



THE ASCLEPION EFFECT

Studies Book MCL31 Dermablade

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DERMAL LESIONS

Erbium YAG laser treatment of periorbital syringomas by using the multiple ovoid-shape ablation method.

Kitano Y. J Cosmet Laser Ther. 2016 May 12:1-6.

INTRODUCTION: Syringomas are benign tumours that develop predominantly in the periorbital areas of women. As periorbital syringoma is adjacent to the appendages, Erbium YAG (Er:YAG) laser treatment should be an ideal tool for its precise ablation, although its use has not previously been reported. We retrospectively analysed our new ovoid-shape Er:YAG laser ablation method for the treatment of syringoma.

MATERIALS AND METHODS: We developed an extirpation method in which multiple, 2- to 4-mm, egg-shaped ablation fields were created. This method was used to treat 49 patients, 35 of whom had predominantly accumulated syringomas, and 14 had disseminated syringomas. Treatment was repeated every 2 months.

RESULTS: Our approach was successful in both disseminated- and accumulated-type syringoma as well as plaque-type syringoma, which is considered to be the most difficult to treat. After an average of 3.77 treatments, more than 75% of the syringoma in the treated area had disappeared in 43 of 49 patients.

CONCLUSION: Our ovoid-shape ablation method gives good cosmetic results even in the most difficult type of syringoma.

Ablation of cutaneous lesions using an erbium:YAG laser.

Khatri KA. J Cosmet Laser Ther 2003; 5:1-4

BACKGROUND AND OBJECTIVE: This study was performed to evaluate the effectiveness and safety of erbium:YAG laser in removal of cutaneous lesions.

STUDY DESIGN: Data were collected after removing 363 benign, pre-malignant and malignant lesions in 27 patients at a dermatology and cosmetic laser surgery center.

RESULTS: All lesions were completely removed. Eight of 363 lesions recurred and the histological analysis showed complete removal of one malignant lesion with erbium:YAG laser ablation. There were no long term or permanent complications.

CONCLUSION: Erbium:YAG laser is safe and effective in removal of cutaneous lesions.

Erbium:YAG Laser Therapy of Skin Lesions

Kaufmann R, Beier C.. Med Laser Appl 2001;16:252-263

SUMMARY: Owing to its high versatility and precision in combination with an extremely tissue sparing skin-ablative work the Er:YAG laser has rapidly been recognized as an ideal tool to treat a large variety of skin disorders. Among others, indications include various epidermal lesions, benign dermal and adnexal tumors, melanocytic disorders, scar revisions, or resurfacing procedures in photodamaged skin. This review article deals with technical aspects of Er:YAG laser use, its preferential use in the field of Dermatology and also with potential hazards and side effects.

Treatment of melanin-induced benign dermal lesions by an Erbium-YAG laser system

Doi H, Ogawa Y, Hatoko M. J Plast Reprod Surg 2000; 0:90-95

SUMMARY: Electrocautery and the carbon dioxide (CO₂) laser have been used to treat many outpatients with benign pigmented lesions due to melanin pigmentation. We used an Er:YAG laser to treat such lesions, clinically, studying the treatment efficiency and safety of the laser system. There was no evidence of significant scarring, severe complications, or pain during treatment, but a few cases had post-treatment side effects, such as temporary pigmentation and minimal scarring. In this clinical trial, the effects of the Er:YAG laser were equal to or better than those of a CO₂ laser. The Er:YAG laser will be useful for treatment of benign pigmented lesions due to melanin pigmentation.

Treatment of common warts and actinic keratosis by Er:YAG laser.

Wollina U, Konrad H, Karamfilov T. J Cutan Laser Ther 2001;3:63-66

BACKGROUND AND OBJECTIVES:

The use of ablative lasers in the treatment of common warts and precancerous actinic keratoses has been reported in the literature, showing variable response rates and relapse rates. The erbium:YAG laser (Er:YAG) with a wavelength of 2.94 μ m allows precise ablation avoiding strong inflammation. The authors have evaluated the potential benefits of Er:YAG laser treatment for difficult-to-treat warts and actinic keratoses.

PATIENTS AND METHODS:

A total of 69 patients with difficult-to-treat warts (periungual or plantar) with a mean age of 30.1 \pm 16.1 years (range 11-58 years), and 29 patients with actinic keratoses with a mean age of 73.5 \pm 9.7 years (range 58-90 years) were treated by Er:YAG laser. Ablative therapy was performed with a spot size of 3 mm, a frequency between 8 Hz and 15 Hz, and a fluence of 5.7-11.3 J cm⁻² (warts) or 5.7-7.1 J cm⁻² (actinic keratoses).

RESULTS:

After a single laser treatment a complete response (CR) was observed in 50 patients with warts (72.5%). Plantar warts were more resistant (13.5% non-responder) compared with periungual warts (5.9% non-responder). Twelve patients with a CR showed a relapse within 3 months after treatment (24.0%). All but one suffered from plantar warts. Twenty-six patients with actinic keratoses showed a CR after a single laser treatment, and in three patients a partial response (PR) was achieved. None of the patients treated with Er:YAG laser developed pigment changes, wound infections or scarring.

CONCLUSION:

Treatment of common epithelial lesions such as common warts or actinic keratoses by Er:YAG laser is safe and effective. In patients with plantar warts, however, a significant rate of relapse may occur, requiring additional therapy.

Efficacy of erbium:YAG laser ablation in Darier disease and Hailey-Hailey disease

Beier C, Kaufmann R. Arch Dermatol. 1999; 135(4):378-80

Background

Among different surgical approaches, dermabrasion and carbon dioxide laser vaporization have been used to treat Hailey-Hailey disease (HHD) (familial benign chronic pemphigus) and Darier disease (DD) (keratosis follicularis), with various results. Because of the erbium:YAG laser's unique absorption characteristics in tissue water, erbium:YAG laser ablation combines the advantages of both techniques, avoiding thermal injury of vaporization and also allowing selectively deeper tissue removal in the follicular lesions of DD. Therefore, good results should be expected in both types of acantholytic disorders.

Observations

Four patients (2 with HHD and 2 with DD) with different affected areas were treated with laser ablation. During a follow-up period ranging from 8 to 20 months, complete remission was achieved in 3 patients—2 with DD and 1 with HHD—and significant improvement was achieved in 1 patient with HHD. Histological examination of control biopsy specimens after ablation in 1 patient with DD revealed no signs of the disease and only a slight fibrosis in the papillary dermis.

Conclusions

Erbium:YAG laser ablation effectively removes lesions of both HHD and DD and can also yield excellent long-term results in chronic, recalcitrant cases.

DARIER DISEASE (DD) (keratosis follicularis) and Hailey-Hailey disease (HHD) (familial benign chronic pemphigus) are autosomal dominant disorders characterized by specific alterations corresponding to seborrheic areas of the body and intertriginous areas.¹⁻³ The histological features consist of dyskeratosis, suprabasal acantholysis, papillomatosis, and suprabasal separation with extensive loss of intercellular bridges.⁴ Despite the clinical and histological overlap of the 2 diseases, the underlying mutations of both affect different genes.⁵

Conventional therapeutic approaches consist of topical and systemic steroids, antibiotic agents, vitamin A acid cream, and oral retinoids. Nevertheless, prolonged remission is difficult to achieve.¹⁻³

Good results for both diseases were obtained from such surgical interventions as excision^{6,7} or excision with subsequent split-thickness skin grafting,⁸ electrodesiccation,⁹ and dermabrasion.¹⁰⁻¹⁴

According to the observations of other authors, our own experiences have confirmed the value of dermabrasion, particularly in the treatment of HHD. However, DD frequently requires selective removal of keratotic papules and circumscribed deeper ablation in follicular lesions, which is not feasible with dermabrasion. Moreover, the treatment of certain areas, such as the upper trunk area or the neck, is limited because of the risk of scar formation.

Recent case reports have advocated the use of carbon dioxide laser vaporization in the treatment of HHD and DD,¹⁵⁻¹⁷ a procedure that could compensate for some of the disadvantages of dermabrasion. However, carbon dioxide laser vaporization, even in pulsed mode, leaves residual thermal damage, especially with deeper tissue removal, and therefore increases the risk of scar formation and prolonged wound healing. In contrast, erbium:YAG laser ablation, operating at a wavelength of 2.94

μm , combines the most efficacious stepwise etching of the skin surface with the least thermal damage owing to its unique absorption characteristics in tissue water.^{18,19} This technique should therefore allow the precisely controlled removal of lesions in both HDD and DD and limit the injury in widespread lesions or in those located on areas prone to keloid formation. We decided to treat 4 patients (2 with HDD and 2 with DD) with pulsed 2.94- μm erbium:YAG laser ablation and found this approach to be of special advantage in patients with DD.



Figure 1.
Patient 2 with typical signs of Darier disease. Left, Lower back area. Right, frontal view of neck area



Figure 2.
Patient 2, 18 months after erbium:YAG laser ablation at 5 J/cm² with up to 7 stacked passes. Left, Lower back area. Right, Frontal view of neck area.

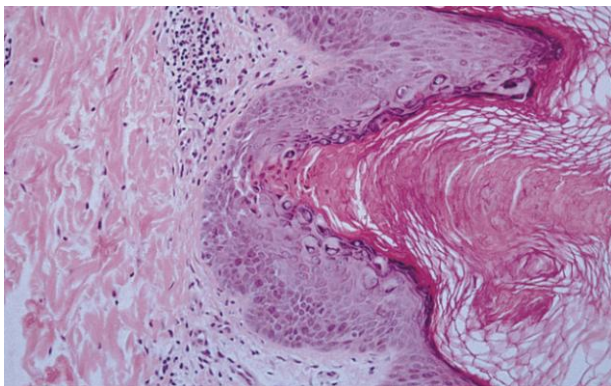


Figure 3.
Dyskeratosis and suprabasal acantholysis in Darier disease (hematoxylin-eosin, original magnification $\times 200$).

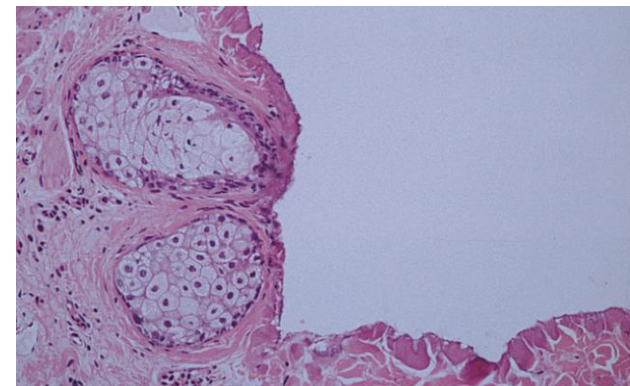


Figure 4.
Patient 2, immediately after laser ablation, with no significant thermal tissue damage (hematoxylin-eosin, original magnification $\times 200$).

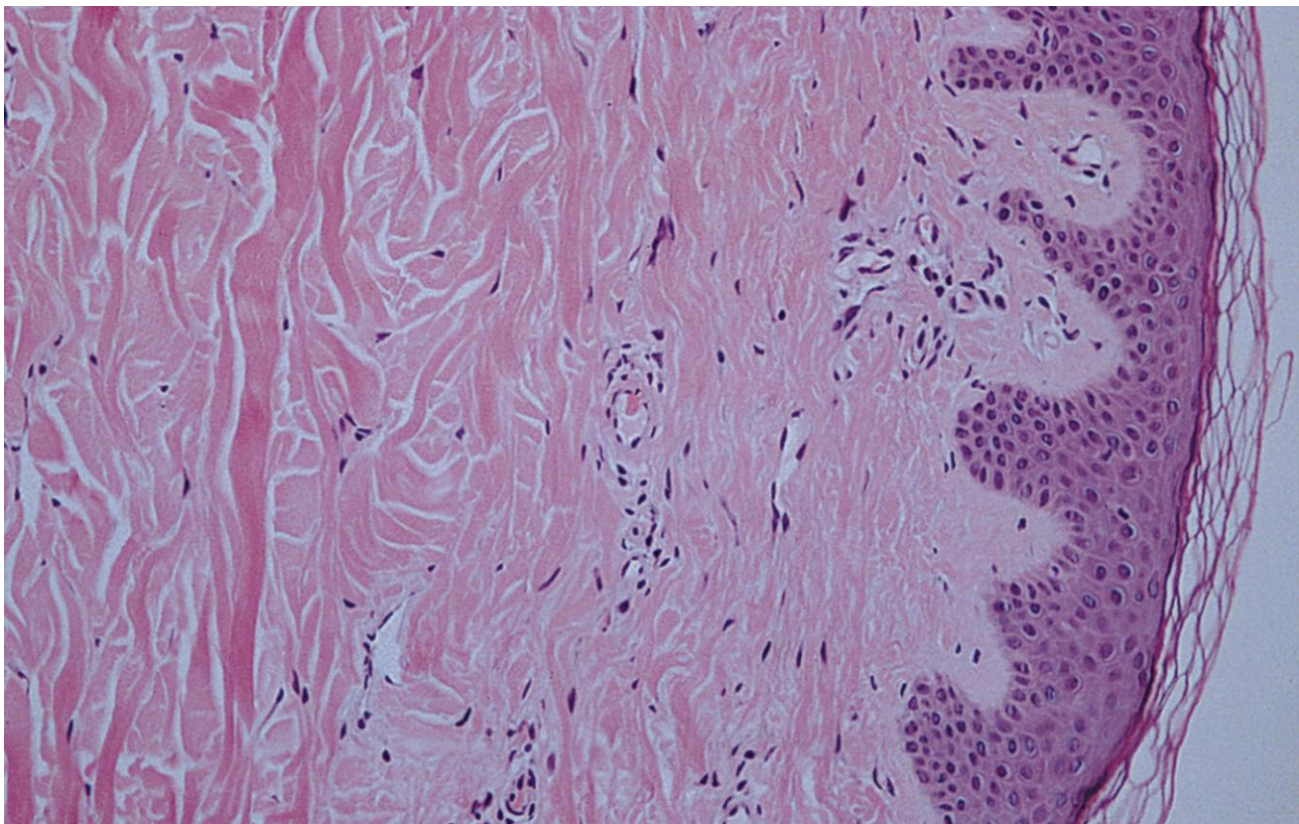


Figure 5.

Patient 2. Biopsy specimen of a treated lesion 18 months after laser ablation. No signs of Darier disease and only slight fibrosis of the upper dermis (hematoxylin-eosin, original magnification $\times 100$).

Erbium:YAG Laser Ablation: Treatment and Results

Patient No.	Treatment Sites	Fluence, J/cm ²	Maximum No. of Pulse Series	Results	Follow-up, mo
1	Axilla, scapular, and upper arm region	7.1	6	Complete remission	11
2	Trunk, extremities, ventral aspect of neck	5.0	7	Complete remission	20
3	Axillae, groins, scrotum	8.5	5	Complete remission	15
4	Axillae, groins	7.1	5	Partial remission	8

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Treatment of Striae Distensae Using an Ablative Erbium-Yag Fractional Laser versus a 585-nm Pulsed-Dye Laser

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J Cosmet Laser Ther. 2014 Jun;16(3):117-9. doi: 10.3109/14764172.2013.854621. Epub 2013 Nov 18.

Abstract

Striae distensae represent a common disfiguring cutaneous condition characterized by linear reddish smooth bands of atrophic appearing skin. Most often striae distensae develop in areas of dermal damage produced by stretching. Numerous treatment modalities have been applied with varying success. Novel approaches include treatments with of various types lasers with the flashlamp-pumped pulsed dye laser (PDL; 585 nm) being the most commonly reported. Very recently, fractional photothermolysis has been suggested as an effective method for the treatment of striae distensae. Here, we report on the effect of an ablative Erbium:Yag fractional laser in two cases of axillary striae distensae in comparison to a 585-nm PDL.

Introduction

Striae distensae (SD) are flat, cutaneous scars characterized by loss of elastic fibres and atrophy of the overlying epidermis. SD are commonly observed in association with pregnancy, obesity, rapid growth during adolescence, increased adrenocortical function or corticosteroid therapy. The exact cause of SD remains unclear, even though a combination of hormonal factors associated with lateral stretch due to increased size of the various portions of the body has been suggested (1). Early SD present as flattened or slightly raised pink or red lesions (striae rubrae). Histopathologically, they appear as inflammatory alterations with elastolysis and mast cell degranulation (2). Over time, the lesions usually become atrophic and white (striae albae). The latter histopathological findings are similar to those of dermal scarring characterized by thinning of the overlying epidermis with fine dermal collagen bundles arranged in straight parallel arrays (2, 3). SD do not cause any significant medical problems but are frequently the source of significant distress to those affected. Thus, various therapeutic approaches have been proposed for the improvement of this common skin condition, including topical application of tretinoin, intense pulsed light, and the 585-nm flashlamp-pumped pulsed-dye laser (PDL) with variable results (4-6). Recently, non-ablative 1550-nm erbium-doped fractional photothermolysis (FP) and ablative 10,600-nm carbon dioxide fractional laser have been proposed as successful approaches for improving the appearance of SD (1, 7-9). For the first time, we report on the effects of an ablative 2940-nm Erbium:Yag fractional laser in two cases of axillary striae distensae in direct comparison to a 585-nm PDL.

Case report 1

A 23-year-old Caucasian male with Fitzpatrick skin type II presented with reddish striae distensae on both axillae which he had recently noticed. His medical history was unremarkable except that he had been suffering from atopic eczema for years, predominantly treated with topical corticosteroids. Upon physical examination, except for 5 purple linear, atrophic markings in his axillary area no other findings were noticed (Figure 1A, B). After obtaining informed consent and treating an unaffected, representative areas of 2x2 cm² with similar settings of the below mentioned lasers

(which were well tolerated), treatment was initiated four weeks later. The patient received a total of five sessions with an Erbium:YAG fractional laser using the MCL 30 Dermablade (Asclepion Laser Technologies GmbH, Jena, Germany) in the left axillary region with 4 to 5 weeks of elapsed time between treatments. During each treatment session, the laser fluences were delivered at settings of 72 J/cm^2 . For the corresponding area in the right axilla, PDL (Candela Vbeam Perfecta, Candela Corp., Wayland, MA) treatments were started simultaneously at 585-nm wavelength delivering a fluence of 7.0 J/cm^2 with pulse duration of 1,500 ms and 7-mm spot size. For local anesthesia, the lesions were cleansed with 70% alcohol and topical EMLA cream (eutectic mixture of 2.5% lidocaine HCl and 2.5% prilocaine; AstraZeneca AB, Södertälje, Sweden) was applied under occlusion an hour prior to each laser treatment. After a total of five laser applications the texture of the lesions on the left side had markedly improved and erythema had faded while appearance of striae distensae of the right axillary area had not markedly changed (Figure 1C, D). Evaluation of a questionnaire addressing subjective improvement in texture, color, overall satisfaction and pain demonstrated superior effects for the treatment of striae distensae using the ablative 2940-nm Erbium:Yag fractional laser.

Case report 2

A 18-year-old healthy male bodybuilder consuming several protein and amino acid preparations for the past 5 years presented with disseminated striae distensae in his axillae, on upper arms and lower back (Figure 2A, B). After discussion of the possible treatment options, potential side effects and after signing informed consent, treatment with the Erbium:YAG fractional laser in the right axillary region and the 585-nm Pulsed-Dye Laser for the corresponding area in the left axilla was initiated following the same treatment protocol as described above. Importantly, no side effects were noticed four weeks after the first treatment. Photographs taken 2 months after the third treatment (Figure 2C, D) demonstrated moderate improvement of lesions treated with both lasers compared to baseline. However, both therapies resulted in marked hyperpigmentation within the treated areas thus no further treatments were delivered. Nevertheless, based on the subjective evaluation the patient favored the use of the fractional Erbium:YAG laser.

Discussion

Striae distensae are dermal scars characterized by linear atrophic depressions. Many treatment modalities have been proposed, with variable results (10). Of the many modalities used to ameliorate and improve SD, lasers have recently become a popular therapeutic alternative. The PDL is the most commonly reported laser used in treatment of SD. Based on the characteristically dilated blood vessels at the early stage of SD formation, particularly striae rubrae constitute a good candidate for PDL treatment (11). Based on the experience of McDaniel et al. and Alster, aesthetic improvement of immature SD can be achieved after several courses of 585-nm flashlamp PDL therapy (12, 13). Jiminez and colleagues documented a moderate beneficial effect in reducing the degree of erythema in striae rubrae. They also found an increase in total collagen in the extracellular matrix, which has been postulated as another possible mechanism of action of PDL therapy for SD (10, 14). In our two patients, the effect of repeated 585-nm flashlamp PDL therapy revealed only moderate results. This may be in part due to the fact that SD in patient two had existed for longer periods of time and thus early stage inflammatory changes, which respond best to PDL treatment may have already subdued.

Fractional photothermolysis (FP) represents a novel technique which utilizes the separation of a single laser beam into an array of smaller beams to deliver microscopic treatment zones (MTZs) of

thermal injury into the skin (15). These MTZs selectively damage dermal tissue leading to the formation of new dermal collagen and the repair of tissue defects (15). Today, there are various non-ablative and ablative fractional laser systems available. Recently, the U.S. Food and Drug Administration approved non-ablative 1,540-nm erbium-doped glass fractional photothermolysis systems (FPS) (Lux1540, Palomar Medical Technologies, Inc., Burlington, MA) for the treatment of striae distensae. Various studies have reported on the efficacy and safety of FPSs predominantly for the treatment of striae albae (8, 9, 16, 17). However, multiple treatment sessions are generally required to achieve pronounced clinical improvement. Very recently, similar results have been described using an ablative 10,600-nm Carbon Dioxide fractional laser (18). Here, we found an ablative 2940-nm Erbium:YAG fractional laser to improve texture and color of axillary early and later stage striae distensae after 3 to 5 treatment sessions in two cases. Post-treatment erythema was noticed at the treatment site of both patients for approximately 2 weeks. Short-term side effects included transient pruritus, post-treatment crusting or scaling. However, although the first laser session did not reveal any side effects four weeks after the initial treatment, one patient developed significant hyperpigmentation after the third treatment session in both axillary areas.

Thus, although the use of an ablative 2940-nm Erbium:YAG fractional laser may provide an additional treatment approach particularly for patients suffering from later stage SD, the risk of associated hyperpigmentations should not be underestimated. In general, SD remain difficult to treat and any therapy and associated side effects should be critically discussed with the patient before any therapy.

Figure 1

Er:YAG fractional laser



A) Before



C) After

PDL



B) Before



D) After

Baseline photograph at presentation in our clinic before initiation of laser therapy (A, B). Result after five sessions of Erbium:YAG fractional laser therapy in the left axillary region (C) and PDL treatment on the corresponding area on the right side (D).

Figure 2

Er:YAG fractional laser



A) Before



C) After

PDL



B) Before



D) After

Baseline photograph at presentation in our clinic before initiation of laser therapy of patient 2 (A, B). Result after three treatment sessions with an Erbium:YAG fractional laser in the right axillary region (C) compared to PDL treatment in the corresponding area on the left side (D).

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AESTHETIC LESIONS

Achieving superior resurfacing results with the Erbium:YAG laser

Jasin ME. Arch Facial Plast Surg 2002; 4:262-266

Abstract

Laser skin resurfacing has become increasingly popular. The carbon dioxide (CO₂) laser seemingly remains the most commonly used laser modality for skin resurfacing. Many surgeons still promote the CO₂ laser as being superior to the erbium:YAG laser, particularly for individuals with deeper lines. However, further experience with the erbium:YAG laser has shown the converse to be true. The erbium:YAG laser can be used to treat deep rhytids successfully, many times achieving results superior to those seen with the CO₂ laser, particularly in the perioral region. The theory behind this relates to the 10-fold greater absorption of the erbium:YAG wavelength by water. The greater absorption produces more efficient vaporization, even at low fluences, with greatly reduced adjacent thermal injury. Ablation can be carried to deeper levels of the dermis than is consistently safe with the CO₂ laser. Deliverance of total fluences in the range of 100 to 150 J/cm², or more, produces a marked reduction or elimination of deeper rhytids. Clinically, experience with more than 300 cases indicates collagen remodeling occurs to a similar degree with the erbium:YAG laser as with the CO₂ laser, as improvement in rhytids can be seen for 2 to 3 months after surgery. It would appear that superior results can be obtained without the "heat effect" of the CO₂ laser. The erbium:YAG laser is capable of achieving superior resurfacing results, while offering many advantages to the patient, e.g., reduced anesthetic requirements, shorter healing time, reduced erythema, less risk of pigmentary change, and more flexibility for resurfacing the skin off of the face.

Facial skin resurfacing with the Erbium:YAG laser: new findings

Perez MI, Bank DE. Cosmetic Dermatology 1998;5:27-37

Results

Ten patients were female and four were male. The average age of our patients was 68 years old. The average healing time after Er:YAG laser was 3.8 days (ranging from 2-4 days). Marked redness changed to mild pink in average by 7.7 days (ranging from 6-9 days). All evidence of erythema resolved between 3-8 weeks in all patients. All patients demonstrated some improvement.

Marked improvement was seen in eight of the fourteen patients in whom 50-75% of class III rhytides (sharply defined deep lines with dermal elastosis and skin folds) improved. Moderate improvement was seen in six of fourteen patients in whom 25-50% of class III rhytides improved.

The most dramatic improvement was noticed after full face resurfacing with the Er:YAG laser of a 70 year-old woman with class III rhytides, premalignant skin changes and facial dyschromia as shown in Figure 1 (A and B, before and after). Pre-cancerous lesions and dyschromia disappeared, as well as most of the class III rhytides which either disappeared or became class I rhytides. Figure 2A shows class III rhytides on the outer canthus of a 65 year-old male who works outdoors, and shows extensive sun damage as compared to his marked improvement 5-6 weeks after Er:YAG laser resurfacing of the periorbital region (Fig. 2B). Figure 3A shows perioral and periorbital class III rhytides in a 68 year-old woman who demonstrated 50-75% improvement 8 months after Er:YAG laser resurfacing (Fig. 3B). In contrast with the static improvement observed in patients resurfaced with the high-energy, short-

pulsed CO₂ lasers, the patients resurfaced with the Er:YAG laser keep improving with time up to approximately 6 months after treatment.

The histologic evaluation of the skin grafts donor skin treated with the Er:YAG laser revealed the following findings: Figure 4A shows that after one pass with the Er:YAG laser there is ablation of the epidermis down to the granular layer under which a thin layer of thermal damage lies and the subgranular keratinocytes show intracellular edema. In Figure 4B, after 2-3 passes with the laser there is ablation of the epidermis down to the basal cell layer, minimal thermal damage and swollen basal cell keratinocytes as well as slight reactive changes of the papillary dermis seen as compacted collagen. After 4-5 passes, full thickness ablation of the epidermis and the upper papillary dermis with a reactive papillary dermis demonstrating loss of the fascicle-like arrangement of the collagen and perpendicular orientation of the collagen fibers is shown (Fig. 4C). After 6-7 passes with the laser (Fig. 4D), there is total ablation of the epidermis and the papillary dermis with very little thermal necrosis. The papillary, superficial and mid-reticular dermis shows loss of the fascicle arrangement of the collagen and perpendicular orientation of the collagen fibers.

Laser peel: facial rejuvenation with a superficial erbium:YAG laser treatment

Khatri KA, Machado A, Magro C, Davenport S. J Cutaneous Laser Ther 2000;2:119-123

BACKGROUND: Facial rejuvenation is a popular procedure to temporarily mask the effects of aging. Most patients desiring this treatment are younger and want improvement without any down time. This study was conducted to evaluate the use of Er:YAG laser as a facial rejuvenation tool.

METHODS: The full faces of 18 volunteers were treated with an Er:YAG laser using a fluence of either 5 or 10 J/cm². All volunteers applied EMLA[®] cream (lidocaine 2.5% and prilocaine 2.5%) two hours before the procedure and were treated with a single pass using a pulse duration of about 300µs. Follow-up visits were made in order to evaluate the degree of discomfort, erythema, swelling and improvement in skin aging. Skin biopsy was performed in one volunteer before and two hours after EMLA[®] application, although preceding laser treatment.

RESULTS: Most volunteers experienced moderate discomfort during the treatment. There was mild to moderate erythema and mild swelling. The improvement in general skin appearance, actinic bronzing and photo-damage was mild to moderate. The microscopic evaluation of pre-laser treated skin two hours after EMLA[®] application was suggestive of increased water content in the dermis.

CONCLUSION: The Er:YAG laser is an effective and safe tool for facial rejuvenation. With a superficial treatment, resolution of intense erythema is fairly rapid, averaging two to three days. The improvement, however, is mild compared to full laser skin resurfacing (LSR).

Comparison of erbium:YAG and carbon dioxide lasers in resurfacing of facial rhytids

Khatri KA, Ross V, Grevelink JM, Magro CM, Andersson RR. Arch Dermatol 1999;135(4):391-7

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 (χ^2 , $P < .05$). 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.

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 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



Figure 1.

Subject with erythema, 1 week after resurfacing. Subject's right side was treated with the carbon dioxide laser (fluence, 5 and 3.5 J/cm²; 3 passes) and the left side was treated with the erbium:YAG laser (fluence, 7.6 J/cm²; 5 passes).



Figure 2.

Subject with erythema, 1 week after resurfacing. Subject's right side was treated with the carbon dioxide laser (fluence, 5 and 3.5 J/cm²; 3 passes) and the left side was treated with the erbium:YAG laser (fluence, 7.6 J/cm²; 7 passes).

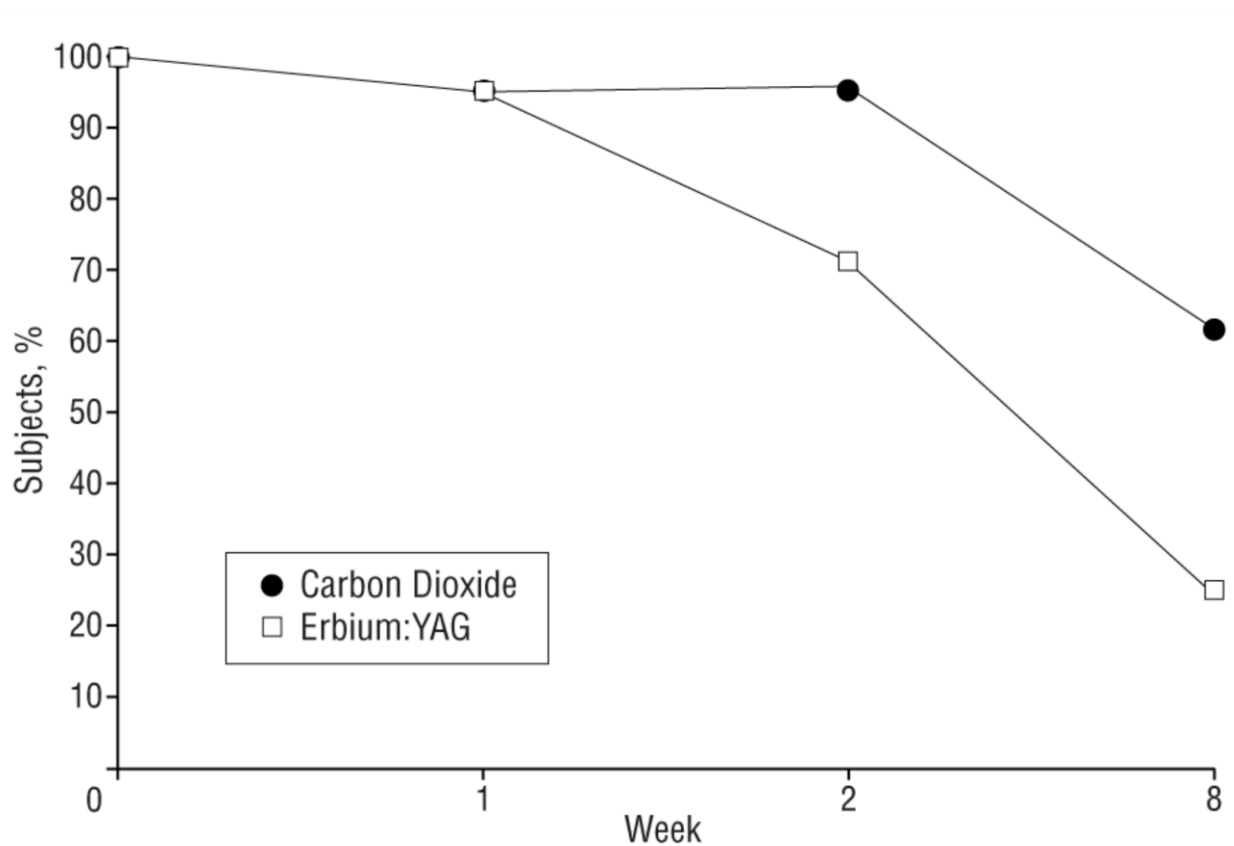


Figure 3.

Percentage of subjects with erythema immediately after resurfacing, and 1, 2 and 8 weeks after resurfacing (n=21).

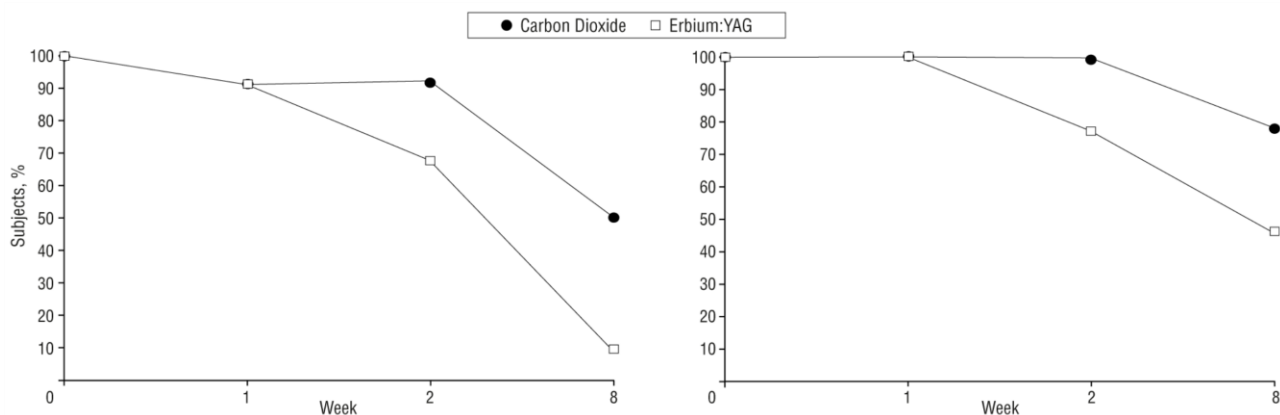


Figure 4.

Percentage of subjects with erythema immediately after resurfacing, and 1, 2 and 8 weeks after resurfacing. Left, Treatment with fewer than 5 passes of erbium:YAG laser and 3 passes of carbon dioxide laser (n=12). Right, Treatment with 5 or more passes of erbium:YAG laser and 3 passes of carbon dioxide laser (n=9).



Figure 5.

Subject with swelling, 1 day after resurfacing. Subject's right side was treated with the carbon dioxide laser (fluence, 5 and 3.5 J/cm²; 3 passes) and the left side was treated with erbium:YAG laser (fluence, 7.6 J/cm²; 5 passes). Subject was unable to open her right eye for 1 day.

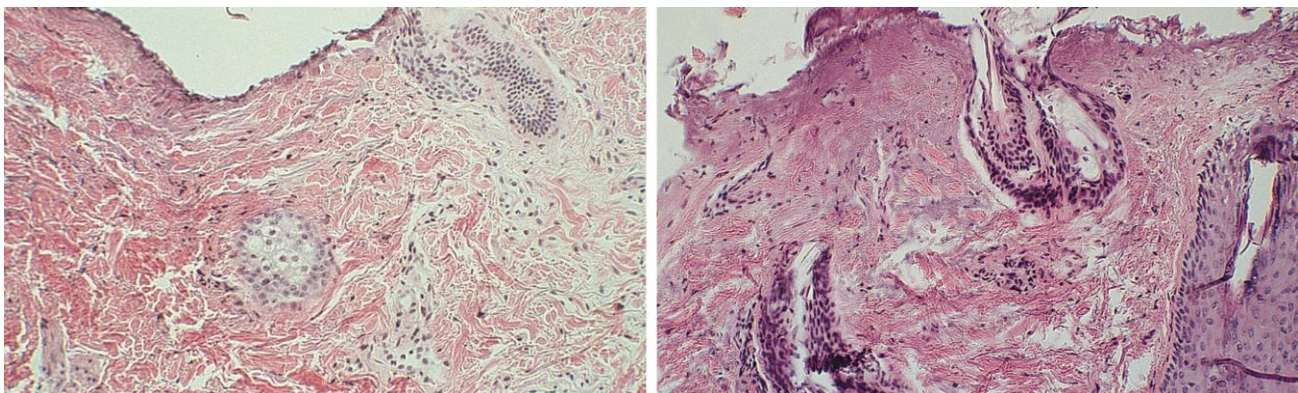


Figure 6.

Photomicrographs of a biopsy specimen immediately after resurfacing showing residual thermal damage (RTD). Left, Erbium:YAG laser-treated side (fluence, 5 J/cm²; 6 passes). Zone of RTD is about 30 μm (hematoxylin-eosin, ×20). Right, Carbon dioxide laser-treated side (fluence, 6.3 and 5 J/cm²; 2 passes). Zone of RTD is about 60 μm (hematoxylin-eosin, ×20).

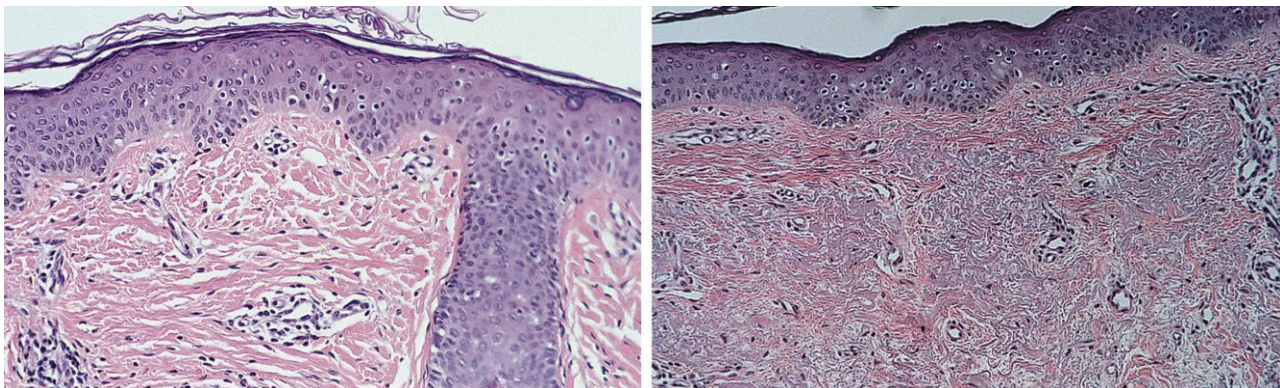


Figure 7.

Photomicrographs of a biopsy specimen 6 months after resurfacing showing fibroplasia. Left, Erbium:YAG laser-treated side (fluence 7.6 J/cm^2 ; 8 passes). Zone of fibroplasia is about 475 μm (hematoxylin-eosin, $\times 20$). Right, Carbon dioxide laser-treated side (fluence, 6.3 and 5 J/cm^2 ; 3 passes). Zone of fibroplasia is about 75 μm (hematoxylin-eosin, $\times 20$).

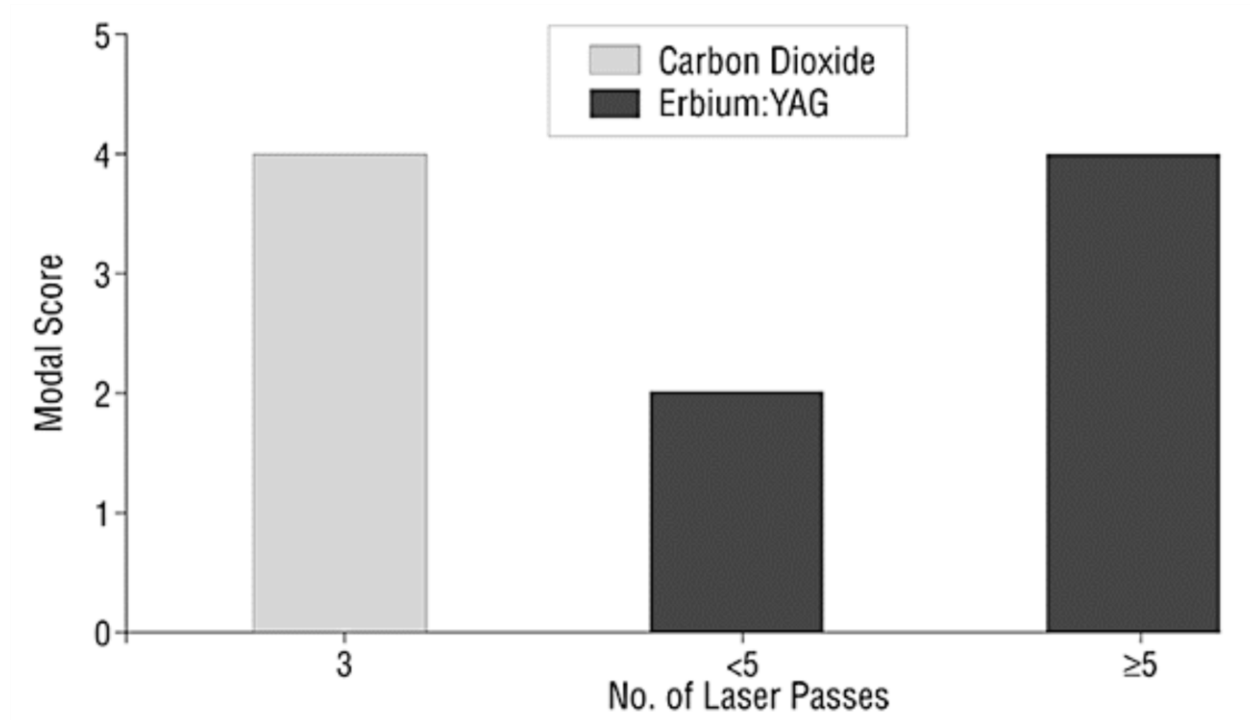


Figure 8.

Wrinkle improvement as graded by a blinded panel with fewer than 5 passes and 5 or more passes of erbium:YAG laser and 3 passes of carbon dioxide laser. Modal scores were graded as follows: 1, poor; 2, fair; 3, good; 4, excellent; and 5, complete clearance.

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Figure 9.

Wrinkle improvement. Left, Subject before resurfacing. Right, Subject 6 months after resurfacing. Subject's right side was treated with the carbon dioxide laser (fluence, 6.3 and 5 J/cm²; 3 passes) and the left side was treated with the erbium:YAG laser (fluence, 7.6 J/cm²; 8 passes). Note the difference in pigmentation between treated and untreated skin. The blinded panel gave an improvement score of 4 (excellent) to both sides.

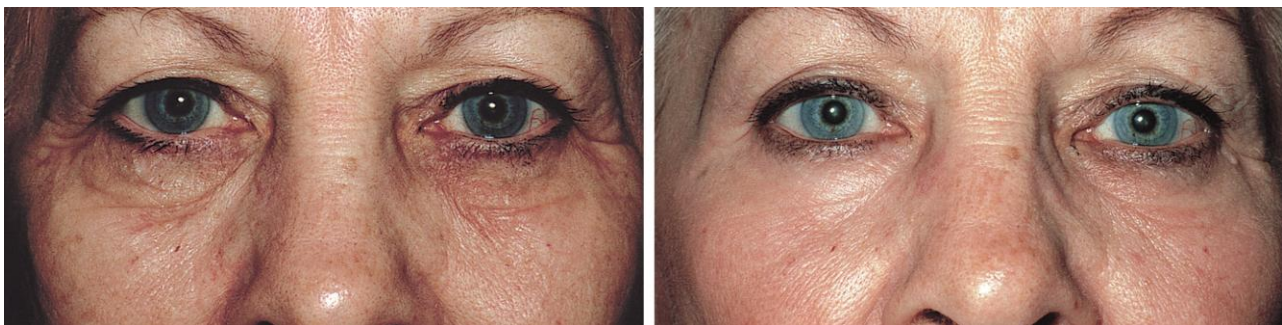


Figure 10.

Wrinkle improvement. Left, Subject before resurfacing. Right, Subject 6 months after resurfacing. Subject's right side was treated with the carbon dioxide laser (fluence, 5 and 3.5 J/cm²; 2 passes) and the left side was treated with the erbium:YAG laser (fluence, 5 J/cm²; 2 passes). Note better improvement on the carbon dioxide laser-treated side. The blinded panel gave an improvement score of 3 (good) to both sides.

Microscopic Evaluation of Biopsy Specimens*

Subject No.	Laser	Fluence, J/cm ² ; No. of Passes	Biopsy After Treatment	Residual Thermal Damage, μ m	Inflammation	Fibroplasia, μ m
1	Erbium:YAG	5; 6	Intermediate	30	NA	NA
	CO ₂	6; 2	Intermediate	60	NA	NA
2	Erbium:YAG	5; 2	Intermediate	50	NA	NA
	CO ₂	5; 3	Intermediate	200	NA	NA
3	Erbium:YAG	8; 8	1 d	NA	+	NA
	CO ₂	6; 3	1 d	NA	++	NA
4	Erbium:YAG	5; 5	2 d	NA	+	NA
	CO ₂	6; 3	2 d	NA	++	NA
5	Erbium:YAG	8; 5	6 mo	NA	NA	0
	CO ₂	5; 3	6 mo	NA	NA	200
6	Erbium:YAG	8; 8	6 mo	NA	NA	475
	CO ₂	6; 3	6 mo	NA	NA	75

* NA indicates not applicable; plus sign, mild; and double plus signs, moderate.

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Intraepidermal erbium:YAG laser resurfacing: impact on the dermal matrix.

Orringer JS, Rittié L, Hamilton T, Karimipour DJ, Voorhees JJ, Fisher GJ.

J Am Acad Dermatol. 2011 Jan;64(1):119-28. doi: 10.1016/j.jaad.2010.02.058.

BACKGROUND:

Various minimally invasive treatments enhance the skin's appearance. Little is known about the molecular mechanisms whereby treatments working at the epidermal level might alter the dermis.

OBJECTIVE:

We sought to quantify the molecular changes that result from erbium:yttrium-aluminium-garnet (Er:YAG) laser microablative resurfacing.

METHODS:

We performed biochemical analyses after intraepidermal Er:YAG laser resurfacing of 10 patients. Immunohistochemical analysis and polymerase chain reaction technology were utilized to measure key biomarkers.

RESULTS:

The basement membrane remained intact after intraepidermal microablation, as demonstrated by laminin $\gamma 2$ immunostaining. Epidermal injury was demonstrated with acute up-regulation of keratin 16. An inflammatory response ensued as indicated by increases in cytokines interleukin 1 beta (IL-1 β) and IL-8 as well as a substantial neutrophil infiltrate. Levels of cJun and JunB proteins, components of the transcription factor AP-1 complex, were also elevated. Up-regulation of extracellular matrix degrading proteinases matrix metalloproteinase 1 (MMP-1), MMP-3, and MMP-9 was noted. A transient increase in keratinocyte proliferation, as indicated by staining for Ki67, was observed. Increased expression of type I and type III procollagen was demonstrated.

LIMITATIONS:

The data presented are those that resulted from a single treatment session.

CONCLUSIONS:

Although microablation was confined to the uppermost epidermis, marked changes in epidermal and dermal structure and function were demonstrated after Er:YAG laser microablative resurfacing. We demonstrated substantial dermal matrix remodeling, including a degree of collagen production that compares favorably with some more invasive interventions. Dermal remodeling and stimulation of collagen production are associated with wrinkle reduction. Thus these results suggest that the skin's appearance may be enhanced by creating dermal changes through the use of superficially acting treatments.

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 Jungner, MD, PhD,² and Christian Raulin, MD, PhD^{1,3*}

Lasers Surg Med. 2010 Feb;42(2):160-7. doi: 10.1002/lsm.20879.

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.

Comparison of clinical outcome parameters, the Patient Benefit Index (PBI-k) and patient satisfaction after ablative fractional laser treatment of peri-orbital rhytides.

Karsai S, Raulin C.

Lasers Surg Med. 2010 Mar;42(3):215-23. doi: 10.1002/lsm.20904.

BACKGROUND:

Laser treatment of facial rhytides has evolved as a major modality of aesthetic surgery. Published results, while generally encouraging, feature highly diverse evaluation methods, which makes an evidence-based assessment of treatment efficacy and safety all but impossible.

OBJECTIVE:

To compare the results of different instruments of measurement.

PATIENTS/METHODS:

Twenty-eight patients were enrolled and completed the entire study. They received a single ablative fractional treatment of the peri-orbital region. The evaluation included the Fitzpatrick wrinkle score, the profilometric measurement of wrinkle depth and the Patient Benefit Index (both before and 3 months after treatment) as well as the assessment of patient satisfaction (1, 3, 6 days and 3 months after treatment).

RESULTS:

All assessment instruments showed a significant, albeit moderate, improvement. The agreement between assessment methods was poor. Despite claiming to assess basically the same parameter, the Fitzpatrick wrinkle score and profilometry differed significantly, and neither assessment instrument showed any appreciable correlation with any other.

CONCLUSIONS:

The outcome assessment of rhytide therapy-regardless of the method used-shows substantial room for improvement. Strict methodological precautions ought to be applied for 'objective' evaluation methods like photographic scoring and profilometry. Subjective methods of assessment are essential and might serve as a main outcome parameter. Finally, critical reappraisal of published treatment results seems warranted to review the quality of their methodology.

FRACTIONAL ER:YAG (DERMABLATE) HISTOLOGICAL IN VIVO STUDY

Daniel Cassuto, MD, Milan, Italy

Objective:

A fractional modality has been developed for the Dermablade Er:YAG laser by Asclepion. Our group demonstrated that a novel non-ablative fractional resurfacing modality with discreet epidermal and dermal lesions, coined microscopic treatment zones (MTZ), could be created using a laser emitting at 2.940 nm wavelength, while sparing the surrounding tissue. This study aimed at determining any correlation between epidermal ablation and effects on the dermis when using Er:YAG laser in ablative fractional resurfacing mode and to prove its safety and efficacy in promoting skin rejuvenation.

Materials and methods:

Abdominal skin was irradiated in vivo under general anesthesia on 20 kg pigs. Samples were cut into smaller specimens and then fixed in 10% v/v neutral buffered formalin.

Skin thickness was 3mm on average. Biopsies were obtained at 0 (immediately after treatment), 2, 7 and 21 days.

The laser device was MCL 30 Dermablade (Asclepion Laser Technology, Jena, Germany). Its beam is fractionated by a microlens array giving a 13x13mm square with a 5% coverage and an individual spot size of 250µm. The settings were as follows: 10, 40 and 80 J/cm² (1; 4; 8 stacked pulses of 10 J/cm² each) with a coverage of 5 and 15%. In all cases, the hand piece was kept in the same position and moved on square by square. The skin was left untreated after the irradiation in order not to interfere with the healing process. Biopsies were routinely processed and stained with haematoxylin and eosin (H&E) at 0 (immediately after treatment), 2, 7 days and 3 weeks after irradiation (Table 1).

Settings Time	10J/cm ² 5%	10 J/cm ² 15%	40 J/cm ² 5%	40 J/cm ² 15%	80 J/cm ² 5%	80 J/cm ² 15%
Immed- iately After	Epithelial thickening	Eschar	Eschar	Eschar	Ulceration	Ulceration
2 days	Eschar	Eschar	Eschar	Eschar	Eschar + Vasculitis	Eschar + Vasculitis
7 days	Hyperkeratosis	Hyperkeratosis	Hyperkeratosis	Hyperkeratosis	Eschar	Eschar
21 days	Vasculitis	Vasculitis	Epithelial Proliferation + Vasculitis	Epithelial Proliferation + Vasculitis	Vasculitis	Vasculitis

Table 1: Relationship between power density and tissue effects

H&E stainings were examined by an independent pathologist (Prof. Marcello Gambacorta, Head of the Pathology department, Ospedale Niguarda, Milano, Italy) blinded to the kind of laser, the fluences and the timing of the biopsy. Two samples were examined for each combination of parameters. Controls were taken from the untreated adjacent skin of each animal.

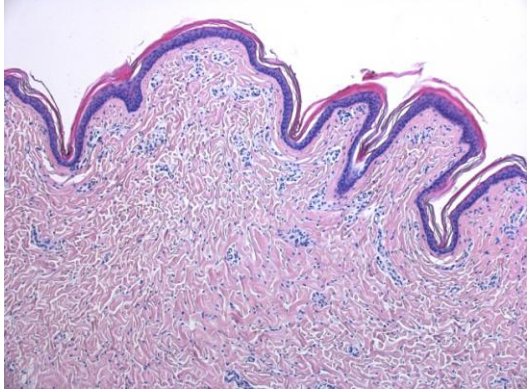
Results:


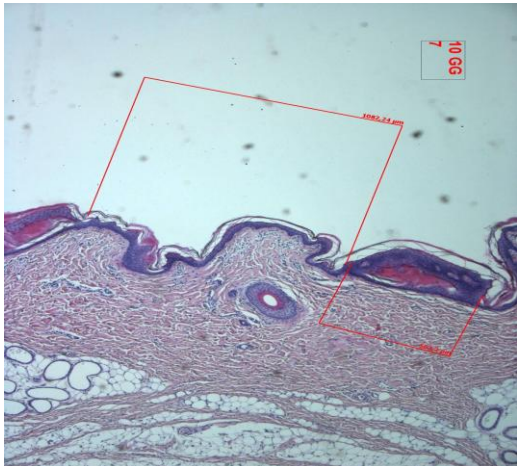
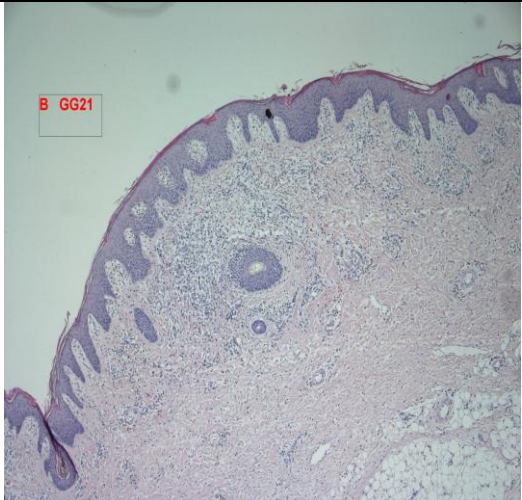
The histological findings were consistent. The findings are described in the following paragraphs according to the used fluence.

10 J/cm²

IMMEDIATELY AFTER: Only minor focal ablation of the stratum corneum is visible, no evidence of structural alterations, complete tissue integrity is present in all examined samples at all different times (2, 7, 21 days). A diffuse inflammatory infiltration (mainly lymphocytic) and vasculitis are present after 3 weeks in the papillary and reticular dermis, i.e. the most superficial layers. (Usually these layers show most signs of aging in humans because they are the ones damaged by UV light); this inflammatory process is the one that usually leads to new collagen formation and remodeling. Previous histological studies done with other fractional ablative lasers have shown a consistent presence of activated fibroblasts, when specific immunohistochemical staining was performed. We can conclude that a significant effect of superficial dermal remodeling can be demonstrated even with a very low power density that is virtually painless on human skin (Table 2). This type of settings doesn't usually cause any downtime and may provide a treatment that is less painful and more effective than nonablative fractional treatments. This kind of repeated "subablative dermal stimulation can be very useful in difficult dark skin types and in patients who can't have any downtime or with a very low tolerance of pain. In fact when epidermal integrity is preserved, make up could be allowed during the immediate post-treatment period.

Table 2

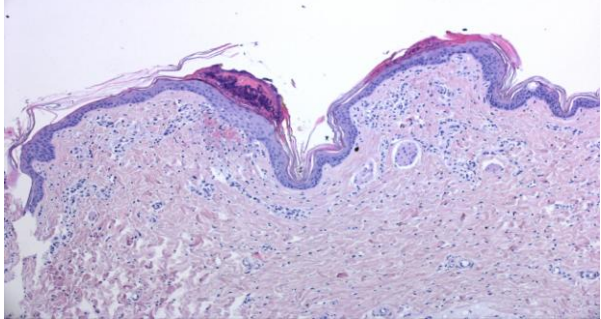
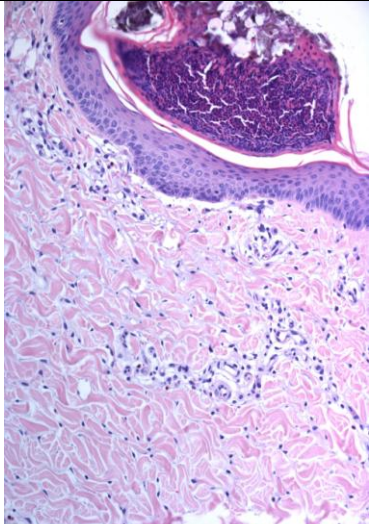
	<p><u>Immediately after irradiation:</u></p> <p>No ablative effect of treatment is seen. Only the stratum corneum is slightly damaged. The epidermis shows only a slight focal thickening. (The effect can be compared to micro-dermabrasion).</p>
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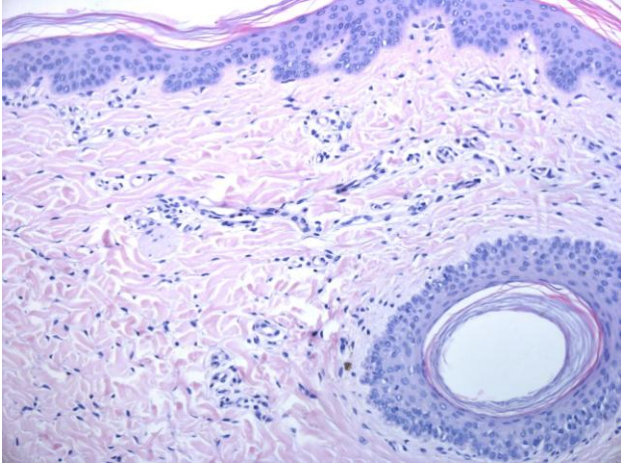
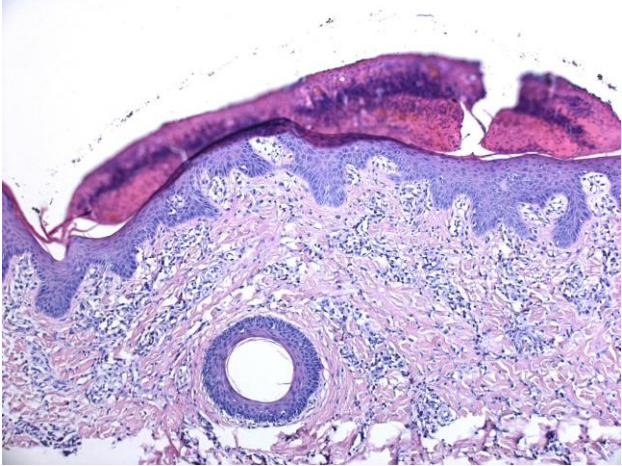
	<p><u>2 days after irradiation:</u></p> <p>A very superficial inflammatory reaction is visible in the epidermis with hyalinization of the collagen fibers (“edema”) and a mild inflammatory infiltration in the papillary dermis (see the area under the measurement red lines). No tissue necrosis is visible. There is no evidence of real damage to the skin.</p>
	<p><u>7 days after irradiation:</u></p> <p>The measurements indicate the diameter of the microcrusts: 562 micron, wider than the 300 micron spot, probably due to movement during treatment or due to the overlapping of two spots in double passing in order to increase the coverage. However, 1000 micron is the space between the spots, compatible with the 5% handpiece used. The inflammatory reaction in the papillary dermis is still mild.</p>
	<p><u>3 weeks after irradiation with 15% coverage (double crossed pass at 5%):</u></p> <p>The whole upper half of the dermis is showing significant inflammatory lymphocytic infiltration. Collagen remodeling is about to begin in the relevant dermal layers. The depth of the reaction is around 1500-2000 microns. This was probably the depth of dermal heating even though the real damage was much more superficial. It shows that deep ablation is not only risky but also unnecessary for effective rejuvenation.</p>

40 J/cm²

Immediately after laser irradiation at 40 J/cm² the histological slides show an ablation depth of 50-80µm in the upper epidermis and homogenous vacuolization of the remaining epidermis with superficial thermal coagulation in the papillary dermis, caused by conducted/diffused heat by the stacked pulses. This is not a normal feature of the classic single pulse at 2940 which typically shows almost pure ablation. At 7 days epithelialization was complete and a mild inflammatory infiltration was seen in the papillary dermis. The infiltration was still present in the upper layers of the papillary dermis at 3 weeks (see table 3). This demonstrates a dermal inflammation indicating significant dermal remodeling has been initiated in all the relevant dermal layers, in contrast with the “prejudicial” conception of classical 2940 nm resurfacing being very superficial and not capable of deeply influencing new dermal collagen formation.

Table 3

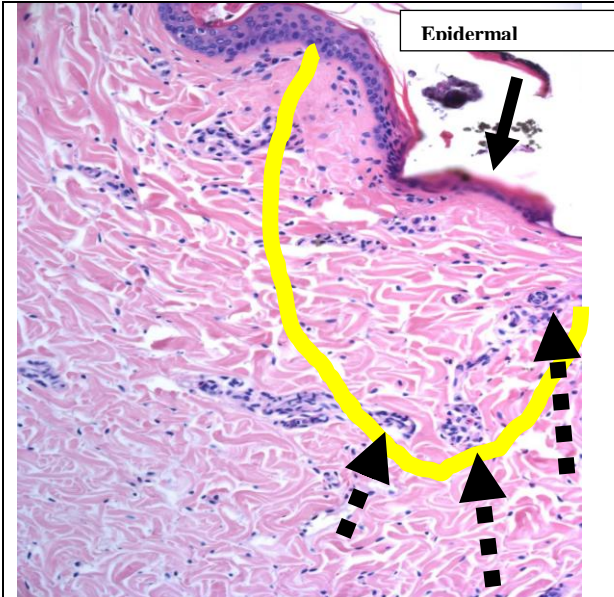
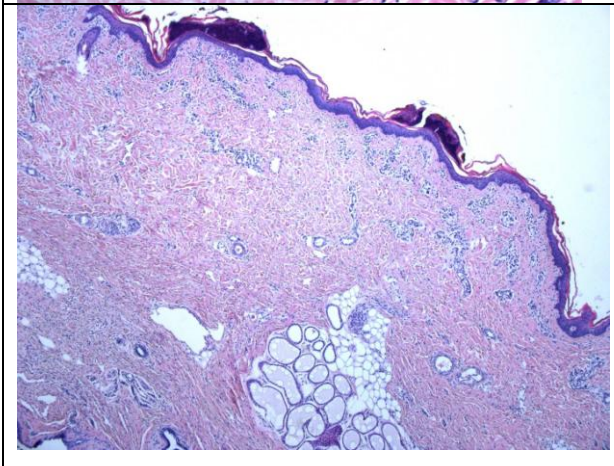
	<p><u>Immediately after irradiation:</u></p> <p>About half (average 100 micron) of the epidermis is ablated or necrotized and exchanged by a thin eschar. The papillary dermis is damaged apparently down to a depth of 350 microns. Dermal tissue coagulation is evident under the spot together with damage to superficial vessels with vasculitis (predicts good inflammatory response in depth.)</p>
	<p><u>2 days after irradiation:</u></p> <p>The eschar is still visible on the epidermis which is edematous. The inflammatory infiltration in the papillary dermis is evident. Papillary dermal coagulation is visible down to about 300 microns of depth, compatible with the immediate findings. The epidermis is already repaired by about 70 percent.</p>

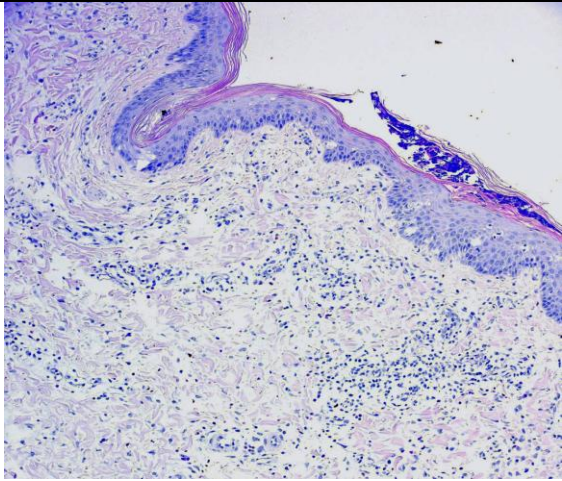
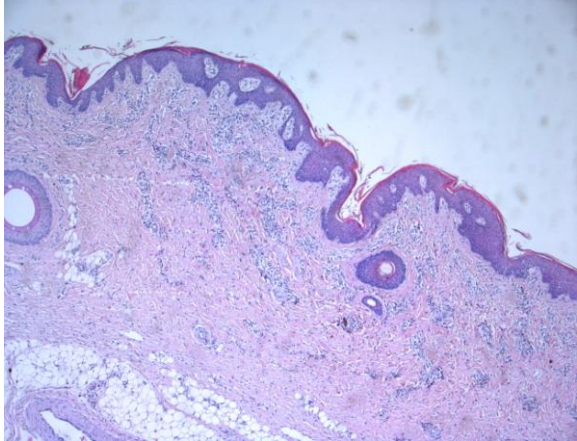
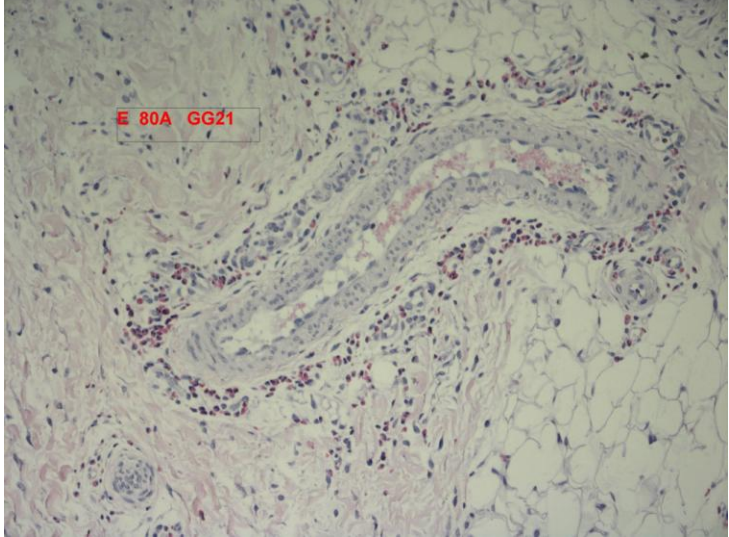
	<p><u>7 days after irradiation:</u></p> <p>The epidermis is completely repaired. The inflammatory reaction in the papillary dermis is still mild to moderate. Coagulation depth still looks around 300 microns but healing. Mild vasculitis is also present.</p>
	<p><u>3 weeks after irradiation with 15% coverage (double crossed pass at 5%):</u></p> <p>The whole upper half of the dermis is showing a diffuse intense inflammatory lymphocytic infiltration. Collagen remodeling is about to begin in the relevant dermal layers. The depth of the reaction is around 1500-2000 microns. It confirms that the treatment is capable of causing full thickness dermal remodeling while causing only a partial epidermal ablation initially.</p>

80 J/cm²

The skin treated at 80 J/cm² showed total epidermis removal with evident residual thermal damage in the superficial dermis comprising a layer of frank collagen coagulation in the superficial dermis, followed by tissue with clear signs of eosinophilia. The epidermis was completely healed at 7 and 21 days. The mild to moderate inflammatory infiltrate was present in the upper papillary dermis, with a slightly higher density compared to the 40 J/cm² specimens (see table 4).

Table 4

	<p>Immediately after irradiation: About 170 microns of epidermis are ablated (arrow). The papillary and reticular dermis are coagulated apparently down to a depth of 450 microns (yellow line). Dermal tissue coagulation is evident under the spot together with damage to superficial and deeper vessels (dotted arrow: predicts good inflammatory response in depth).</p>
	<p>2 days after irradiation: The eschars are visible the epidermis which is already regenerating almost completely. The inflammatory infiltration of the full thickness of the dermis is evident down to about 2000 microns of depth, compatible with a full dermal coagulation whose intensity is degrading with depth but reaches the full thickness. The epidermis is already repaired by about 70 percent.</p>

	<p><u>7 days after irradiation:</u></p> <p>The epidermis is completely repaired even though some thin eschars are still visible. The inflammatory reaction throughout the dermis is still evidently increasing. Hyalinization of the collagen fibers (i.e. evidence of initial damage and successive reaction) is visible down to a depth of 600 microns. Vasculitis is diffusely present as an adjunctive sign of significant inflammation leading to collagen remodeling.</p>
	<p><u>3 weeks after irradiation with 15% coverage (double crossed pass at 5%):</u></p> <p>Even the deepest part of the dermis, adjacent to the subcutaneous fat (average depth 2 mm) is showing a diffuse intense inflammatory process infiltration and evident vasculitis. Collagen remodeling is beginning in tall dermal layers. The depth of the reaction is around 1500-2000 microns. It confirms that the treatment is capable of causing full thickness dermal remodeling while initially causing only epidermal ablation.</p>
 <p>E 80A GG21</p> <p>Fat</p>	<p><u>Close up: 3 weeks after irradiation with 15% coverage (double crossed pass at 5%).</u></p> <p>The deepest part of the dermis is visible, adjacent to the subcutaneous fat (average depth 2 mm). The diffuse intense inflammatory process is focused up around a deep blood vessel. The depth of the reaction is around 1500-2000 microns. It confirms that the treatment is capable of causing full thickness dermal remodeling while initially causing only epidermal ablation.</p>

Discussion:

In this study, we have demonstrated that high density Er:YAG laser microbeams achieved by various fluences, target not only the skin surface with elimination of epidermis, but also produces photothermally related effects in the dermis. The dermis was thus affected by heat diffusion although the epidermis was the first target for the Er:YAG laser, because of the water absorption associated with the Er:YAG wavelength, and the different tissue water content between the epidermis and dermis. Once the epidermal 'window' was created, the Er:YAG beam directly targeted the dermis, with its much higher water content, creating a very superficial zone of frank coagulation and adding to the overall residual thermal damage zone. This region of dermal RTD results in inflammation which in turn induces fibroblast-driven collagen neo-formation at the time that the dermal wound repair takes place. The effect seen in the dermis, was a 'doubled' effect caused by direct absorption of the Er:YAG energy through the newly created epidermal window, associated with heat propagation inwards from the beam repeatedly targeting the epidermis. Histologically, a microshrinkage of collagen fibers was noticed in the superficial dermis as a possible consequence of its higher water content index, when compared to the somewhat less-hydrated epidermis where the appearance of vacuoles was noticed. Complete epidermal healing was observed even at the higher fluences after 1 week in all examined specimens, regardless of the extent of the initial epidermal damage due to the different fluences and percentages of coverage. The basal layers of the epidermis were not destroyed and favoured the prompt epithelialization. No residual tissue damage was visible after 1 or 3 weeks in any of the examined samples.

Conclusions:

Ablative fractional resurfacing shows promise for skin resurfacing and tightening and also to improve treatment of epidermal and dermal pigmentary disorders. Ablative laser resurfacing with the CO₂ and/or the Er:YAG is an effective therapeutic method for treating the signs of skin ageing, and is still the gold standard in severe photoaged skin. However, the excellent results obtained are often associated with an unacceptably long patient downtime, and ablative resurfacing is not complication free. Fractional resurfacing has been proposed as an alternative ablative method of treatment because it produces less aggressive photothermal side effects allowing for faster recovery of tissue and much shorter downtime. The Er:YAG laser at the wavelength of 2.94 μ m is very strongly absorbed in water. This study was designed to determine the possible correlation between various laser settings with a fractional Er:YAG system, which could lead to epidermal ablation and deliver thermal effects into the dermis, thus offering the potential to induce collagen synthesis and remodeling to rejuvenate photoaged skin. Based on these observations and because of the precise vaporization characteristics of the Er:YAG wavelength, highly predictive elimination of the epidermis and delivery of Residual Thermal Damage to the dermis could be monitored closely to ensure more precise efficacious clinical results in skin rejuvenation, while limiting side effects and decreasing downtime. The classical conception of the 2940 nm Er:YAG laser as a relatively pure ablative tool, incapable of causing tissue coagulation is hereby contradicted. Stacking pulses can effectively coagulate the upper dermis, and diffuse heat to the remaining skin layers.

The clinical implications of these observations are far reaching:

- The physical parameters usually mentioned, such as depth of ablation and coagulation, are relatively imprecise. The diameters and depths are variable and impossible to quantify exactly. The epidermal injury is often observed as almost reaching 600 micron, i.e. twice the spot. The possible causes are inclination of the handpiece on the skin resulting in a non perpendicular laser-tissue interaction, inadvertent movement of the hand between the stacks or close positioning of two adjacent “stamps” of pulses. This observation must be conveyed, and the users should be aware of the fact that the effect of treated tissue is not always as perfectly geometric as in the laboratory. For these reasons an extensive measurement of all the possible effects was not performed in all samples. The great variability would have imposed to calculate averages that would not have represented reality in a precise way. In order to get a statistically significant average measurement the necessary added work and number of added slides would have increased the cost of the study far beyond the agreed budget. Furthermore, the importance of the tridimensional effect of the treatment on all skin layers outpowers the importance of the single spots diameter or depth of penetration of its coagulative effect. The global effect on tissue is much more important and its clinical implications as far as efficacy and safety are concerned. This variability is obviously accentuated when treating large and curved areas, such as the face, whereas the décolleté, the dorsum of the hands and the sides of the neck can be treated in a relatively more precise manner due to their being flatter.
- Achieving residual thermal effect beyond the ablated tissue has not been a typical feature of the 2940 nm laser. This limit has been tackled by other companies by simultaneously generating another coagulating beam from a parallel Er:YAG source, with increased costs. When an appropriated elongation of the exposure time is applied (in this case by stacking pulses) a very significant deep thermal effect can be obtained with this wavelength. This is probably the most striking result of this study, and it confirms the clinical experience gathered so far: the efficacy on moderately deep wrinkles and acne scars, skin tightening and the lack of immediate bleeding cannot be obtained without a thermal effect that reaches far beyond the depth of ablation.
- The latter also proves that ablation deeper into the dermis is rarely indicated or mandatory, even when more dramatic improvement is needed. The primary importance of global 3D skin remodeling versus bidimensional deep channels formation is confirmed. This has a great impact in reducing the pain level and improving the safety profile of ablative fractional resurfacing.

The *in vivo* histological evaluation of the Dermablade Er:YAG LASER fractional modality showed that the device is safe and efficacious for skin treatments.

Laser-assisted drug delivery: Enhanced response to ingenol mebutate after ablative fractional laser treatment

Braun SA1, Hevezi P2, Homey B3, Gerber PA4. Am Acad Dermatol. 2015 Feb;72(2):364-5. doi: 10.1016/j.jaad.2014.09.055.

To the Editor: We have read with great interest the articles of Micali et al^{1, 2} concerning topical pharmacotherapy for skin cancer that included an evaluation of the therapeutic response of ingenol mebutate (IM). In this context, we call attention to the evolving field of laser-assisted drug delivery (LADD). Togsverd-Bo et al³ demonstrated in their study that pretreatment of skin with ablative fractional lasers (AFXLs) is an effective technique to enhance the inflammatory reaction of photodynamic therapy, which resulted in an improved response of actinic keratoses in field-cancerized skin.

Here, we applied the concept of LADD to IM therapy. A patient presenting with actinic field cancerization underwent AFXL treatment (fractional 2.940 nm Er:YAG laser, MCL 30 Dermablade, Asclepion Laser Technologies, Jena, Germany; spot size: 350 µm; density: 10%; total fluence: 63 J/cm²; estimated depth of ablation: 280 µm; 1 pass) with consecutive application of IM.

The patient was a 68-year-old man with multiple actinic keratoses on the occiput. We treated the left side of the occiput with the combination of AFXL and IM at a concentration of 0.015% applied on 3 consecutive days, while the right side of the occiput was treated with IM (0.015%) on 3 consecutive days with no LADD. Notably, the combination of AFXL and IM led to a marked increase of the inflammatory reaction compared with IM alone after 3 weeks (Fig 1). The patient experienced no systemic side effects or safety concerns.

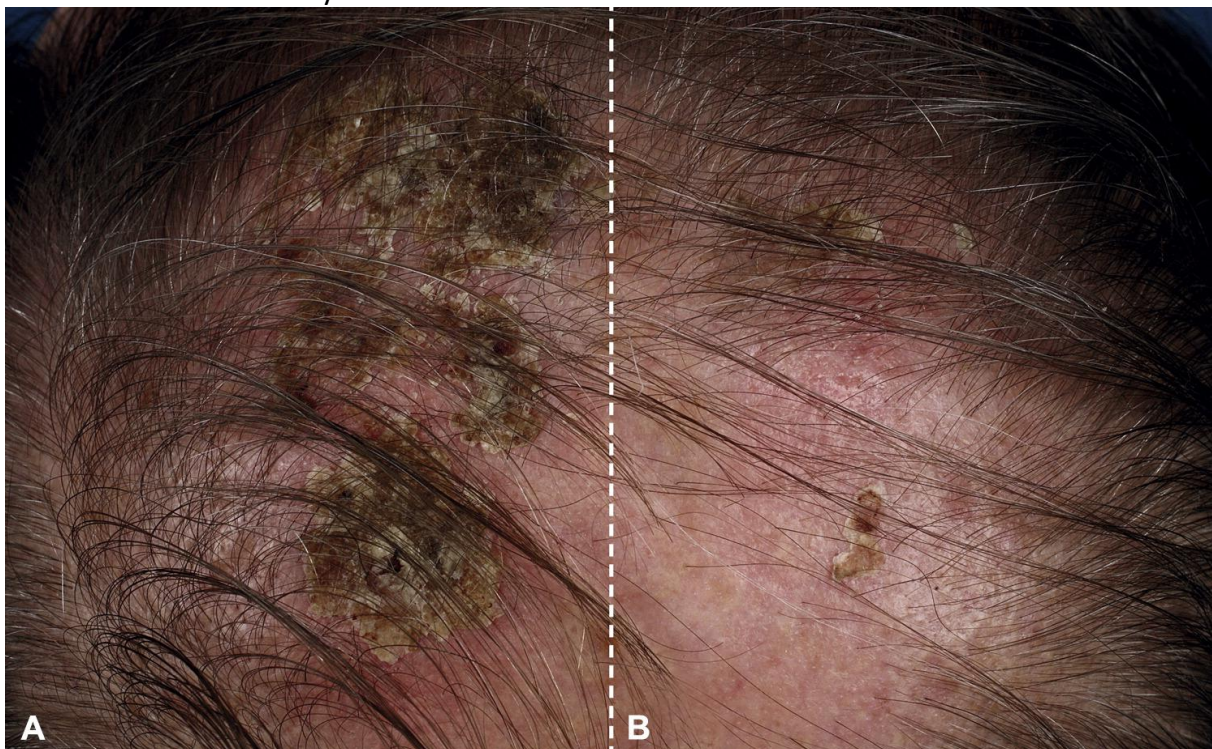


Fig. 1. A, Enhanced inflammatory reaction with thick yellowish crusts on the combined ablative fractional lasers and ingenol mebutate (IM) treated left side of the occiput after 3 weeks. **B,** Reaction to IM monotherapy on the right side after 3 weeks.

Our clinical observations demonstrate that pretreatment of skin with AFXL enhances the inflammatory reaction of IM and that side effects are tolerable. Because the penetration of IM into intact skin is limited, biologically relevant concentrations that induce cell death are only generated in the epidermal compartment.⁴ Accordingly, we propose that the temporary opening of the epidermal barrier (TOR), which is achieved by AFXL, may enable the diffusion of IM into deeper compartments of the skin, leading to a higher bioavailability of IM. This may increase the effect on IM on thicker lesions. Clinical trials are urgently needed to assess the potential and limitations of combination AFXL-IM therapy.

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Reply to: “Laser assisted drug delivery: Enhanced response to ingenol mebutate after ablative fractional laser treatment”

To the Editor: Braun et al show in their letter that pretreatment with fractional 2.940 nm Er:YAG laser enhanced the inflammatory reaction of ingenol mebutate (IM) in a patient with actinic keratoses. However, because information about clinical outcome is not available, it remains unknown whether this approach may effectively improve actinic keratoses clearing. It is also unclear whether the observed increased inflammation was due to boosting of IM delivery or to a cumulative effect resulting from the 2 treatments.

Ablative lasers have the ability to remove the stratum corneum, the main barrier to the passage of chemicals through the skin, in a predictable and controlled manner.¹ For this reason, laser-assisted drug delivery (LADD) has been proposed as an evolving modality that may allow a greater penetration of topically applied drugs.¹ However, available studies exploring the potential role of LADD in the topical treatment of skin cancer are

scant, with most of them performed on animal models. Some authors have demonstrated, on a nude mouse model, an increased transdermal delivery of 5-fluorouracil (5-FU) following pretreatment with conventional Er:YAG, conventional CO₂, and Q-switched ruby (594 nm) lasers, respectively achieving a 53- to 133-fold, a 36- to 41-fold, and a 5- to 10-fold increase with each device.² Another study, performed on porcine and nude mouse

skin, showed an improvement of imiquimod skin delivery by low-fluence fractional Er:YAG laser. In this study, an imiquimod concentration of 0.4% from aqueous vehicle with laser treatment approximated the flux from the commercial 5% imiquimod cream without laser treatment, reducing the drug dose 125-fold.³ Finally, other authors have obtained, using a rabbit ear model, a significant increase of transdermal permeation by applying

5-FU after nonablative Q-switched Nd:YAG laser treatment.⁴

In regard to in vivo human studies supporting the efficacy of LADD in the treatment of skin cancer, the ability of ablative laser pretreatment to enhance the efficacy of photodynamic therapy with 5-aminolevulinic acid (ALA) and methylaminolevulinate (MAL) has been demonstrated in some clinical trials.⁵ A single case report has demonstrated improved efficacy of topical 5-FU following Er:YAG laser pretreatment in Bowen disease. Three target lesions from a patient with multiple plaques were selected for a half-side comparison study, and the laser-pretreated areas showed more rapid clinical and histologic responses to topical 5-FU compared to those treated with 5-FU alone.⁶

These preliminary results suggest that placebo controlled trials on the use of LADD for skin cancer that demonstrate improved clinical outcome rather than simple enhanced drug delivery and/or inflammatory reaction would be necessary to establish their efficacy.

Giuseppe Micali, MD, Francesco Lacarrubba, MD, and Maria Rita Nasca, MD, PhD

Clinical experience in the use of Er: Yag 2940 «Dualmode» combined with an injectable form of PRP for treatment of post-acne symptoms.

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Abstract

The below results describe the treatment of post-acne symptoms of a young man, 16 years old, with Er: Yag (2940 nm), using laser and plasma enriched with thrombocytes (PRP). The subject matter of the case is the use of Er: Yag 2940 nm laser in ablation and non-ablative mode, combined with an injectable form of PRP.

Introduction

Acne is the most common cause of scarring and other cosmetic facial blemishes. In recent years, dermato-cosmetology specialists have coined the term "post-acne", referring to a secondary symptom of rashes that have developed due to the evolution of the various forms of inflammatory acne. The most common symptoms of post-acne are hyperpigmentation, pathological scars, as well as the formation of atheroma, and milia.

The duration of inflammatory acne is directly linked to the risk of scarring, which is formed by different authors of 11-95% of cases^[1]. In the case of pustules and papules and forms of nodular cystic acne, 100% of patients have post-eruptive skin changes^[2].

In modern society, physical attractiveness plays a major role and helps in achieving professional success as well as in one's private life^[3].

The range of means and methods of post-acne treatment is extremely broad and includes external treatment, systemic medications, physical therapy, peels, etc. In recent years, physicians have devoted a great deal of time to the development of technologies based on the use of physical factors in the treatment of skin diseases. At the same time, methods using medical equipment are now not only part of, but often the main element of the treatment process of dermatological patients. In this regard, a promising high-energy pulsed laser method has been successfully used in dermato-cosmetology and, in particular, for the correction of scarring, pigmentation, and vascular disorders^[4].

Laser skin resurfacing is a modern method of removing surface defects of the skin, such as scars, tattoos, actinic keratoses, xanthelasma, pigment spots and nevi. As the skin consists of 77% water, for resurfacing we use lasers which emit radiation which is well absorbed by water and thus also by the skin. The energy and duration of the laser pulses are selected so that the radiation is completely absorbed in the epidermis. During absorption, there is a rapid temperature rise to several hundred degrees, whereby the tissue vaporizes almost instantly. The rate of evaporation (vaporization) is so high that the heated layer converts to steam, without transferring the heat to the deeper layers of the skin.

Since 2004, global specialists have started to use laser devices with the option of fractionating the laser radiation which is known as the Erbium (Er: YAG) laser. The laser beam, unlike other lasers, does

not cause tissue ablation. It forms microthermal therapeutic areas (MTA) – a microscopic zone in the form of columns with a width of 50 - 150 mm, and a depth of 382 to 1359 microns. MTA depth and diameter are determined by the energy of the laser beam, controlled by a physician during the treatment.

For the Er: YAG laser, the penetration depth of ablation and coagulation component varies according to the technical capacity of the laser system. However, in each case, the penetration depth per flash is less than the depth of the basal membrane. The number of passes to the basal membrane varies from 2 to 4-5, allowing different procedures to be performed such as peels, aesthetic dermabrasion, laser dermabrasion, depending on the disease pattern.

An additional point is that it is necessary to specify three types of ablative effects:

The "cold" ablation - a physical phenomenon of vaporization of the soft tissue to the penetration depth of the laser and the minimum (7 μ) zone of coagulation.

"Warm" ablation - a physical phenomenon of vaporization of soft tissue and coagulation zone of up to 15 microns.

"Hot" ablation - a physical phenomenon of soft tissue vaporization and coagulation zone to 30 microns.

Realization of cold ablation phenomenon is only possible when using the Er: YAG laser, with a pulse duration less than the thermal relaxation time of the surface layers of the epidermis (e.g., pulse duration of 100 ms, the thermal relaxation time of the corneous epithelium 250 ms) and the energy density of more than the ablation threshold (more than 2.5 J/cm²).

The use of Er: YAG laser with variable pulse duration (100, 300, 600, 1000 ms.) allows the use of procedures combining ablation and coagulation components, and non-ablative rejuvenation treatments which are based on the coagulation effects, leading to a reduction in the area of the skin flap and unusually powerful stimulation of neocollagenesis in the superficial dermis.

In LLC "Professor Yutskovskaya's Clinic" we use the 6th generation MCL-31 (Asclepion Laser Technologies, Germany) Er: YAG laser (2940 nm).

One of the most promising developments in medicine in general and in particular of regenerative medicine is the use of growth factors to accelerate the regenerative processes in the wound. The most accessible source of autologous growth factors are platelets^[5]. All these factors are in the alpha granules of platelets. These include - platelet derived growth factor (PDGF - Platelet Derived Growth Factor), two transforming factor beta (TGF-beta I, 2 - Transforming Growth Factor), insulin-like growth factor (IGF - Insuline like Growth Factor), epidermal growth factor (EGF - Epidermal Growth Factor), fibroblast growth factor (FGF - Fibroblast Growth Factor), vascular endothelial growth factor, aitigeparinovy factor, platelet activating factor^[6].

Autogenic platelet concentrate stimulates collagen formation, accelerates the regeneration of the skin and mucous membranes, induces the growth of blood vessels, stimulates the rapid and full formation of connective tissue, provides hemostasis, reduces pain, reduces the risk of infectious complications, and helps achieves the best results during invasive surgery in order to prevent surgical complications.

In order to optimize the treatment of patients with post-acne symptoms, we conducted testing of a new method using Er: Yag 2940 «Dual mode» in combination with an injectable form of PRP.

Clinical case study

Patient S. 16 years. The patient visited the LLC "Professor Yutskovskaya's Clinic" complaining of a rash on the face and neck. He repeatedly visited dermato-venereologists and cosmetologists, where treatment was prescribed, but no results were achieved.

At the clinic he was examined by a dermato-venereologist, endocrinologist, and a gastroenterologist.

During the examination:

Before treatment - facial skin is characterized by hyperexcretion of fat and the presence of multiple efflorescence of an inflammatory nature, different sizes from 0.3 to 0.5 cm in the form of papules and pustules with marked infiltration of a stagnant red color. On the skin of the lower jaw with the transition to the skin of the cheeks there are cystic pustular blemishes of bluish color, 0.5 cm size. Other areas showed congestive erythema cores, post-inflammatory hyperpigmentation, and atrophic round scars of different sizes. On the skin of the anterior surface of the chest and back on an oily skin base, there are inflamed papules and pustules, some of which are on the infiltrated and hyperpigmented spots and atrophic scars on parts of the rash.



Fig. 1. The disease pattern before medical treatment.

We conducted a comprehensive clinical and laboratory examination, including skin tests, ultrasound of the skin, blood count, blood chemistry, hormonal profile, skin scraping on demodex, skin scraping for sowing with sensitivity to antibiotics, antibody testing to *Lamblia*, antibody testing to *H. pylori*. Taking into account the medical history, disease pattern and clinical data and laboratory examination, the diagnosis was third degree acne (see Fig. 1).

The patient was prescribed treatment with isotretinoin (Roaccutane) at a daily dose of 20 mg. After 2 months of treatment, the dosage was increased to 40 mg per day, and after 4 months following start

of treatment, the daily dose was increased to 60 mg. After 8 months of treatment, the cumulative dosage was reached - 7200 mg. During the therapy, we observed some negative side effects during treatment such as cheilitis, allergic "Retinoid" dermatitis, dry eye syndrome, rhinitis. The use of supplementary treatment reduced some undesirable effects.

8 months after medical treatment - skin and mucous vermilion borders are dry, sprinkler elements are hyperpigmented spots, and atrophic scars. In the area of the left cheek, close to the lower eyelid there is induration of stagnant-bluish color, size 0.3 x 1.0 cm. (Fig 2).



Fig. 2 The disease pattern after 8 months of medical treatment.

Taking the post-acne symptoms into account, it was decided to carry out the treatment with the erbium laser in combination with PRP. We selected "cold ablation" laser treatment methods (pulse width 100 μ s, the momentum density of 3 J/cm²), which allows the dysfunctional layer to be carefully removed without causing heating of the subcutaneous layer, and a method of non-ablative fractional photothermolysis. For the preparation of PRP we used Plasmolifting tubes and followed standard procedures. PRP injections were administered using mesotherapeutic 30G syringes, immediately after non-ablative laser photothermolysis, for one procedure we injected 4 ml of the drug.

AESTHETIC LESIONS

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The first stage of post-acne symptom treatment:	
09.01.2014	Plasma treatment of face and neck:
09.02.2014	Plasma treatment of face and neck:
09.03.2014	Ablative fractional laser "cold" photothermolysis of face and neck (N25) - 25 J/cm ³ .



Fig 3. The disease pattern after the 1st phase of post-acne treatment.

After the first stage of the treatment - there are papular elements on the skin of the face, back, and on the neck, with signs of inflammation and the presence of serous and hemorrhagic crusts. Hyperpigmented spots and atrophic scars of various sizes can be seen in the affected area (Fig 3). It was decided to continue the therapy.

The second stage of post-acne symptom treatment:	
24.03.2014	Plasma treatment of face and neck+ non-ablative fractional laser photothermolysis of scar lesions of the face and neck (W25) - 4 J/cm ³ .
16.04.2014	Plasma treatment of face and neck+ non-ablative fractional laser photothermolysis of scar lesions of the face and neck (W25) - 4 J/cm ³ .
19.05.2014	Plasma treatment of face and neck+ non-ablative fractional laser photothermolysis of scar lesions of the face and neck (W25) - 4 J/cm ³ .
03.06.2014	Ablative fractional laser "cold" photothermolysis of face and neck (N25) - 25 J/cm ³ .



Fig. 4. The disease pattern after the 2nd stage of treatment of post-acne symptoms.

Some improvement could be seen on the skin of the face where there are multiple atrophic scars (Fig. 4).

Results of procedures are rated as excellent by the physician and the patient. The results obtained allow us to confirm the efficiency of the laser treatment procedure in combination with an injectable form of PRP.

The above treatments of post-acne symptoms are recognized by dermatologists, but are often used separately. The right therapy depends on the individual characteristics of the scar and aims to achieve good clinical results. Today, it is impossible to achieve complete regression of post-acne skin changes; future treatments will use combined techniques that will aim to achieve better results in comparison to monotherapy.

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