Photorejuvenation by Intense Pulsed Light with Objective Measurement of Skin Color in Japanese Patients

Kei Negishi, MD,^{*†} Nobuharu Kushikata, MD,^{*†} Kaori Takeuchi, MD,[†] Yukiko Tezuka, MD,^{*†} and Shingo Wakamatsu, MD^{*†}

BACKGROUND AND OBJECTIVES This study had two objectives: subjective evaluation of overall skin rejuvenation effects of relatively short-wavelength intense pulsed light (IPL) and objective changes in basic skin tone as measured by a spectrophotometer.

STUDY DESIGN/MATERIALS AND METHODS Twenty-five women selected at random received a series of three IPL treatments. Efficacy was evaluated over a 3-month follow-up period. Concurrently, a spectrophotometer was used to measure "lightness" (L^{*}) to quantify the lightening effect changes to pretreatment and posttreatment basic skin tone.

RESULTS Subjective improvement of 50% or more was seen in 18 of 25 patients for pigmentation. One patient showed exacerbation of latent epidermal melasma as a complication. In the spectrophotometric analysis, the mean value of L^* increased from a baseline value of 60.86 to 63.22, at 3-month follow-up period, with statistical significance.

CONCLUSION IPL skin rejuvenation using relatively shorter wavelengths and pulse widths brought about significant macroscopic and quantitative improvements, especially in the treatment of epidermal pigmentation and improvement of basic skin tone.

The equipment used in the study was provided by Darish Dermatologic Development.

Tt is widely known that skin re-L juvenation by intense pulsed light (IPL) improves various symptoms of photodamage. In our department's facility, the improvement of pigmented lesions and irregular pigmentation is the most frequent and primary request of patients seeking IPL treatment. Methods for obtaining satisfactory results with high efficacy include increasing fluence or using relatively short wavelengths for enhanced melanin absorption. It is also possible to use shorter pulse widths to more aggressively affect the melanin-saturated epi-

dermis. In Japanese patients with darker skin types, however, careful attention must be paid to balance fluence and other parameters to prevent complications such as thermal burns. In contrast, if fluence is set too low, results may be unsatisfactory.

In the current study, the authors investigated the efficacy of using relatively short wavelengths when the main objective was the improvement of pigmentation. Patients and physicians provided subjective evaluations, and a spectrophotometer was also used to quantify changes to what is called "baseline skin tone lightning effect." By way of background, there is tremendous demand among Japanese females for a "lightening improvement" of basic skin tone (concurrently referred to as "whitening"). This demand has been clearly demonstrated by the large variety of retail cosmetics offered for sale for whitening improvement.

Japanese basic skin tone varies from fair to dark due to geography and ethnicity, and it is suspected that prolonged exposure to

*Tokyo Women's Medical University Aoyama Institute of Women's and Natural Medicine, Tokyo, Japan; [†]Department of Aesthetic Surgery, Tokyo Women's Medical University Tabata NSK Clinic, Tokyo, Japan

© 2006 by the American Society for Dermatologic Surgery, Inc. • Published by Blackwell Publishing • ISSN: 1076-0512 • Dermatol Surg 2006;32:1380–1387 • DOI: 10.1111/j.1524-4725.2006.32283.x

ultraviolet (UV) rays increases the darkness of basic skin tone. Patients undergoing IPL therapy see subjective improvements in areas with obvious dyschromia, but they also consistently remark that basic skin tone improves (that is, that it becomes lighter than pretreated skin). As such, spectrophotometric readings were taken to measure what patients call the "whitening effect" that results from facial IPL therapy.

Materials and Methods

Patients

Twenty-five Japanese women (ages 31–68 years; mean age, 50 years; SD, 9.0 years) with Fitzpatrick skin types III and IV were randomly recruited and underwent IPL treatment and skin color measurement. Informed consent was obtained from all patients. Patients that had received any skin rejuvenation procedure during a 6-month period before the study, patients with severe melasma, and patients with conditions such as photosensitivity that might affect treatment were excluded from the study.

Regarding sunscreen usage, the authors allowed subjects to decide if they would use or not use sunscreen after treatment in accordance with the subject's prior experience and lifestyle habits. For habitual users, continued use was allowed, while for nonusers, usage was not required. Sunscreen users were 5 cases with the remaining 20 cases nonusers. To more objectively segment subjects in accordance with their relative degree of photodamage, the authors developed a unique threestage visual classification system. Using the photo model scale



mild

moderate

severe

shown in Figure 1, classified by photodamage, 3 cases were severe, 6 were moderate, and 16 were mild, and UV photography revealed 4 cases with latent melasma.

Treatment Method

Equipment The authors used an intense pulsed light [Ellipse Flex, Danish Dermatologic Development (DDD), Hoersholm, Denmark] with a PR applicator that emitted 530 to 750 nm (peak wavelength, 661 nm) in a 10 × 48-mm spot.

IPL Treatment

The authors performed repeated full-face treatments at intervals of 3 to 4 weeks. The patients were instructed to completely remove makeup and to wear goggles during irradiation. Relatively short 2.5-ms double pulses with a delay time of 10 ms were employed to elicit a sufficient response in the melanin-saturated epidermis. A chilled colorless gel was applied to the filter to effectively couple light delivery to the skin, and irradiation was performed with only slight contact between the filter and the skin surface. Test irradiations were performed on a preauricular area to establish the optimal fluence. A slightly pinkish reaction was considered to be the irradiation end point on skin with no pigmented lesions. For skin with pigmented lesions, a brown, slightly darker color change was considered to be the irradiation end point. If this reaction was not



Figure 2. Photofixation and lighting system.

obtained at a pigmented lesion site after full-face irradiation had been performed at the set fluence, irradiation was repeated two or three times on the sites. The fluences set by this end point determination method at each treatment were 5.5 to 7.0 J/cm² (mean, 6.40; SD, 0.32) at the first, 5.5 to 7.0 J/cm² (mean, 6.76; SD, 0.39) at the second, and 6.5 to 8.0 J/cm² (mean, 7.38; SD, 0.33) at the third treatment.

If the patient felt a burning sensation immediately after the treatment, the area was cooled with an ice pack until the symptoms resolved. The only restriction on daily activities after treatment was to avoid irritating areas with pigmented lesions until the superficial fine crust (so-called "microcrust"¹) that formed in the area naturally sloughed off (typically after a mean of 5 days postirradiation). The use of makeup was permitted immediately after treatment. Digital photographs were taken at each visit using an original facial photo and fixation system (DDD; Figure 2). The system was used under the same lighting system in the same condition.

Skin Color Measurement

The authors used a spectrophotometer (Model 2600d, Minolta, Osaka, Japan) to analyze basic skin tone. This spectrophotometer employs a xenon arc lamp emitting wavebands from 460 to 760 nm at 10-nm intervals. Reflected light is detected by a silicon photodiode array housed in a dual 40 glass element structure. This device calculates tristimulus color analysis from spectral reflectance data for the "lightness" (L*), a*, and b* values. The conventional parameter of L* shows skin reflectance or lightness on a gray scale with values from 0 (totally black) to 100 (totally white). Use of a spectrophotometer to measure skin spectral and colorimetric

values for a variety of research purposes is well documented.^{2–6} The sensitivity and accuracy of the spectrophotometer employed in this study was with a standard deviation for colorimetric values of $\Delta E^*ab 0.04$.

Two measurements of skin with no obvious pigmented lesions or other dyschromias were taken by a trained physician before the first treatment (baseline value), additionally at 1 month after the third treatment, and finally at 3 months after the third treatment. The same area for all patients—an 8-mm-diameter spot at the midpoint of the line between the outer canthus of the eye and the border of nasal ala—was measured each time.

Clinical Evaluation

Efficacy was evaluated by both physicians and study subjects. Two physicians with extensive experience in IPL and other light sources who did not treat any cases in this study assessed digital photographs, and study subjects completed questionnaires at 1 and 3 months after the third treatment. Evaluations were performed according to the following five parameters using a five-grade percentage improvement scale from A to E: A = 75% - 100%, B = 50% - 74%, C = 25% - 49%, D = 1% - 24%, and E = no change or worse. Evaluations were performed at 1 and 3 months after the third treatment.

Images were taken before treatment with a UV camera (Canfield Imaging Systems, Fairfield, NJ) to assess the presence of very subtle epidermal melasma, and these images were used as an aid in considering the relationship between therapeutic efficacy and complications.

Spectrophotometric Analysis

Two measurements with the spectrophotometer were taken at each visit, and readings were averaged and used to evaluate the changes between the baseline L* values and the values 1 and 3 months after the third treatment. The patients were divided into two cohorts based on high and low baseline melanin and L* values, and the differences in numerical values between the two cohorts were evaluated. The results were then subjected to statistical analysis (Student's t test).

Results

Clinical Efficacy

Subjective patient evaluations versus physician evaluations of B or better were, respectively, as follows: for pigmentation improvement, 72.0% versus 64.0%; for fine wrinkle reduction, 21.7% versus 17.3%; for skin texture improvement, both 96.0%; and for enlarged pore reduction, 32.0% versus 20%. Overall satisfaction was evaluated by patients only, and 36.0% reported "extreme satisfaction," 52.0%

"very satisfied," 12.0% "satisfied," and no cases reported either "slight satisfaction" or "unsatisfied." In the results three months after the third treatment (Table 1), physicians observed a regression (darkening) in basic skin tone in two patients. Both patients were diagnosed to have latent melasma based on a comparison to pretreatment UV camera photo images. One of these patients reported a subjective exacerbation of melasma as a complication. Three patients reported further improvement in fine wrinkles in the patient evaluations, and one of those also reported an improvement in skin texture and elasticity. There was no correlation between the evaluated results and severity of photodamage.

For skin areas with pigmented lesions, 3 to 5 days elapsed before the superficial fine crust sloughed off. The only complication was a burning sensation that persisted for more than 2 hours after irradiation in two patients. In one patient erythema that persisted for more than 2 hours after irradiation was reported as a complication, and in that patient an exacerbation of very subtle epidermal melasma was seen at a visit of 3 months after the third treatment. According to the patient, worsening of the skin color (darkening) gradually emerged beginning 4 to 5 weeks after the third treatment. In the other patient, erythema was observed but without other complication. No other complications such as blisters, hypopigmentation, or skin atrophy were observed.

Spectrophotometric Analysis

Twenty-two of 25 cases showed an increased L* value at the 1- and 3-month follow-up periods. The recorded L* values were as follows: mean at baseline, 60.68 (range, 57.45-66.02; SD, 2.11); mean at 1 month after the third treatment, 62.82 (range, 58.60-68.19; SD, 2.32); and mean at 3 months after the third treatment, 63.22 (range, 59.68-68.17; SD, 2.32). Student's t test analysis showed a statistically significant increase in lightness between the baseline (pretreatment) value and the value at 3 months after treatment (p = .001), and there were no significant differences between the 1- and 3-month follow-up data. Two cohorts of 12 patients each were formed based on high or low baseline L* values, and an intergroup comparison of the improvement rate 3 months after treatment was performed. The mean improvement rate in the cohort with the high L* values was 2.10% (range, 2.20%-5.23%; SD, 0.02%), and the mean improvement rate in the cohort with low L* values was 5.15% (range, 0.75%-9.81%; SD, 0.02%). The cohort with the lower baseline L* values showed a higher improvement rate (p = .005).

Clinical Cases

Case 1 Figure 3 shows a 55-year-old woman (sunscreen nonuser)

TABLE 1. The Results after the Third Treatment st	ts after the	e Third Treat	ment*									
	Pigmenta	Pigmentation (n = 25)		Fine Wrii	Fine Wrinkles (n = 23)		Skin Textu	Skin Texture (n=25)		Enlarged	Enlarged Pores (n=25)	(
	Combined	q		Combined	q		Combined			Combined	ł	
Measure	Patients	Patients Physician	(%)	Patients	Patients Physician	(%)	Patients	Physician (%)	(%)	Patients	Physician (%)	(%)
Percent improvement												
A: 75%–100%	8 (32.0)	8 (32.0) 4 (16.0)	24.0	(0) 0	1 (4.3)	2.2	17 (68)	12 (48)	58.0	(0) 0	1 (4)	2
B: 50%–74%	10 (40.0) 12 (48.0)	12 (48.0)	44.0	5 (21.7)	5 (21.7) 3 (13.0)	17.4	7 (28)	12 (48)	38.0	8 (32)	4 (16)	24.0
C: 25%–49%	7 (28.0)	7 (28.0)	28.0	16 (69.6) 15 (65.2)	15 (65.2)	67.4	1 (4)	1 (4)	4.0	14 (56)	18 (72)	64.0
D: 1%–24%	0 (0)	2 (8.0)	4.0	2 (8.7)	2 (8.7) 4 (17.4)	13.0	0 (0)	(0) 0	0	3 (12)	2 (8)	10.0
E: 0%	(0) 0	(0) 0	0	(0) 0	0 (0)	0	0 (0)	(0) 0	0	(0) 0	(0) 0	0
Degree of satisfaction $(n=25)$	(n = 25)											
Extremely	9 (36.0)											
Very	13 (52.0)											
Satisfied	3 (12.0)											
Slightly	(0) 0											
Unsatisfied	(0) 0											

Data are reported as number (%).

with conspicuous pretreatment pigmented areas. These were clearly improved after three treatments with approximately 4-week intervals between treatments. The improvement rate of the L* value was 5.81% (before, 59.31; after, 62.75).

Case 2 Figure 4 shows a 49-yearold woman (sunscreen nonuser) with enlarged pores and diffuse redness before treatment. Improvement was seen in these areas, but seborrheic keratosis, however, did not completely clear. The improvement rate of the L* value was 0.81% (before, 61.92; after, 62.43).

Case 3 Figure 5 shows a 50-yearold woman (sunscreen user) with subtle epidermal melasma. Three months after the third treatment with approximately 4-week intervals between treatments, improvement in skin texture and an overall lightening effect were obtained, but melasma-like pigmentation or exacerbated melasma can be observed.

Discussion

One feature of IPL full-face rejuvenation is that multiple symptoms of photoaging can be improved concurrently by repeated treatments. The effect of IPL full-face rejuvenation does not completely eliminate any of the symptoms, but it improves them comprehensively. Japanese patients (skin typically classified as III to IV according to the Fitzpatrick Skin Type scale⁷) run a high

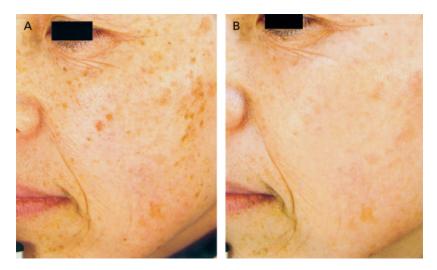


Figure 3. A 55-year-old woman, 1 month after three treatments at approximately 4-week intervals. There was marked improvement in pigmented spots. (A) Before and (B) 1 month after the third treatment.

risk of postinflammatory hyperpigmentation as a result of the excessive inflammation caused by laser therapy. In comparison, the authors have not encountered postinflammatory hyperpigmentation in our treatment of agerelated pigmentation problems (excepting patients exhibiting latent or subtle epidermal melasma) when using IPL, so this modality is an extremely desirable option even though the efficacy of removing dyschromias is slightly less than when lasers are employed.⁸ In addition, when melasma is encountered, the authors have been able to obtain satisfactory results by adjusting parameters and using combination

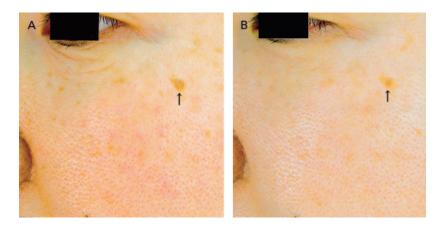


Figure 4. A 49-year-old woman, 3 months after three treatments at approximately 4-week intervals. Improvement in enlarged pores accompanied with improvement in diffuse redness. (A) Before and (B) 3 months after the third treatment. Arrow shows the seborrheic keratosis.

therapies.^{9,10} It is believed that these reasons underscore why IPL treatment is easily accepted by both patients and physicians.

When using relatively shorter wavelengths and shorter pulse widths, it is necessary to lower fluence to perform safe and effective treatment of Japanese patients (and other patients of Asian ethnicity). The shorter wavelengths and pulse widths have a powerful effect on melaninsaturated keratinocytes, leading to epidermal burns and potentially postinflammatory hyperpigmentation. When this study is compared with the report of Bjerring and colleagues¹¹ in which the same filter and pulse width settings were used, the mean fluence setting in their study was 7.9 J/ cm^2 , whereas the mean fluence setting in this study was 6.5 J/cm². The authors were initially concerned that lowering fluence would result in decreased efficacy with respect to related parameters other than pigmentation such as skin texture, enlarged pores, and fine wrinkles, but it was found that the results are similar to those in our previously conducted study of IPL using longer wavelengths (560-1200 nm).⁸ It is suspected that very good results were seen in the improvement of skin texture and elasticity because a relatively rapid temperature rise in the superficial dermis stimulates fibroblast activity better than a slow rise. Normally, skin texture improvement is attributed to der-

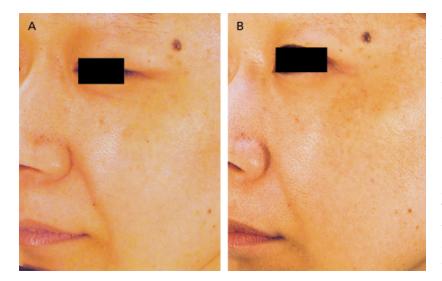


Figure 5. A 50-year-old woman. (A) Pretreatment findings. (B) The findings 3 months after the third treatment. Exacerbated melasma can be seen on the upper cheek.

mal remodeling and proliferation of the dermal component, but it is believed change in epidermis is experienced subjectively as an improvement in skin texture, and it should be given further consideration. Hernandez-Perez and Ibiett¹² have reported that turnover of the epidermis is accelerated, loss of polarity in keratinocytes is corrected, and an increase in epidermal thickness is seen with IPL treatment. It has been found that patients nearly universally remark that post-IPL-treated skin is noticeably smoother and that pores appear smaller, and it is surmised that visual improvement (reduction) of fine wrinkles and skin pore appearance comes from the dual benefits of collagen synthesis and regeneration of epidermal skin.

Human skin color is determined mainly by melanin and hemoglobin. Both of these are reflected in the parameters obtained by the spectrophotometer used, and the value that expresses nominal whiteness is the L* value.¹³ Therefore, L* was selected as a parameter in this study, and the measurement results showed a statistically significant increase in the L* value in basic skin tone. Many patients of Asiatic ethnicity suffer not only from specific dyschromias and maculae but also from diffuse and irregular pigmentation over the entire face due to chronic sun exposure. This study demonstrates that IPL treatment can arrest and even potentially reverse the progression of darkening skin (as measured by lightness) due to cumulative ultraviolet exposure.

When the patients were divided into two cohorts with high and low L* values and an intergroup comparison of the difference in lightness values was performed, a higher rate of change was seen in the cohort with lower baseline values. According to the report by Alaluf and coworkers,¹⁴ melanin content and L* value do not have a linear correlation but an exponential relationship, and in persons with lighter skin color, a small change in melanin content is manifested as a large change. Therefore, if the melanin content was decreased by about the same extent in both cohorts by IPL treatment in this study, the results are puzzling. When it is considered that the cohort with the high baseline value included many patients with severe photodamage, delayed epidermal turnover, and often mixed with diffuse erythema as a complication, however, it is not a logical contradiction that the cohort with the lower L* value, which reflects both the melanin and the hemoglobin values, would show a high rate of improvement. In any event, although the change in skin color was evaluated objectively in this study, changes to basic skin tone requires further investigation.

Complications

In the current study, one patient showed exacerbated melasma as a complication. In this patient, subtle epidermal melasma was present before treatment. Other patients with latent melasma, however, showed improvements. As has been reported previously, it is believed that inflammation due to IPL irradiation acts as a trigger and that melasma is manifested as postinflammatory hyperpigmentation.¹⁵ It has been our clinical experience that most subtle or latent melasma cases do not, however, develop or show exacerbated melasma as the result of IPL therapy. That is why the authors did not exclude all patients showing subtle or latent melasma in this study. It has been found that most patients diagnosed with latent or subtle melasma will typically not suffer exacerbation provided that irradiations are not performed with excessive fluence. To minimize complications in these patients and all patients, it is necessary to ascertain the treatment end point carefully through progressive test shots and to actively cool irradiated areas immediately after treatment.

Conclusion

Patients obtained a high level of satisfaction with three repeated treatments of IPL skin rejuvenation using an Ellipse Flex intense pulsed light with a PR filter. In comparison to the eight different IPL devices that have been used at our facility, the device in the current study is unique in that its wavelength band for skin rejuvenation is relatively short. In comparison with longer-wavelength bands employed on other IPL devices, it was found that the short range is actually well suited for treating pigmentation-related disorders. Even for patients exhibiting latent melasma, with careful

setting selection, the device is both safe and effective. In addition, the design of the applicator head is well conceived to enhance visualization of the treatment area as well as being lightweight. Through employment of spectrophotometry, the authors also showed that repeated IPL treatments could alter basic skin tone values. Since Japanese patients desire improvement of obvious pigmented areas as well as "lighter" or "whiter" skin, spectrophotometry is a useful method to quantify changes.

References

- Kawada A, Shiraishi H, Asai M, et al. Videomicroscopic and histopathological investigation of intense pulsed light therapy for solar lentigines. J Invest Dermotol 2002;29:91–6.
- Chan HH, Wong WS, Lam LK, et al. The use of pulsed dye laser for the prevention and treatment. Dermatol Surg 2004;30:987–94.
- Park SB, Huh Ch, Choe YB, et al. Time course of ultraviolet-induced skin reactions evaluated by two different reflectance spectrophotometers: Derma-Spectrophotometer and Minolta spectrophotometer CM-2002. Photoderm Photoimmun Photomed 2002;18: 23–8.
- Chambers MA, Jahans K, Whelan A, et al. Simple objective measurement of the cutaneous delayed-type hypersensitivity reaction to tuberculin using spectrophotometry. Skin Res Ther 2002;8:89–93.
- Oliveira GV, Chinkes D, Mitchell C, et al. Objective assessment of burn scar vascularity, erythema, pliability, thickness, and planietry. Dermatol Surg 2005;31:48–58.
- 6. Takiwaki H, Serup J. Measurement of color parameters of psoriatic plaques by narrow-band reflectance

spectrophotometry and tristimulus colorimetry. Skin Pharmacol 1994;7:145–50.

- Fitzpatrick TB. The validity and practicality of sun-reactive skin types one through six. Arch Dermatol 1988;124:869–71.
- Negishi K, Wakamatsu S, Kushikata N, et al. Full-face photorejuvenation of photodamaged skin by intense pulsed light with integrated contact cooling: initial experiences Asian patients. Lasers Surg Med 2002;30:298–305.
- Negishi K, Wakamatsu S. Pigment-control therapy for melasma in Asian skin: a new treatment approach. Lasers Surg Med 2003;Suppl 15:72.
- Wang CC, Hui CY, Sue YM, et al. Intense pulsed light for the treatment of refractory melasma in Asian persons. Dermatol Surg 2004;30:1196–200.
- Bjerring P, Christiansen K, Troillius A, et al. Facial photo rejuvenation using two different intense pulsed light (IPL) wavelength bands. Lasers Surg Med 2004;34:120–6.
- 12. Hernandez-Perez E, Ibiett EV. Gross and microscopic findings in patients submitter to nonablative full-face resurfacing using intense pulsed light: a preliminary study. Dermatol Surg 2002;28: 651–5.
- Yoshimura K, Harii K, Masuda Y, et al. Usefulness of a narrow-band reflectance spectrophotometer in evaluating effects of depigmentation treatment. Aesthetic Plast Surg 2001;25:129–33.
- Alaluf S, Atkins D, Barrett K, et al. The impact of epidermal melanin on objective measurements of human skin color. Pigment Cell Res 2002;15:119–26.
- Negishi K, Kushikata N, Tezuka Y, et al. Study of the incidence and nature of "very subtle epidermal melasma" in relation to intense pulsed light treatment. Dermatol Surg 2004;30:1–6.

Address correspondence and reprint requests to: Kei Negishi, MD, Tokyo Women's Medical University Aoyama Institute of Women's and Natural Medicine, 2-7-13 Kita-aoyama, Minato-ku, 107-0061 Tokyo, Japan, or e-mail: keinegishi@aol.com