Combined Nonablative Skin Rejuvenation with the 595- and 1450-nm Lasers

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BACKGROUND. Histologic findings are not echoed in the visible effect in the epidermis after skin rejuvenation.

SUBJECTS AND METHODS. Ten women (Group A) received five treatment sessions with a 595-nm pulsed dye laser immediately followed by a 1450-nm diode laser. Two other demographically similar groups of 10 patients each, Groups B and C, were treated with the 595-nm pulsed dye laser or the 1450-nm diode laser alone, respectively.

RESULTS. Good dermal collagen remodeling was observed in Group A. Overall better and faster results were seen in Group A. The 6-month clinical outcome was best in Group A followed by Group C and Group B.

CONCLUSIONS. Wavelengths of 595 plus 1450 nm for skin rejuvenation produced good results with much higher patient satisfaction than those obtained with the 595- or 1450-nm wavelengths alone.

M. A. TRELLES, I. ALLONES, J. L. LEVY, R. G. CALDERHEAD, AND G. A. MORENO-ARIASHAVE, INDICATED NO SIGNIFICANT INTEREST WITH COMMERCIAL SUPPORTERS.

ABLATIVE LASER resurfacing produces very good results, but the associated downtime, the persistent erythema, and the risk of complications and side effects are very negative factors for patients.[1,2] In the past few years, nonablative skin rejuvenation has been introduced with a variety of modalities in the treatment of photoaged skin.

The aim of nonablative skin rejuvenation is to deliver a controlled dermal wound without harming the overlying epidermis, so that all stages of wound healing occur under the biologic protection of an intact epidermis. In addition to wrinkles, the treatment must include the entire photoaged skin and associated conditions including elastosis and pigmentary changes.[3] It is also clear that the zone of residual thermal damage associated with the ablative laser procedures must be at least in part delivered in the nonablative modalities to stimulate the necessary remodeling of the upper dermal collagen fibers, which will in turn tighten the overlying epidermis.[4,5] Hence we refer to this as delivered thermal damage.

Various modalities have been used, with and without skin cooling, including the continuous-wave Nd:YAG at 1064 nm, radiofrequency, electrosurgery, the 1320-nm line of the Nd:YAG, the 1450-nm diode laser, and the pulsed dye laser, both in its original form and in a model specifically developed for facial skin rejuvenation.[6–19] The use of intense pulsed light sources has also been reported.[20,21]

The major problem associated with the use of all types of nonablative skin rejuvenation is that the excellent dermal histology, with good collagen remodeling, is not always echoed in epidermal rejuvenation and patient satisfaction.[10,12–14,20] The long treatment regimens associated with this method also cause some problems with patient compliance.

Light powder micropeel, moisturizing, and antipigmenting creams have been reported to improve the result with intense pulsed light skin rejuvenation.[22] A more effective method is obviously needed to improve patient satisfaction to a level concomitant with the excellent histologic results reported in the upper dermal collagen.

This study was thus designed to examine and assess the efficacy of nonablative skin rejuvenation with a combination of two lasers at different wavelengths (595 and 1450 nm) compared with each wavelength used on its own.

Subjects and Methods

Subjects

The inclusion criteria included Fitzpatrick's skin phototypes I to IV inclusive, solar elastosis, telangiectasias, solar lentigos/lentigines, and wrinkles Types I to III. Type I wrinkles were defined as fine wrinkles seen with motion in association with mild elastosis, fine textural

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changes, and subtle accent of skin lines. Type II wrinkles were defined as a moderate number of fine wrinkles at rest, plus moderate-to-deep wrinkles with motion in association with moderate elastosis (visible translucent yellow papules under direct lighting) and some dyschromia. Type III wrinkles type were defined as a large number of fine-to-moderately deep wrinkles at rest and very deep wrinkles with motion in association with severe elastosis (thickened yellow multipapular skin under direct lighting and coarse on palpation) and a significant number of dyschromic lesions. Informed consent was obtained from all subjects. The study protocol conformed to the guidelines of the 1975 Declaration of Helsinki and was approved by our institutional review board.

The exclusion criteria included pregnancy, nursing, inflammatory skin diseases, open wounds, active herpes simplex, facial congenital/acquired nevi, and refusal to give signed informed consent.

Patients were enrolled in the trial and were allocated to three demographically similar groups of 10 patients each as follows. Group A was treated with a combination of the 595-nm pulsed dye and 1450-nm diode lasers. Group B was treated with the 595-nm pulsed dye laser alone and Group C was treated with the 1450-nm diode laser alone.

Group A (595+1450 nm)

Ages ranged from 29 to 64 years with a mean of 42.6 years. Skin phototype ranged from II to IV (II = 3, III = 3, and IV = 4). Wrinkle evaluation was graded II in two patients and III in the remaining subjects. Dyschromic lesions (actinic lentigos and lentigines) were more noticeable in Patients 1, 4, and 9.

Group B (595 nm)

Mean age was 43.8 years (range, 30–67 years). Skin phototype was II in two, III in five, and IV in three subjects, respectively. Dyschromic lesions were more evident in Patients 2, 7, and 10.

Group C (1450 nm)

Mean age was 44.7 years (range, 30–61 years). Phototype ranged from II to IV (II = 3, III = 5, and IV = 2). Wrinkle evaluation was graded II in four, III in five, and IV in one patient, respectively. Lentigos and lentigines were more evident in Patients 4, 6, and 9.

Laser Systems and Treatment

The lasers applied were, first, the 595-nm V Beam pulsed dye laser (Candela Corp., Wayland, MA) delivering 10 J/cm^2 per pulse, 10 ms per pulse, with a 7-mm-diameter spot size, and a 20-ms cooling cryospray before each laser pulse. The other system used immediately after the pulsed dye laser was a 1450-nm diode laser (Smoothbeam, Candela Corp.), also 10 J/cm^2, 4-mm-diameter incident beam with the system set to program 3 in which each 210-ms laser macropulse is accompanied by three 60-ms micropulses of cryogen spray that are delivered before, during, and after the laser pulse. In both systems overlapping was 0%. In Groups B and C only the 595-nm diode laser and the 1450-nm diode laser, respectively, were used on their own at the same parameters as above.

Treatment Protocol

Two days before the first session in all three groups, a light aluminum powder micropeel was administered using a device named Gentlepeel (Candela Corp.) once only, with the aim of giving the epidermis the “same” condition before starting the whole program of sessions. Two days after, patients were appointed to begin the treatment session, and in Group A the 595-nm pulsed dye laser was applied followed immediately by the 1450-nm diode laser at the parameters given above. In the case of Groups B and C, the 595-nm pulsed dye laser and the 1450-nm diode laser, respectively, were indicated on their own. No patient required anesthesia. There were five treatment sessions, with 2 weeks between Sessions 1 and 2 and 4 weeks between Sessions 2 through 5. Patients then returned on the 24th week after the 1st session (10 weeks after the 5th session) for final assessment and evaluation. All patients were advised to begin a regimen of adjunctive epidermal care using creams and to continue the regimen until the final assessment session. Advice was also given regarding avoiding solar exposure and the use of a UVA/B sun blocker with solar protection factor of 60 (SPF60).

Clinical Photography

Digital clinical photography and macrophotography (Sony MAVICA MVC-FD91) were carried out before each treatment session and then at the 24-week final control, maintaining uniformity in patient position, lighting, and camera setup. A separate diskette was kept for each patient to enable accurate repetition of the photography and follow-up. For histologic assessment, three patients as a cross-section of each group consented to having 1-mm punch biopsies taken from the preauricular region before the first session and at the 24-week final control. Clinical photography ensured that the same point was not biopsied more than once. The bilateral preauricular area was also treated in the biopsy volunteers in addition to the normal treatment areas.

Efficacy Assessment

The efficacy of skin rejuvenation was assessed objectively from the clinical photography by a panel consisting of two independent "blinded" dermatologists not involved in the trial and, subjectively, to assess patient satisfaction index, in two sets of structured patient interviews carried out at the 6th, 14th, and 24th weeks after the first treatment session by the same clinician each time. For all 30 patients, objective assessments were made before the first treatment session and Sessions 2 through 5 and at the 24-week final control. The external symptoms of elastosis, the degree of dyschromia, and the homogeneity or inhomogeneity of skin color were all assessed, together with the number of lines. The histologic specimens, stained with hematoxylin and eosin, were randomized, coded, and assessed by an independent blinded pathologist, who was asked first of all to rate the specimens according to the extent of the interfibrillary spaces, in addition to commenting on dermal architecture.

For the subjective analyses, first the patient satisfaction index was recorded on a five-level scale (worse, dissatisfied, fairly satisfied, satisfied, and very satisfied), and the total of "satisfied" and "very satisfied" was used to calculate the overall satisfaction as a percentage. Second, with the first treatment standardized at 20%, patients were asked to rate the percentage of improvement in each of five categories to a subjective maximum improvement of 100%: overall skin color, skin softness, wrinkles, melanin abnormalities, and blood vascular abnormalities. The results before treatments 3 and 5 and the final control point were averaged and charted.

Results

Thirty female patients were enrolled in the trial, 10 patients in each treatment group. All enrolled patients completed the course of treatments. Owing to the comparatively low power and energy densities associated with this treatment modality, no patient reported any side effects. During laser treatment, some patients reported slight discomfort, particularly when the 1450-nm diode was indicated. No patient refused further treatment.

In the case of Group A (Table 1), at the 6-, 14-, and 24-week points the overall satisfaction index was progressively better and at the last control: five (50%) were satisfied and two patients (20%) were very satisfied (overall satisfaction index 70%). Figure 1 shows graphically the patients' subjective assessment of the improvement in the individual items of melanin and vascular anomalies, skin softness, wrinkles, and skin color for Groups A (Figure 1A), B (Figure 1B), and C (Figure 1C). When comparing these graphs, obvious differences can be observed. Interpretation of the results demands remembering that each patient had her own idea of what "the best possible improvement" might mean, but none expected 100% improvement with nonablative versus ablative rejuvenation following our patient education program implemented and put in place at the beginning of the study. The low finding for melanin-pigmented anomalies in all groups should be noted. Also, there was a linear relation between the fifth treatment checkpoint and the 24-week checkpoint because there was no intermediate checkup during this 10-week period. The findings from the graph, however, echo fairly well the satisfaction index ratings. Results of Group A indicate higher satisfaction scores, when compared to those of Group B (overall satisfaction index 30%) and Group C (overall satisfaction index 40%), as presented in Tables 2 and 3, respectively.

Table 1. Five-Grade Subjective Patient Satisfaction Index (SI) in 10 Patients in Group A (595+1450 nm)

	Weeks after First Treatment					
	6		*14*		*24*	
SI Grade	*No.*	*Overall Satisfaction* (%)*	*No.*	*Overall Satisfaction (%)*	*No.*	*Overall Satisfaction (%)*
Worse	0	20	0	50	0	70
Dissatisfied	3		2		1	
Fairly satisfied	5		3		2	
Satisfied	2		4		5	
Very satisfied	0		1		2	

*Overall satisfaction = "very satisfied"+"satisfied" scores.

Tables 4 through 6 give the "blinded" independent assessors' findings in Groups A through C for skin improvement judged from the clinical photography. In Group A (Table 4), a steady improvement was seen in all aspects of the overall skin condition, particularly in the return to better morphology of skin furrows and turgidity and the return of homogeneity of appearance of the treated skin. The same situation was not obvious in Groups B and C as represented in Tables 5 and 6.

The homogeneity and appearance of the treated skin ties in well in Group A with the general skin color and vascular pigmentation improvements as noted subjectively by the study participants, a situation that received some improvement in Group B treated with the 595-nm pulsed dye, but not in Group C, treated

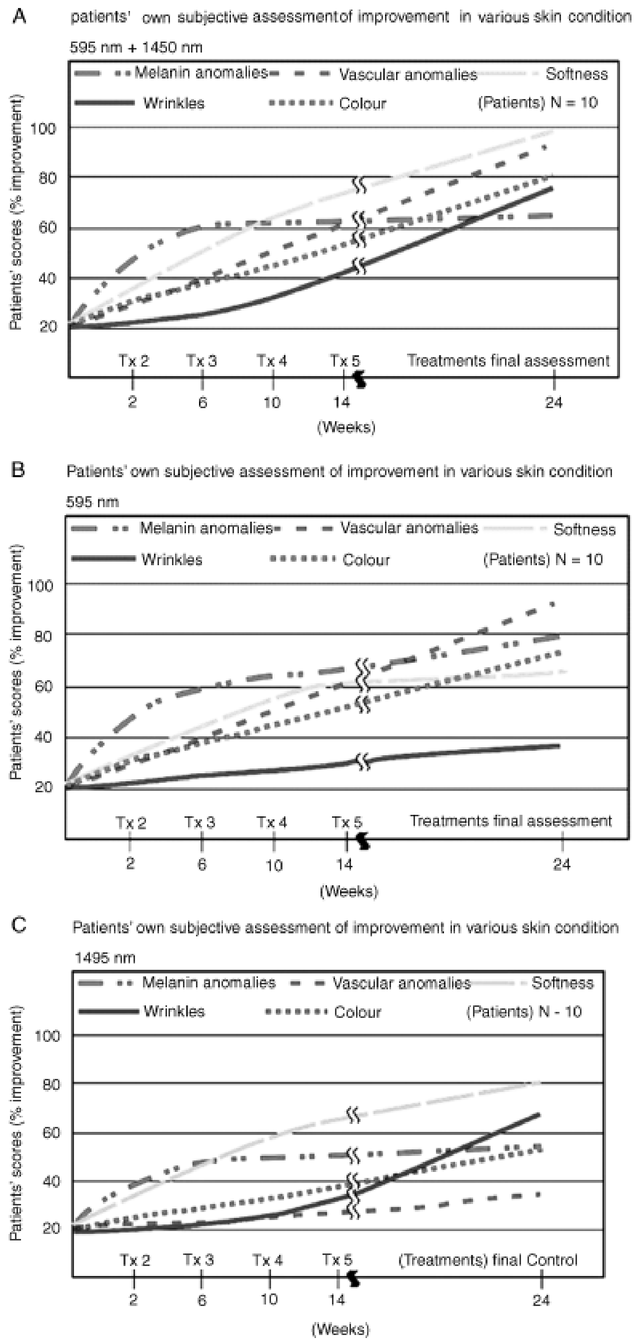

Figure 1. Patients' own subjective assessment of improvement.

with the 1450-nm diode laser. As for wrinkles, the improvement rate in Group A in the "numerous" ratings in Table 4 correlated well with the improvement seen in the wrinkle scores. In contrast to this, Group B (595 nm) did not show improvements in any of the patients treated, whereas in Group C (1450 nm), 4 patients of 10 were satisfied, with favorable changes to their wrinkle condition.

Typical histology before treatment and at the final control is shown in Figure 2 (Group A). Clinical photographic evaluation before treatment and 24 weeks after the first treatment session is shown in Figure 3 (Group A).

Table 2. Five-Grade Subjective Patient Satisfaction Index (SI) in 10 Patients in Group B (595 nm)

	Weeks after First Treatment					
	6		14		24	
SI Grade	*No.*	*Overall Satisfaction* (%)*	*No.*	*Overall Satisfaction (%)*	*No.*	*Overall Satisfaction (%)*
Worse	0	0	0	20	0	30
Dissatisfied	8		7		5	
Fairly satisfied	2		1		2	
Satisfied	0		2		3	
Very satisfied	0		0		0	

*Overall satisfaction = "very satisfied" + "satisfied" scores.

Discussion

This study presents a trial combining lasers of visible yellow (595 nm) and near infrared (1450 nm) wavelengths in the nonablative skin rejuvenation of photoaged skin. The aim of the treatment was not only to improve the appearance of wrinkles, but to remove comprehensively other symptoms of photoaging, meeting the criterion of "skin rejuvenation" as proposed by Bitter.[3] To achieve this, our goal is to use the "useful," minimally aggressive photothermal reactions which occur below the survival threshold of the laser-targeted cells to deliver a precise thermal damage and subsequent stimulative response to the upper layers of the target dermis. Rather than residual thermal damage associated with ablative laser resurfacing, we therefore

Table 3. Five-Grade Subjective Patient Satisfaction Index (SI) in 10 Patients in Group C (1450 nm)

	Weeks after First Treatment					
	6		14		24	
SI Grade	*No.*	*Overall Satisfaction* (%)*	*No.*	*Overall Satisfaction (%)*	*No.*	*Overall Satisfaction (%)*
Worse	0	0%	0	30%	0	40%
Dissatisfied	7		6		3	
Fairly satisfied	3		1		3	
Satisfied	0		3		4	
Very satisfied	0		0		0	

*Overall satisfaction = "very satisfied" + "satisfied" scores.

Table 4. Evolution of Aging Skin Signs According to Objective Panel Assessment from Clinical Photography in Group A (595+1450 nm)*

Item	*Treatment 1*	*2*	*3*	*4*	*5*	*Final Assessment*
Skin elastotic signs and texture						
Yellow translucent	3	3	4	5	6	7
Thickened yellow	4	4	3	3	2	1
Folds and furrows/turgidity	3	3	3	2	2	2
Homogeneity of skin color						
Homogeneity	2	2	2	4	5	3
Inhomogeneity	8	8	8	6	5	7
Number of lines						
Numerous	7	7	7	5	3	3
Moderate	3	3	3	5	7	7

*Numbers indicate number of patients.

suggest the term "delivered thermal damage" as a better term to describe the aim of this treatment.

The single micropeel of the epidermis with an aluminum powder based system 2 days before starting our series of treatments in all three groups serves two purposes: it first removes the rather disorganized and highly reflective top layer of keratin from the stratum corneum and, second, it improves the "dull" appearance of a photoaged epidermis, immediately improving the patients' appearance from the first treatment session, extremely important when assuring patient compliance with a comparatively long treatment process. Although micropeeling has also been shown to bring about beneficial morphologic changes to both the epidermis and the superficial dermis,[21] we do not believe that it caused any skewing of the data in this study, because it was carried out 2 days before starting the laser sessions and in all patients of all three groups.

Table 5. Evolution of Aging Skin Signs According to Objective Panel Assessment from Clinical Photography in Group B (595 nm)*

Item	*Treatment 1*	*2*	*3*	*4*	*5*	*Final Assessment*
Skin elastotic signs and texture						
Yellow translucent	5	5	5	6	6	6
Thickened yellow	3	3	3	2	2	2
Folds and furrows/turgidity	2	2	2	2	2	2
Homogeneity of skin color						
Homogeneity	2	2	3	3	5	5
Inhomogeneity	8	8	7	7	5	5
Number of lines						
Numerous	5	5	5	5	5	5
Moderate	5	5	5	5	5	5

*Numbers indicate number of patients.

Table 6. Evolution of Aging Skin Signs According to Objective Panel Assessment from Clinical Photography in Group C (1450 nm)*

Item	*Treatment 1*	*2*	*3*	*4*	*5*	*Final Assessment*
Skin elastotic signs and texture						
Yellow translucent	4	4	4	6	6	6
Thickened yellow	3	3	3	1	2	2
Folds and furrows/turgidity	3	3	3	3	2	2
Homogeneity of skin color						
Homogeneity	3	3	3	3	3	3
Inhomogeneity	7	7	7	7	7	7
Number of lines						
Numerous	6	6	6	4	3	3
Moderate	4	4	4	6	7	7

*Numbers indicate number of patients.

We deliberately chose lower power and energy densities for this study and elected to give five treatment sessions rather than any fewer to control patient discomfort and enhance patient compliance with the protocol. The fact that no patient reported any complications and all completed the protocol also justified our protocol parameters.

Infrared lasers stimulate dermal collagen remodeling with minimal or no postoperative sequelae.[23] Tanzi and Alster[24] have shown that both long-pulsed 1320-nm Nd:YAG and 1450-nm diode lasers offer clinical improvement for patients with atrophic scarring. Nevertheless, the 1450-nm diode laser showed greater clinical scar response. Moreover, the 1450-nm diode laser is a noninvasive safe treatment to induce clinical improvement of photoaging skin but results are in general modest as described by Tanzi et al.[25] The same author reports that clinical improvement is seen at 6 months after a series of treatments but results had

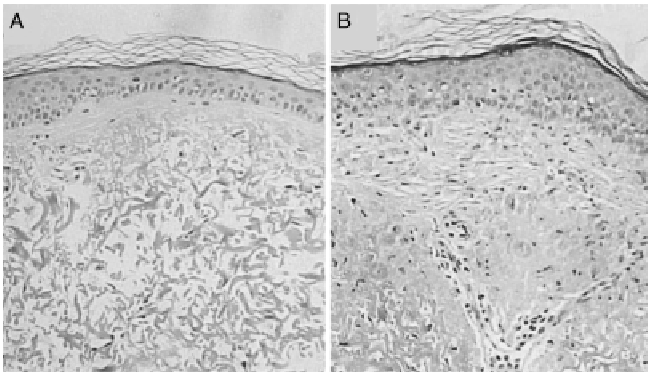

Figure 2. Representative histology of skin before and after treatment with combined nonablative 595- and 1450-nm laser skin rejuvenation. Hematoxylin and eosin, skin × 250. (A) Pretreatment findings; (B) 24-week control.

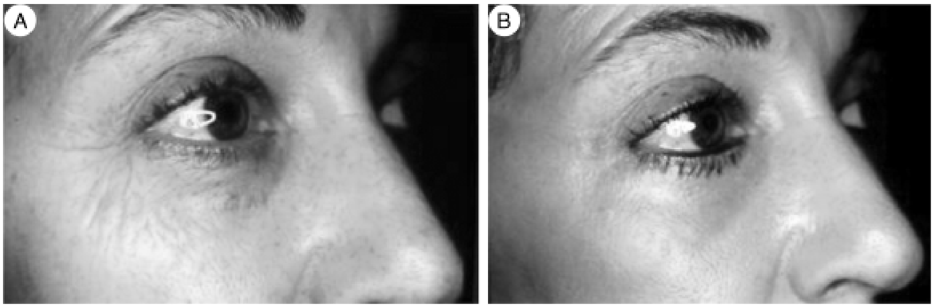

Figure 3. A 38-year-old woman with Caucasian skin type IV in Group A (595+1450 nm). (A) Before treatment; (B) after treatment.

diminished by the 12th month after the initial treatment session. This suggests that good maintenance of the repair process, particularly the proliferative and remodeling stages, caused by delivered thermal damage-mediated tissue stimulation combined with a stronger initial stimulus may well solve this problem. This justifies the rationale behind our method of treatment, which stimulates more neocollagenesis and subsequent remodeling in tissue via the synergistic action of 595- and 1450-nm laser energy delivered sequentially in the same treatment session. This phenomenon has been also noticed by Katz[26] who has reported that a combination of both wavelengths is more effective for nonablative cutaneous rejuvenation when compared with the 1450-nm diode or the 595-nm pulsed dye laser used alone.

The typical histologic findings we found following 1450-nm diode laser treatment on its own correlate well with the conclusions of Hardaway and colleagues[27,28] in which they stated that the 1450-nm diode laser was capable of targeting collagen stimulating fibrosis deep in the dermis, corresponding to a maximum depth of 644 μm from the skin surface.[27] Although the good histologic effects induced by the 1450 m diode laser were not translated into equally good clinical results as far as the appearance of rhytides[27] when energy of the same wavelength is applied in combination with the more superficial action of the 595-nm wavelength of the pulsed dye laser, as presented in our study, the result was good improvement in all aspects of the photoaged skin, including the appearance of rhytides, which was echoed in the better patient satisfaction index recorded for the combination Group A compared with the 1450 nm Group C.

The two laser wavelengths have different biotargets. The 595-nm subpurpuric pulsed dye laser targets the relatively superficial chromophores of this visible yellow light wavelength, namely, hemoglobin and melanin chromophores. The near-infrared wavelength of 1450-nm has as its chromophores the macromolecular proteins that are found in abundance in the dermis. In addition, this wavelength is significantly absorbed in water. The combination of these absorption characteristics helps limit the local, nonspecific dermal heating to depths of around 400 to 600 μm,[27] an ideal depth to ensure the delivered thermal damage-mediated wound repair process. The combination of the two wavelengths, coupled with the epidermal cooling systems used in both lasers, gives a controlled and enhanced buildup of upper dermal heat under an intact, cooled epidermis, resulting in a high level of controlled accumulative heat damage leading to enhanced collagenesis, elastinogenesis, and angiogenesis in the superficial and upper reticular dermis during the proliferative phase of wound healing, followed by good linear alignment of the collagen fibers running under the dermal-epidermal junction and firmly attached to its basement membrane.

Although the yellow beam concentrates on treating the vascular and mild pigmentary changes in the superficial dermis, pulsed yellow light has also been associated with the release of photoproducts important in the wound healing process from the targeted microvasculature.[17] After the removal of the vascular-associated pigment from the superficial dermis, the subsequent shot of 1450-nm light might penetrate deeper. In addition to the dermal chromophores of near-infrared wavelengths mentioned above, this waveband is also associated with induction of long-lasting heat-shock proteins of a specific type (Hsp 70) in the animal model,[22] and this may well be extrapolated to the human skin, although this has yet to be proved experimentally and maybe only a epiphenomenon of stress. Nevertheless, heat-shock proteins are associated with the de novo synthesis of protein in dermal structures, particularly around sebaceous glands, hair follicles, and blood vessels,[29] which cannot be anything but beneficial to the wound healing process in general and collagenesis in particular. The distribution of a further dose of delivered thermal damage (delivered thermal damage) over and above that already deposited by the 595-nm pulsed dye laser will substantially raise the temperature in the upper dermis, while leaving the cooled epidermis unharmed.

Patients who received the joint treatment (Group A) actually received two times as many laser treatment sessions as the other individuals in Groups B or C. Consequently, it could be argued that the dual treatment was better only because it required more treatments. Our combined treatment, however, could be thought of as more aggressive than has been previously reported in similar studies.[30,31] Additionally, we believe that the combination of these wavelengths produces an increased level of nonselective stimulative photothermal dermal irritation that acts as a stimulus to accelerate and enhance the wound healing process, and no undesirable side effects were reported by any patient.

Conclusions

Each of the two wavelengths used in this study on nonablative skin rejuvenation has been associated on their own with good histology but less patient satisfaction than the histology warrants. A skin rejuvenation regimen of a combination of 595 and 1450 nm produced good patient satisfaction with this process compared with result obtained in another two groups of patient of similar skin characteristics in which treatments were performed with only one laser wavelength. We therefore suggest that combining different laser wavelengths is a useful tool to boost the effect in the nonablative skin rejuvenation arena. The disadvantages of this protocol are that two laser systems are required, and the time taken for the two treatments in the one session is obviously greater than with a single modality. Nevertheless, the very much higher patient satisfaction may well compensate for this. Patient satisfaction, we believe, should not be neglected by clinicians in favor of "pure science," and so any demonstrated benefit to the patients of any particular protocol should outweigh its scientific validity, plus the cost-effective nature of the protocol for the patient.

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