BI.LA.P. (BIOSTIMULATION LASER PEELING): MULTIDRUGS BIOSTIMULATION AND ERBIUM: YAG SUPERFICIAL LASER PEELING. A NEW TECHNIQUE TO TREAT MODERATE PHOTODAMAGED SKIN.

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Summary

Deeper resurfacing techniques, including medium depth chemical peels, dermabrasion and laser resurfacing have clearly been efficacious in treating photodamage. However, the need for intravenous sedation or general anaesthetic and the protracted post-operative course and frequent complications associated with deeper procedures have caused many physicians and patients to seek alternative approaches. More and more patients are seeking non-invasive, no downtime techniques to obtain smoother skin and diminish age spots. The authors sought to use a new technique, described by Paolo Mezzana MD 2005 based on vitamin C, low weight hyaluronic acid, betaglucan dermal injections ten minutes before a double pass low fluence, Er:YAG laser with a new thermal subsurfacing function to ascertain its efficacy in treating mild to moderate photoaging. On the basis of the data presented in this article, the authors conclude that the BI.LA.P technique seems to be a safe and effective method to correct skin textural changes of photoaging and improves superficial Er:YAG laser resurfacing results that in previous studies appear to play an important role in the treatment of mild to moderate photodamage. The short recovery time makes this procedure attractive for busy persons.

Riassunto

Le tecniche di resurfacing profondo, inclusi i peeling chimici, la dermabrasione e il laser resurfacing, hanno dimostrato chiaramente in passato la loro efficacia nel trattamento della cute fotodanneggiata.
Gli autori sperimentano una nuova tecnica messa a punto dal Dott. Paolo Mezzana nel 2005, basata su iniezioni dermiche di vitamina C, acido ialuronico a basso peso molecolare e betaglucano, dieci minuti prima di un doppio passaggio a bassa energia di un laser erbium yag.
Sulla base dei dati raccolti, gli autori concludono che la tecnica è sicura ed efficace per correggere i cambiamenti strutturali superficiali cutanei indotti dal foto invecchiamento.
INTRODUCTION

Non-ablative skin rejuvenation using laser, intense pulsed light or RF techniques is becoming increasingly popular due to the aging population’s desire for fresher, younger looking skin (1-2-3-4). Light, chemical peels and microdermabrasion have enjoyed recent popularity for the treatment of mild photodamage. Deeper resurfacing techniques, including medium depth chemical peels, dermabrasion and laser resurfacing have clearly been efficacious in treating photodamage. However, the need for intravenous sedation or general anesthetic and the protracted post-operative course and frequent complications associated with deeper procedures have caused many physicians and patients to seek alternative approaches. More and more patients are seeking non-invasive, no downtime techniques to obtain smoother skin and diminish age spots. Laser skin resurfacing is an effective treatment option for many patients with cutaneous photodamage, wrinkles, and acne scarring (5-6). Several laser systems are currently available for cutaneous laser resurfacing, including high-energy pulsed and scanned carbon dioxide (CO₂) and erbium:yttrium-aluminum-garnet (Er:YAG) lasers. Although excellent improvement of photodamaged skin, rhytides, and atrophic scars can be achieved after multiple pass treatment technique with these laser systems (7-8-9), an extended recovery period and, in some cases of CO₂ laser resurfacing, prolonged erythema have diminished the enthusiasm for multipass CO₂ procedures (10-11).

In 1997, a minimally traumatic single-pass CO₂ laser resurfacing procedure was described that resulted in faster re-epithelialization and an improved side-effect profile than typically observed after use of the multiple-pass technique (12). In addition to the development of minimally traumatic CO₂ laser techniques, the search for alternative methods of cutaneous resurfacing led to the development of the Er:YAG laser. At a wavelength of 2940 nm, the Er:YAG laser corresponds to the peak absorption coefficient of water and is absorbed 12 to 18 times more efficiently by cutaneous water-containing tissue that is the 10,600-nm wavelength of the CO₂ laser (13). At a fluence of 5 J/cm², a typical short-pulsed (250 ms) Er:YAG laser reliably ablates 10 to 20 mm of tissue per pass, producing a residual zone of thermal injury not exceeding 15 µm (14-15). In contrast, CO₂ laser skin resurfacing produces 20 to 60 mm of tissue ablation and up to 150 mm of residual thermal injury per pass. As a result of the minimal thermal injury induced by short-pulsed Er:YAG laser resurfacing, faster re-epithelialization and an improved side effect profile are effected (as compared with CO₂ laser skin resurfacing) (16-17). On the other hand, minimal thermal injury in the dermis provides insufficient vascular coagulation (resulting in poor intraoperative homeostasis) and reduced collagen contraction and remodeling (resulting in less impressive clinical results) (6, 18). Two recent studies of superficial Er:YAG laser resurfacing, using topical anesthesia, showed improvement in treating photodamage of variable degrees (19-20).

We sought to use in this study was used a new technique, described by Paolo Mezzana MD in 2005 based on vitamin C, low weight hyaluronic acid, betaglucan dermal injections ten minutes before a double pass low fluence, Er:YAG laser with the new thermal sub-surfacing function to ascertain its efficacy in treating mild to moderate photodamage.

MATERIALS AND METHODS

The data were collected over a 1-year period (April 2005 to April 2006). 92 patients (80 women and 12 men) with ages ranging from 35 to 60 years old, underwent two sessions, delayed of three months, of full face resurfacing with
B.L.A.P. (Biostimulation and Laser Peeling MEZZANA 2005) technique under topical anesthesia. The patients answered the questionnaire, and permit to take digital photographs before, one months, and three months after the last session and were included in the study. The patients included had Fitzpatrick skin types II to IV: 20% percent type II, 65% percent type III, and 15% percent type IV. All procedures were performed by one physician. Patients with any suspicion of skin cancer, skin pathology or in doubt of pregnancy were not included. The patients signed a detailed informed consent.

The mixture of drugs for biostimulation (vitamin C, low weight hyaluronic acid, betaglucan) was HCG 2000® (Mavi Sud srl, Italy). The patients underwent 2 sessions, three months delayed, of full-face laser resurfacing according to B.L.A.P. technique. No subjects were pre-treated with hydroquinone or retinoic acid. However all the subjects did receive prophylactic antivirals (aciclovir 400 mg BID) and continued their use for three days after the procedure. Topical anesthesia of 5% lidocaine was placed on the skin for 45-60 minutes under occlusion prior to laser treatment. The topical anesthetic was then removed and laser eye and skin safety precautions were observed (Oculoplastik, Montreal, Canada).

Multi-drugs biostimulation was done with 5 ml intradermal injections in net manner of the solution described before in every anatomic site of the face 10 minutes before every laser procedure. Injections were repeated as single procedure one month after the second session of laser resurfacing.

All subjects underwent the two sessions of Er:YAG laser resurfacing (Burane XL™, WaveLight Laser Technologie AG, Germany) using a beam diameter of 5 mm a repetition rate of 15 Hz. 2 passages with 1st mode: Pure ("cold") ablation of the epidermis (resurfacing) for reduction of fine wrinkles and 1 passage 3rd mode: Thermal sub-surfacing. The energy was between 200 to 300 mJ.

At the end of each session, cold wet gauzes were applied to the skin for a few minutes. Antibiotic-corticosteroid ointments were prescribed after the procedure to be applied three times a day for three days and after this, the patients were allowed to apply hypoallergenic makeup and an hydrating moisture cream. Sun exposure was avoided for as long as possible after each treatment, and a total sun block was applied during daily normal life.

The patients filled out a detailed questionnaire concerning their satisfaction level, side effects, and complications, one months, and three months after the last session. In the questionnaire, patient satisfaction was evaluated and graded on a scale from 0 to 5, with 5 excellent, 4 very good, 3 good, 2 moderate improvement, 1 mild improvement, and 0 no improvement. A nurse collected the patient rating at the office visit and had no connection with the physician rating performed also at the office visit. A blinded physician rated the results using the same parameters. An accurate analysis of the images before and after, was done by the same physician, using the same scale of the questionnaire from 0 to 5 (no improvement) to 5 (excellent).

RESULTS

All subjects were clinically improved. No viral, bacterial nor fungal infections were observed. No contact or allergic dermatitis was noted; no permanent pigmented change or scarring was seen.

The satisfaction rate is demonstrated in Table I. The rates given by the neutral physician were not significantly different from the patients’ rates. The most common side effect was persistent redness (at least 8 days), a sensation of dry skin for the first one week, some echymosis in the injection sites and an oedema for the first three hours after the procedure. No major complications.
TABLE I

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Patient

Physician

DISCUSSION

Certainly facial rejuvenation is an evolving art as well as a science. Unfortunately photoaging is a complex process, so the treatments involved in its correction have to be done at different levels. Patients with minimal to moderate photodamage have more commonly been treated with a light, chemical peel or repeated treatments of microdermabrasion rather than undergoing a procedure requiring an anesthetic. With the Intense pulsed lights most of the improvement was noticed for pigmented lesions and telangiectasias and much less for the skin texture, unlike Weiss et al., noticed skin textural improvement in 83 percent of the patients from their study (21).

The new technique described above, shows good results, in skin texture changes compared with the use of Intense Pulsed Light alone, that shows good results especially in telangiectasias and pigmented lesions. It is possible to use it for the treatment of mild to moderate photoaging and to insert B.I.L.A.P. technique inside protocols of Intense Pulsed Light in order to create a "global care" of the skin. The idea of the multidrug biostimulation immediately before superficial erbium laser peeling was born from some considerations. Photoaging is that damage done to the skin by the direct effects of ultraviolet light. Wrinkles and textural modifications are a major cosmetic concern to patients, and the cause of these problems can be traced back to sun exposure.(2) These structural changes will often be accompanied by other stigmata of sun damage including brown spotting (solar lentigines), telangiectasias as well as actinic and seborrheic keratosis. Solar elastosis is the histological equivalent to clinical photoaging, and the terms are often used synonymously. Solar elastosis consists of deposition of massive amounts of abnormal elastic material, in the upper reticular dermis (22). The abnormal elastic fibers being deposited are accompanied by massive amounts of a chondroitin sulfate molecule (versican). This increase in versican and abnormal elastic fibers are accompanied by a corresponding decrease in amounts of collagen and a collagen associated proteoglycan (decorin) (23). The primary mutagen seems to be ultraviolet light. UVB and UVA radiation differ in their photophysical properties and penetrate into human skin to different extents. Accordingly, the shorter-wavelength UVB radiation is mostly absorbed in the epidermis and predominantly affects epidermal kerati-
nocyes and Langerhans cells, while the longer-wavelength UVA radiation penetrates more deeply and can interact with both epidermal cells and dermal fibroblasts. Recent studies indicate that a direct interaction of UVA radiation with the latter cell population is of enormous relevance for photoaging of human skin. This newly recognized pathway through which UVA radiation triggers photoaging of human skin is initiated in dermal fibroblasts by alterations at the level of mitochondrial (mt) DNA (24).

Evidence for a critical role of mtDNA mutations in photoaging of human skin originates from studies which demonstrate that chronically sun-exposed skin showing clinical signs of photoaging has a higher mutation frequency of the mtDNA than sun protected skin. Miyachi (24) noted that there was evidence that cumulative ultraviolet light insults result in generation of reactive oxygen species (free radicals) and that the presence of these species are associated with cumulative structural changes associated with photoaging. Wlaschek, et al. (25) noted that exposure to ultraviolet light type A (UVA 320-360 nanometers) led to an increase in reactive oxygen species, which in turn led to an upregulation and synthesis of interstitial collagenase in vitro. Increased activity of interstitial collagenase would correlate with increased collagen degradation and connective tissue damage. Another type of damage caused by solar UV radiation on the skin is immunosuppression (26-27), which is characterized by depleted counts of Langerhans’ cells (28-29) and inhibited contact hypersensitivity (30-31).

Biostimulation by dermal injection of different drugs is a well known procedure in order to reestablish the normal balance in collagen synthesis and re-absorption, to control melanogenesis and to contrast the oxidative effects of UV exposure. Ascorbate derivatives (vitamin C) suppress the effects of UV on human keratinocytes and fibroblasts (32), regulate epidermalization (33), make a free radical scavenging and stimulate extracellular matrix construction (34), stimulate collagen synthesis (35), inhibit melanogenesis in vitro and in vivo (36-37).

Low weight hyaluronic modulates proliferation, collagen and protein synthesis of fibroblasts (38), is a strong sub-cutaneous moisturizes, protects collagen against IL-1-induced inhibition of biosynthesis (39), represents a multifunctional carbohydrate mediator of immune processes (40).

Betaglucan appears to stimulate the large white blood cells called macrophages into action. These cells are a primary defense system for our bodies, identifying abnormal conditions and activating the appropriate therapeutic response. They literally devour bacteria, foreign cells, dead and dying cells, mutated cells, cancerous cells, and other negative invaders. Betaglucan's stimulation of macrophage cells produces a cascade of immune events, boosting immune response, stimulating the production of immune cells and improving host resistance. Besides the immunomodulatory effects, it has additional antioxidant properties (41), and stimulates human dermal fibroblast collagen biosynthesis through a nuclear factor-1 dependent mechanism (42).

Beyond biochemical correction of the damages due to sun exposure always present in skin photoaging, the biostimulation promotes the neocollagenesis together with the thermal subsurfacing action of the laser used in this protocol and helps the reduced collagen contraction and remodeling that results by the traditional erbium resurfacing (6-15). Thermal subsurfacing involves the thermal activation of collagen neogenesis. Several ablative pulses that heat up the stratum corneum. This heat is then transmitted to the upper dermis where the temperature of the tissue is raised to approximately 50 °C for a period of more
than 150 milliseconds. This leads to an activation of the fibroblasts and results in collagen neogenesis. The irritation of the upper epidermis represents another promoting factor of collagen neogenesis. The multidrugs dermal injections reduce the inflammation and the frequency of hypermelanosis due to the laser treatment. Moreover the oedema due to water recall done by low weight hyaluronic acid, spread out the skin and led us to do the laser peeling homogeneously over the skin surface.

**CONCLUSIONS**

On the basis of the data presented in this article, we conclude that the BI.LA.P technique seems to be a safe and effective method to correct skin’s textural changes of photoaging and improves superficial Er:YAG laser resurfacing results that in previous studies appear to play an important role in the treatment of mild to moderate photodamage. The short recovery time makes this procedure attractive for busy persons. The possibility of the thermal subsurfacing of the Burane XL™, WaveLight, certainly strengthen the results. This is a method of global skin care and let us to obtain better results in skin texture and firmness changes compared with the use of Intense Pulsed Light alone. A long-term follow-up study will determine how long the good endpoints will last.

![Fig. 1 A-B: 40 years old woman. A pre B 5 months after two sessions of BI.LA.P. technique.](image)
References


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