and should spur debate and encourage further scientific efforts in the field of cutaneous laser resurfacing.

References
Commentary

This excellent study reaffirms that CO₂ laser resurfacing (LSR) can be performed safely with a range of laser cavity configurations, cavity excitation mechanisms, beam profiles, and delivery devices. It also suggests that subtle histologic and clinical differences tend to abate with time. The common features that allow these four lasers to produce similar injury depths are (1) the range of available fluences (3–7 J/cm²) and (2) the laser-tissue interaction times, which spanned over a relatively narrow window from 90–1000 μsec. Based on principles of heat transfer, this interval is sufficient time for a thin layer of tissue to cool (experiments have shown that the actual time for cooling is somewhat longer). Accordingly, all four devices produced dermal residual thermal damage (RTD) confined to 30–100 μm after multiple passes. It follows that as long as serial laser passes are delivered with sufficient cooling intervals, the lower limits of thermal damage will be achieved and scarring is unlikely, even over a broad range of fluences. This is supported by a recent paper, which showed that shrinkage and RTD increased with fluence until a “threshold” was reached, beyond which both remained relatively constant.1 Alster et al.’s results support this threshold concept, since both Gaussian and flat beam profiles produced relatively constant thermal damage across biopsy specimens. It follows that controlled dermal heating (and not dermal ablation) is most responsible for the uniformity of injury and subsequent predictable wound healing after CO₂ LSR. In fact, most studies have shown that for fluences of 3–7 J/cm², dermal ablation is barely measurable after three passes.

Arguably the most “different” laser in this study is the TruPulse, whose pulse duration is an order of magnitude less than its three counterparts. This laser also caused the least residual thermal damage, the least postoperative erythema, and the greatest thickness of fibroplasia per depth of RTD, suggesting that the shorter pulse duration might be responsible. Overall, however, there was a lack of correlation between RTD, duration and degree of erythema, and final thickness of fibroplasia. All of this should provide further impetus to explore the intricacies of wound healing after CO₂ and other resurfacing modalities, particularly from a biochemical perspective. Also, particular emphasis should be placed on the role of thermal damage, independent of the depth of total injury (heating plus ablation), in wound healing.

All four respective laser manufacturers have ingeniously satisfied the criteria for successful resurfacing. Still, despite the similarities in long-term results, the physician should become very familiar with one or two of these systems, as there are subtleties that distinguish each device from each other. It follows that having complete command of any resurfacing laser should optimize the final cosmetic outcome.

E. Victor Ross, MD
San Diego, CA

References