

Eyelid Healing After Carbon Dioxide Laser Skin Resurfacing

Histological Analysis

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Objective: To clarify in vivo healing of eyelid skin after carbon dioxide (CO₂) laser resurfacing.

Design: Patients requesting upper eyelid blepharoplasty consented to undergo previous CO₂ laser skin resurfacing of the upper eyelid skin segments to be excised at various time intervals. After blepharoplasty, the skin specimens were analyzed histopathologically by 2 masked pathologists.

Patients: Eight patients with Fitzpatrick skin types I and II.

Intervention: Upper eyelid CO₂ laser resurfacing 1, 2, 4, or 12 weeks before planned upper eyelid blepharoplasty.

Main Outcome Measures: Epidermis: thickness, po-

larity, contour, and constituents. Dermis: repair zone thickness, vascular and inflammatory pattern, collagen deposition, and elastic fiber changes.

Results: The epidermis regenerated within 7 to 10 days. By 3 months, the epidermis revealed flattening of the rete peg pattern with restoration of polarity, keratinocytes, and melanocytes. The 3-month dermis demonstrated a fibrotic repair zone (500-700 µm), new elastic fibers, and telangiectatic capillaries.

Conclusions: Eyelids heal similarly to other skin regions treated by CO₂ laser resurfacing. This cutaneous healing is analogous to that previously reported with use of chemical peels. Histological changes may explain the skin smoothing and wrinkle reduction seen clinically.

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THE ADVENT of new laser technology has made laser skin resurfacing popular in the nonmedical press and media. Numerous scientific articles^{1,2} in various branches of medicine describe the clinical aspects of carbon dioxide (CO₂) laser skin resurfacing. Most histopathologic studies deal only with the depth of ablation at surgery. Few articles describe histological changes in human eyelid skin after cosmetic laser skin surgery. This study evaluates early histopathologic changes in eyelids resurfaced with a CO₂ laser.

RESULTS

No patient experienced any adverse reaction to laser skin resurfacing or blepharoplasty. All patients were satisfied with their final aesthetic outcome. Mean patient age was 63 years (range, 45-84 years). All patients except 1 were classified as Fitzpatrick skin type II. Mean duration of reepithelialization was 6.9 days after resurfacing (range, 4-10 days). No significant sex differences in the duration of

reepithelialization or in the histopathologic changes were noted. Because the specimens obtained 1 week after laser skin resurfacing did not reveal much epidermal healing, these data are not included herein. Healing in the epidermis and in the dermis are discussed separately (**Table 1** and **Table 2**). The 4-week results are discussed without providing the illustrative histological specimens.

Two weeks after laser resurfacing, there were pronounced changes in the epidermis (**Figure 1**). There was loss of the normal rete pattern, and the epidermis was focally thickened. The thickness of the new epidermis averaged 100 µm compared with 80 µm in adjacent nonlasered skin. No columnar basal keratinocytes were noted, consistent with a reepithelialized epidermis. There were few melanocytes, but occasional clusters were evident. Epidermal polarity was abnormal. Four weeks after laser resurfacing, foci of acanthosis persisted, but in other areas, the epidermis was of normal 80-µm thickness. In the basal layer, keratinocytes had become columnar again, and there were conspicuous melanocytes. Also, the normal undu-

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PATIENTS, MATERIALS, AND METHODS

Eight patients (4 women and 4 men) requesting cosmetic upper eyelid blepharoplasty were examined to exclude dry eye, exposure keratopathy, eyelid malposition, brow ptosis, and blepharospasm. All patients denied previous herpes simplex infection, systemic fungal disease, immune compromising diseases, tobacco smoking, facial irradiation, skin disease, hypertrophic scarring or keloid formation, and use of isotretinoin (Accutane; Hoffman-LaRoche, Nutley, NJ). Patient skin types were classified as Fitzpatrick types I or II. Patients were given the option to undergo cosmetic laser resurfacing of the eyelids 1, 2, 4, or 12 weeks before blepharoplasty. The risks and benefits of cosmetic laser resurfacing and blepharoplasty were discussed with each patient, who gave informed consent for each procedure.

Carbon dioxide laser skin resurfacing was conducted in standard fashion.² Patients were pretreated with a 2% hydroquinone (metahexamide [Melanex; Neutrogena Inc, Los Angeles, Calif]) cream and a broad-spectrum (UV-A and UV-B) sunblock with a sun protective factor of 15 for 6 weeks before laser treatment. In an office setting, patients received regional nerve block with up to 10 mL of 2% lidocaine hydrochloride with 1:100 000 epinephrine

in addition to topical ophthalmic anesthesia (Ophthaine; Alcon Corp, Dallas, Tex).

After standard surgical preparation and installation of protective eye shields, laser resurfacing of the upper eyelids was begun. A CO₂ superpulsed laser (NovaPulse; Luxar Corp) set at 9 W was delivered via a collimated handpiece in a standard periorbital pattern. Two passes were applied to each eyelid. Patients received an oral antibiotic (cephalexin hydrochloride, 250 mg twice daily) and an oral antiviral medication (acyclovir hydrochloride, 400 mg three times per day) beginning the day of laser resurfacing and lasting until full reepithelialization occurred. Patients were seen daily until reepithelialization occurred, and then weekly until their planned blepharoplasty.

One man and 1 woman each underwent standard upper eyelid blepharoplasty 1, 2, 4, or 12 weeks after laser skin resurfacing in an ambulatory operating room. The upper eyelid skin removed at blepharoplasty included skin previously treated with the CO₂ laser. Skin segments were removed, placed in 10% buffered formalin, and processed for light microscopy with hematoxylin-eosin, Luna-Ishak, Verhoeff-van Gieson (EVG), and Shikata stains. A dermatopathologist (R.G.P.) and an ophthalmic pathologist (A.H.F.), masked to the time intervals between laser resurfacing and blepharoplasty, analyzed each slide.

Table 1. Eyelid Healing in the Epidermis After Carbon Dioxide Laser Resurfacing

Variable	Weeks, No.		
	2	4	12
Thickness, μm	100	80	80
Acanthosis	Severe	Moderate	Minimal
Basal keratinocytes	Flat	Columnar	Columnar
Melanocytes	Few	Some	Full
Polarity	Abnormal	Variable	Normal
Rete peg pattern	None	Slight	Present and flat

lating rete peg pattern was reemerging. Polarity was variable. Three months after laser resurfacing, there was almost complete normalization of the previous changes in the epidermis, with only minimal acanthosis (**Figure 2**). The rete peg pattern was slightly undulating but flatter than that of healthy, untreated skin. A full complement of melanocytes and normal polarity were noted.

Two weeks after CO₂ laser resurfacing, the dermis demonstrated profound changes (**Figure 3**). The repair zone measured up to 700 μm and was poorly circumscribed. The fibroblasts in this repair zone varied from thin and fusiform to polygonal with stellate cytoplasm and large nuclei. There was also a pronounced inflammatory infiltration consisting primarily of small mononuclear cells and occasional foreign body giant cells. Small capillaries within this infiltrate were prominent. The collagen matrix was edematous and full of glycosaminoglycans. An elastic fiber stain indicated variable focal loss of fibers in the papillary and superficial reticular dermis

Table 2. Eyelid Healing in the Dermis After Carbon Dioxide Laser Resurfacing

Variable	Weeks, No.*		
	2	4	12
Thickness, μm	500-700	500-700	500-700
Fibroblasts	Many	Some	Few
Inflammatory cells	Moderate	Focal	Few
Blood vessels	Small capillary	Small capillary	Telangiectasia
Matrix	+++ Edema	+ Edema	No edema
New collagen	+	++	+++
Elastic fibers	Focal loss	Widespread loss	New

*Symbols are as follows: + indicates slight amount; ++, moderate amount; and +++, substantial amount.

(**Figure 4**). In some areas, damaged elastic fibers seemed to be "pushed down" by the infiltrate.

Four weeks after laser resurfacing, the dermis showed a clear diminution in cellularity of the infiltrate. Fusiform fibroblasts were present but much reduced in number. Also, there was an increase in the collagenous matrix, between these cells, and less stromal edema and glycosaminoglycan deposition. Thickness of the repair zone was at least 500 μm . Scattered mononuclear cells were present but much less than before. Occasional ectatic capillaries were noted. Elastic fibers in the repair zone were diminished, if not absent. Three months after laser resurfacing, the dermis revealed only scattered mononuclear infiltrates with little fibrosis evident (**Figure 5**). There was pronounced vascular telangiectasia with large-bore, ectatic blood vessels without overt angiogenesis. Shikata stain demonstrated newly formed elastic fibers in the superficial papillary dermis (**Figure 6**).

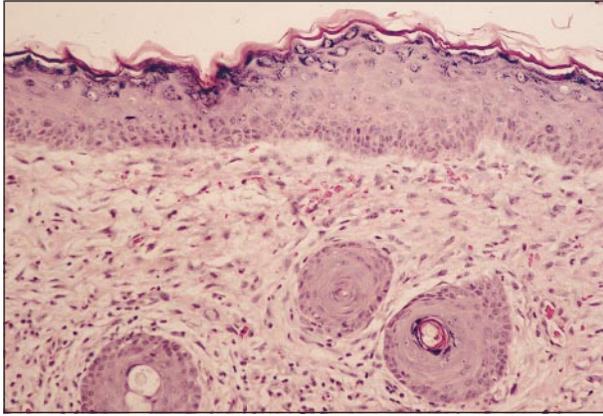


Figure 1. Upper eyelid skin 2 weeks after carbon dioxide laser resurfacing reveals loss of the normally undulating rete peg pattern and loss of polarity at the dermis-epidermis junction. Few melanocytes and no columnar basal keratinocytes are present (hematoxylin-eosin, magnification $\times 10$).

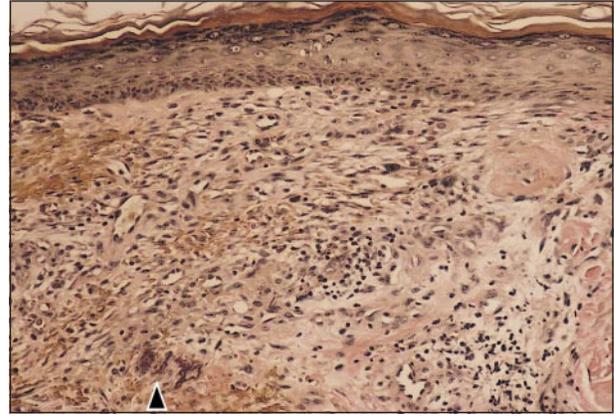


Figure 4. Two weeks after eyelid carbon dioxide laser resurfacing, there is almost complete loss of elastic fibers, with only rare residual elastic fibers present (arrowhead) (Verhoeff-van Gieson [EVG], magnification $\times 5$).

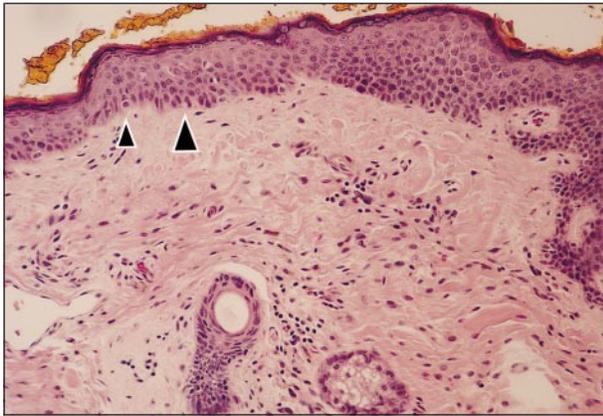


Figure 2. Three months after eyelid carbon dioxide laser resurfacing, an almost normal rete peg pattern is evident. Some basal keratinocytes appear columnar with normal maturation (large arrowhead). Scattered melanocytes (small arrowhead) are visible at the dermis-epidermis junction (hematoxylin-eosin, magnification $\times 8$).

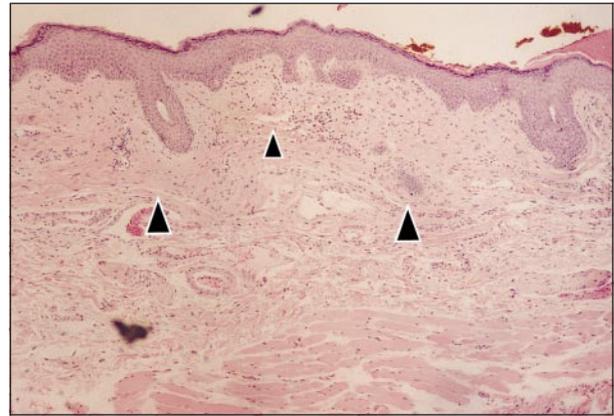


Figure 5. Three months after eyelid carbon dioxide laser resurfacing, the repair zone (large arrowheads) is barely visible as a paucicellular band of fibrosis, with rare inflammatory cells and telangiectatic capillaries (small arrowhead) (hematoxylin-eosin, magnification $\times 4$).

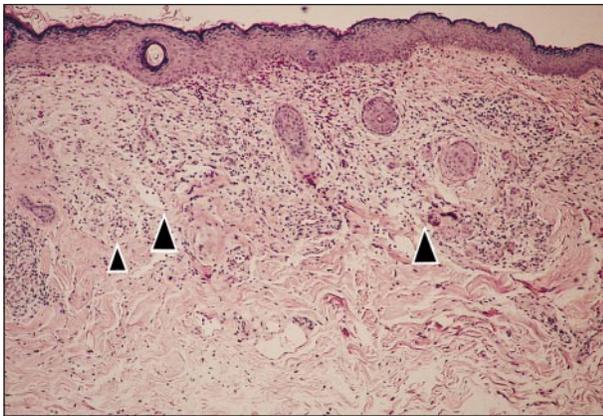


Figure 3. Two weeks after eyelid carbon dioxide laser resurfacing, the repair zone extends to superficial reticular dermis (large arrowheads) and is composed of loosely arranged fusiform cells in an edematous and inflamed stroma. Scattered, thick-walled capillaries (small arrowhead) are present (hematoxylin-eosin, magnification $\times 4$).

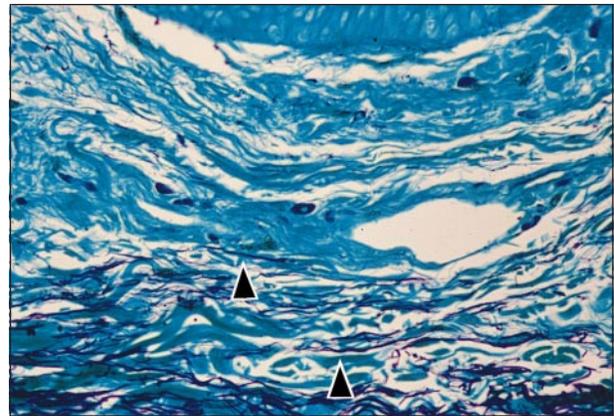


Figure 6. Three months after eyelid carbon dioxide laser resurfacing, there is deposition of new elastic fibers (arrowheads) (Shikata, magnification $\times 4$).

COMMENT

Previous histological studies³⁻⁹ demonstrated that 50 to 150 μm of skin may be ablated with a single pass of a

CO_2 laser. The zone of residual thermal (coagulative) damage can extend a further 20 to 120 μm , depending on the particular laser variables used.³⁻⁹ Because the various CO_2 lasers currently available differ in their biophysical properties, their documented depth of histological ablation and thermal effects vary. Some studies^{3,5,7} document a

progressively increasing zone of thermal damage with each subsequent laser pass, whereas others do not.^{8,9} We found that profound epidermal and dermal changes occur in the first month after laser resurfacing (Tables 1 and 2).

During the first month after laser skin resurfacing, the epidermis and dermis were significantly altered by cellular atypia, abnormal polarity and differentiation, tissue edema, elastin disruption, and collagen deposition. Three months after treatment many of these changes resolved, and the new epidermis and dermis became more like their untreated counterparts. The contour of the rete pegs remained flatter and smoother than that of healthy, untreated skin. Also, the dermis was thickened by new collagen and elastic fibers parallel to the epidermal surface. Furthermore, abnormal telangiectatic vessels of unknown significance were noted in the dermis 3 months after laser treatment.

Previous studies¹⁰⁻¹⁴ evaluating skin healing after CO₂ laser resurfacing in other parts of the face consistently demonstrated similar changes to those described herein. One week after laser resurfacing, the dermis-epidermis junction was not seen because of loss of organization.^{12,13} Three weeks after laser resurfacing, the epidermis was distinct from the dermis, but there is still active inflammation, edema, and immature cells.¹²⁻¹⁴ Neither the epidermis nor the dermis are normal in appearance. Invariably, all such studies^{10,11,14} document an increase in collagen and elastin deposition 3 months after laser resurfacing, with a mean increase of 150% to 190%.¹⁴ Eyelid skin response to laser resurfacing is similar to that of other facial skin regions, even though eyelid skin lacks a distinct interface between papillary and reticular dermis and subcutis.

Some histological changes reported by others¹⁵⁻¹⁹ and herein may be responsible for the clinical observations made after laser resurfacing. Flattening of the rete pegs can smooth skin.^{16,17} Thermal shrinkage of collagen can reduce the surface area of skin up to 25%.^{11,18} The deposition of new collagen, particularly glycosaminoglycans, in the dermis can produce thicker skin.¹⁶ This may persist beyond 3 months and thus explain the continued wrinkle improvement observed more than 1 year after laser resurfacing.¹¹ Furthermore, the deposition of new elastic fibers in the papillary dermis may improve the appearance of photoaged and elastotic skin. There is also anecdotal evidence²⁰ in 2 patients treated with a different CO₂ laser than we used of complete loss of elastic fibers in patchy areas after full-face laser skin resurfacing. The exact mechanism and reason for this is not yet known.

There are reported anatomic and molecular changes after laser skin resurfacing whose significance is not fully appreciated. Recently, a porcine skin model of laser resurfacing demonstrated that CO₂ laser debridement can reverse the cytologic atypia seen after exposure to a chemical carcinogen.¹⁵ Indeed, results of immunohistochemical analysis revealed the presence of contractile actin filaments within the newly deposited fibroblasts after laser resurfacing. These stromal cells might be able to tighten sagging skin and decrease skin creases.

We can only speculate as to the histological changes responsible for the long-term (ie, >1 year) cosmetic effect of laser skin resurfacing. This might be caused by a massive increase in glycosaminoglycans, dermal remod-

eling, or changes in the newly deposited elastic fibers. Future evaluation of skin healing more than 1 year after laser skin resurfacing may clarify this issue. In addition, biochemical and molecular evaluation of tissue growth modulators and dermal collagen and elastin subunits may elucidate the mechanism of cosmetic skin changes.^{21,22} Knowledge gained from such basic scientific research could provide insights for further improvement in the clinical outcomes of laser skin resurfacing.

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