# Q-Switched 660-nm Versus 532-nm Nd:YAG Laser for the Treatment for Facial Lentigines in Asian Patients: A Prospective, Randomized, Double-Blinded, Split-Face Comparison Pilot Study

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BACKGROUND Q-switched (QS) 532-nm lasers are widely used to treat solar lentigines.

OBJECTIVE To compare the efficacy and safety of 660-nm and 532-nm QS neodymium-doped yttrium aluminum garnet (Nd:YAG) lasers in the treatment for lentigines in Asians.

MATERIALS AND METHODS The halves of each face (randomly chosen) of 8 Korean Fitzpatrick Skin Type III–IV women with facial solar lentigines were treated with either 660-nm or 532-nm lasers. Pigmentation was measured objectively using a profilometric skin analysis tool and subjectively using the pigmentation area and severity index (PSI) score, global assessment of the aesthetic improvement scale (GAIS), and a patient satisfaction score at Weeks 4 and 8.

RESULTS Seven patients completed the study. No significant differences were found in the PSI, GAIS, patient satisfaction score, and melanin average score between the lasers. The melanin average level was significantly reduced by the 660-nm laser but not the 532-nm laser at Week 8 compared with the baseline.

CONCLUSION Both 660-nm and 532-nm QS Nd:YAG lasers effectively reduce pigmentation for up to 8 weeks with high patient satisfaction. The new 660-nm laser therefore increases the treatment options for lentigines in Asian skin.

*The authors have indicated no significant interest with commercial supporters.*

Solar lentigines are a common epidermal pigmentary disorder in Asians and whites and are associated with photoaging processes.[1] Although they are benign, many patients want them removed for cosmetic reasons. Since Anderson and colleagues[2] first demonstrated the effectiveness of a Q-switched (QS) neodymium-doped yttrium aluminum garnet (Nd:YAG) laser in the treatment for cutaneous pigmentation, QS alexandrite, QS ruby, and intense pulsed light (IPL) lasers have all been subsequently used to treat epidermal pigmented lesions.[3–6] Because of the high melanin absorption rates at the 532-nm wavelength, the QS 532-nm Nd:YAG laser has been most commonly used for the treatment for such epidermal pigmented lesions.[7,8] However, because 532-nm light is also highly absorbed by hemoglobin, a 532-nm Nd:YAG laser may increase the risk of superficial vascular damage, which can lead to adverse events such as erythema and postinflammatory hyperpigmentation (PIH). Adverse events are also common in Asian patients with a darker skin type, with the risk of PIH reported to be approximately 25%.[2,6,7,9,10]

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*ISSN: 1076-0512 • Dermatol Surg 2015;41:1389–1395 • DOI: 10.1097/DSS.0000000000000493*

A 694-nm QS ruby laser also shows a relatively high absorption rate by melanin and pigmented lesions such as lentigines, freckles, cafe-au-lait spots, and nevus of Ota have been successfully treated with this type of laser.[11–13] A new 660-nm wavelength rubylike versatile YAG laser, which uses a handpiece equipped with a solid dye to convert the 532-nm QS Nd:YAG laser energy to 660 nm, has been introduced for the treatment for epidermal pigmented lesions. The authors therefore designed our present first randomized, double-blinded, split-face, comparative pilot study to assess the efficacy and safety of a 660-nm versus a 532-nm QS Nd:YAG (660-nm vs 532-nm) laser for the treatment for solar lentigines in middle-aged Asian women.

## Materials and Methods

### *Patients*

Eight Korean women (mean age, 48.6; range, 42–60; Fitzpatrick Skin Types III–IV) with lentigines were enrolled in this clinical study from January 2014 to June 2014. All patients had facial solar lentigines that were diagnosed clinically by 2 independent investigators. Those with clinically prominent dermal melanocytic lesions such as melasma, acquired bilateral nevus of Ota-like macules (ABNOMs), and nevi of Ota were excluded. Patients were also excluded if they were pregnant or nursing; had excessive photosensitivity; were currently receiving oral contraceptive pills, hormone replacement therapy, or oral or topical medications that could affect the response to visible light; were undergoing treatment with topical bleaching agents such as hydroquinone, tretinoin, kojic acid, or triple combination therapy (4% hydroquinone, 0.05% tretinoin, 0.01% hydrocortisone); or had received laser treatment or IPL therapy within the previous 6 months. This study was approved by the Institutional Review Board of Asan Medical Center, Seoul, Korea. Written informed consent was obtained from all patients.

### *Treatments*

All patients were administered local anesthetics (EMLA; a eutectic mixture of 2.5% lidocaine HCl and 2.5% prilocaine; AstraZeneca AB, Sodertalje, Sweden) to the whole face under occlusion for 30 minutes. One side of the face was randomly treated with a 660-nm laser (SPECTRA XT; Lutronic Corporation, Goyang, Korea), using a 660-nm wavelength setting, with a fluence of 2.6 to 3.0 J/cm$^2$, a pulse duration of 10 nanoseconds, and a 3-mm spot size. The other side of the face received a 532-nm treatment (SPECTRA XT) with a fluence of 1.2 to 1.5 J/cm$^2$, a pulse duration of 10 nanoseconds, and a 3-mm spot size. The treatment side (660-nm) and control side (532-nm) were randomly chosen so that the evaluating investigators be blind to the treatments used. The clinical endpoint for both lasers was defined as immediate whitening without bleeding. Immediately after the procedures, the lesions were cooled with icepacks, and antibiotic ointment was applied to the irradiated area. Subjects were advised to avoid sun exposure and apply a broad-spectrum sunscreen.

### *Assessment*

Clinical improvement was assessed by 2 experienced dermatologists who were not involved in the treatment arm of the study and who independently made their ratings. The evaluations were conducted at baseline and 4 and 8 weeks after the treatment. Digital photographs taken at baseline and all subsequent visits were used to document the patients under identical conditions (room, light source, and camera). Thereafter, 2 dermatologists were asked to objectively evaluate clinical improvement from the clinical photography in a double-blind manner at 4 and 8 weeks after the treatment on a 5-point scale as follows: (1) little or no improvement (0%–10%), (2) noticeable improvement (10%–25%), (3) fair improvement (25%–50%), (4) good improvement (50%–75%), and (5) excellent improvement (>75%). Additionally, all patients were asked to subjectively report their satisfaction at the final visit using a 5-point grading system as follows: unsatisfied or subjectively worse (score: 1), no change (score: 2), mild improvement (score: 3), moderate improvement (score: 4), and significant improvement (score: 5). Patients also recorded any side effects.

To more accurately quantify the severity of the pigmentation and any change during therapy, the authors

used a pigmentation area and severity index (PSI) score described previously.[3] The score consists of 3 parameters, namely, the extent, darkness, and density of the pigmented lesions, and was based on the melasma area and severity index score devised for melasma evaluation.[3,14] The area was classified as 0, no involvement; 1, less than 10% involvement of 1 cheek; 2, 10% to 29%; 3, 30% to 49%; 4, 50% to 69%; 5, 70% to 89%; and 6, 90% to 100%. Darkness was defined as 0, absent; 1, slight; 2, mild; 3, marked; or 4, severe. Density was calculated as 0, minimal; 1, slight; 2, mild; 3, marked; or 4, maximum. These values were summed to obtain the PSI score (0–48) as follows: (darkness + density) × area. The improvement rate at the time of evaluation was defined as $(PSI_{pretreatment} - PSI_{posttreatment})/PSI_{pretreatment} \times 100\%$.

### *In Vivo Skin Measurement*

Skin topography and distribution of melanin were measured in vivo with the Antera 3D imaging system (Miravex, Dublin, Ireland), which consists of a handheld imaging device connected to a computer.[15] This analysis is based on multidirectional illumination and computer-aided reconstruction of a surface. Several light-emitting diodes are used to illuminate the skin with different colors and different illumination directions. Unlike traditional imaging techniques, the Antera 3D uses reflectance mapping of 7 different light wavelengths spanning the entire visible spectrum. This approach allows for a more precise analysis of the skin's colorimetric properties, which are determined mostly by 2 dominant chromophores, melanin, and hemoglobin. The reflectance data are transformed into skin absorption coefficients and used to quantify hemoglobin and melanin concentrations using a mathematical correlation with the known spectral absorption data of these chromophores.[15,16] The acquired images can be visualized in both 2 and 3 dimensions in different modes, such as the natural skin color, skin texture, melanin, and hemoglobin.

The authors measured the left and right cheeks of each patient in vivo at baseline and 4 and 8 weeks after the treatment. In the melanin measurement, an identical area was checked in the follow-up image, and the melanin average was calculated from the concentration and distribution of melanin in the selected area using the device software.

### *Statistical Analyses*

Statistical analyses commenced with descriptive statistics, using counts, ranges, percentages, and means and SDs or medians and interquartile ranges. The efficacy of the treatments were compared with the Wilcoxon signed-rank test using the means of the scores recorded by 2 independent physicians at baseline, Week 4, and Week 8. Statistical analysis of the comparison between the 2 treatment groups (660 nm and 532 nm) was performed using the Mann–Whitney *U* test. A $p$ value < .05 was considered statistically significant. SPSS for Windows, version 19.0, was used for all statistical analyses (IBM SPSS, Armonk, NY).

## Results

Seven Korean women (mean age ± SD, 49.4 ± 6.3; range, 42–60) with Fitzpatrick Skin Types III ($n$ = 2) and IV ($n$ = 5) completed this pilot study. One of the 8 patients originally enrolled did not return for the 8-week follow-up visit. There was no significant difference in the baseline severity of the pigmentation between the facial sides receiving different treatments ($p$ > .05). The characteristics of the study patients are listed in Table 1.

The 7 patients who completed this study achieved a clear improvement in PSI scores and all 3 component values after both 660-nm and 532-nm laser treatments. Compared with baseline, both treatment groups showed significant improvements ($p$ < .001; Table 2). The improvement rates and PSI scores after both treatments were similar at Weeks 4 and 8.

**TABLE 1. Baseline Characteristics of the Study Patients**

| | | | |
|---|---|---|---|
| Age, years | | | 49.4 ± 6.3 |
| Skin Types III/IV | | | 2/5 |
| | *660 nm* | *532 nm* | *p* |
| Area value | 3.2 ± 0.9 | 3.1 ± 0.9 | .84 |
| Darkness | 3.4 ± 0.6 | 3.4 ± 0.5 | .91 |
| Density | 2.4 ± 0.5 | 2.4 ± 0.5 | 1.00 |

**TABLE 2. Improvement in Pigmentation Area and Severity Index Scores by Treatment**

| | *660 nm* | *532 nm* | *p* |
|---|---|---|---|
| Baseline | | | |
| PSI score | 19.3 ± 8.1 | 18.7 ± 7.6 | .87 |
| Week 4 | | | |
| PSI score | 6.9 ± 3.2 | 6.9 ± 3.5 | .98 |
| Improvement rate,% | 61.5 ± 18.5 | 61.0 ± 16.3 | .80 |
| Week 8 | | | |
| PSI score | 7.2 ± 3.3 | 7.9 ± 3.7 | .67 |
| Improvement rate,% | 59.8 ± 17.3 | 55.1 ± 19.4 | .57 |

However, the improvement rate at Week 8 in the 660-nm treatment group tended to be slightly higher than that of the 532-nm treatment group. The global assessment of the aesthetic improvement scale (GAIS) (mean ± SD) at the 4-week follow-up was 3.93 ± 0.92 for the 660-nm treatment group and 3.57 ± 0.76 for the 532-nm treatment group. At Week 8, the scores changed to 3.85 ± 0.86 in the 660-nm treatment group and 3.50 ± 0.65 in the 532-nm group. Although pigment improvement was not significantly different between the treatment groups, the 660-nm treatment group showed a slightly better improvement at each visit (Figure 1).

The melanin average score, the main factor of objective evaluation, measured using Antera 3D, was also seen to improve significantly at Week 4 in both treatment groups. Although there was no significant difference in the score between the 2 groups, the melanin average at Week 8 was significantly reduced by the

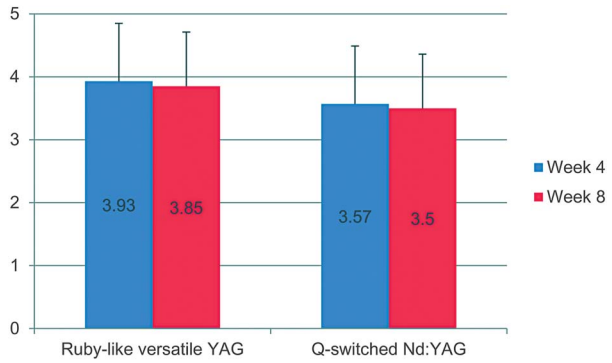


**Figure 1.** Global assessment of the aesthetic improvement scale (GAIS) at 4 and 8 weeks after the indicated laser treatment.

660-nm treatment compared with baseline ($p < .05$) (Table 3). Patient satisfaction scores after 660-nm and 532-nm treatments were similar at Weeks 4 and 8 (Figure 2). Although there was little change in the satisfaction scores, the satisfaction score at Week 8 tended to be slightly higher for the 660-nm treatment group than for the 532-nm group. Representative photographs and Antera 3D images before treatment and 4 and 8 weeks after treatment are shown in Figure 3.

Pain was tolerable in all patients and participants reported that the pain intensity during and after the procedure was similar on both treatment sides. There was no report of serious and/or irreversible adverse events such as scarring. No patients reported any treatment-related disruptions to their routine daily activities.

## Discussion

The authors have compared the clinical efficacy and safety of 660-nm and 532-nm laser treatment for epidermal pigmented lesions in Asian patients. There was no significant difference found between the efficacy of these treatments. In terms of the melanin average measured by profilometric skin analysis, PSI, GAIS, and patient satisfaction scores, 660-nm treatment tended to produce a better therapeutic effect than 532-nm treatment by Week 8. The authors believe that these results were affected by the PIH that started 4 weeks after the laser treatment.

Nd:YAG, alexandrite, and ruby QS lasers selectively destroy melanocytes and melanosome-containing cells while preserving the surrounding tissues, based on the principle of selective photothermolysis. Q-switched lasers and IPL or pulsed-dye lasers were compared in previous studies of facial lentigine treatments in patients with darker skin phototypes.[3–5] These reports found that the 2 laser types had similar effectiveness, although there was a higher risk of postoperative hyperpigmentation with the QS devices. Q-switched lasers reliably release high-powered pulses in the nanosecond range, and this fast heating causes microvaporization and photothermal effects. These processes cause photomechanical damage to the

**TABLE 3. Analysis of the Melanin Average and the Percentage Reduction Before and 4 Weeks and 8 Weeks After the Indicated Treatments**

| *Melanin Average Score* | *Baseline* | *Week 4* | *p* | *Reduction* | *Week 8* | *p* | *Reduction* |
|---|---|---|---|---|---|---|---|
| 660 nm | 0.78 ± 0.08 | 0.71 ± 0.08 | .018* | 8.97 | 0.71 ± 0.06 | .028* | 8.97 |
| 532 nm | 0.78 ± 0.09 | 0.71 ± 0.07 | .018* | 8.97 | 0.73 ± 0.07 | .128 | 6.41 |
| *p* | | 1.00 | | | .38 | | |

*$p < .05$.

adjacent superficial vessels, which induce PIH in the treated area because of an inflammatory cascade and altered melanocyte activity.[3,6,17]

The wavelength is another important factor in selective photothermolysis, affecting treatment efficacy and complications such as PIH.[2] Because the absorption spectrum of melanin is broad and extends continuously from 300 to 1200 nm, the 660-nm beam is only approximately half of an order of magnitude less well-absorbed by melanin than 532-nm light, although this range is still high on the melanin absorption curve. However, the reduced absorbance is more than compensated by the fact that the 660-nm beam is greater than 2 orders of magnitude less well-absorbed by oxyhemoglobin and greater than 1 order of magnitude less well-absorbed by deoxyhemoglobin than the 532-nm laser. This is because hemoglobin has a focally high absorption spectrum between 500 and 600 nm in the ranges of visible light. The absorption by melanin is still high enough to ensure selective photothermolysis by the target melanin compared with surrounding normal skin but, more importantly, significantly lower absorption by the blood should minimize potential inflammation and improve the safety of the 660-nm beam in the treatment for freckles and lentigines. Hence, a 660-nm laser is theoretically expected to offer better absorption by melanin and weaker absorption by hemoglobin, which should minimize the occurrence of PIH.

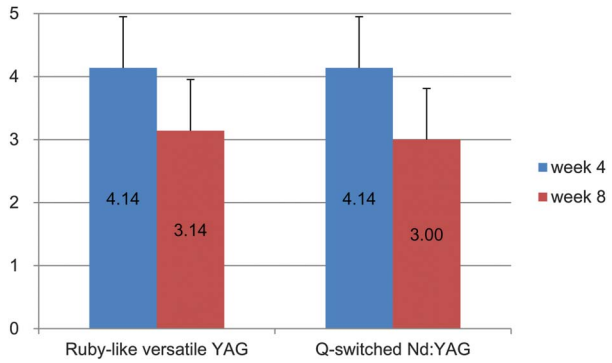


**Figure 2.** Patient satisfaction scores at Weeks 4 and 8 after treatment with 660-nm and 532-nm lasers.

The irradiation strength and pigment lesion category can be associated with the occurrence of PIH. Negishi and colleagues[6] reported that even mild irradiation can lead to microscopic inflammatory skin changes, which is the likely mechanism underlying PIH development. Cytokines, interleukin, endothelin, and reactive oxygen species, and also direct stimulation of melanocytes, may all contribute to the occurrence of PIH.[18] The different incidences of PIH according to the type of lesion—lentigines and freckles—may be due to the differing amount of melanocyte hyperplasia and different genetic background of the 2 entities.[3,19]

All of these potential factors—pulse duration, wavelength, fluence, and type of lesion—should thus be considered to minimize PIH when treating pigmented lesions. In this study, independent of the wavelength, the factors for patients with lentigines were almost equivalent because both approaches involved QS lasers with pulse durations of 5 to 10 nanoseconds and mild irradiation with low fluence. The authors found no significant difference between the efficacy of the 660-nm and 532-nm treatments. Due to the small sample size of our study, the authors could not make a direct comparison between the percentage of our patients who experienced PIH with previous studies, but their objective melanin average measured using profilometric skin analysis showed a higher efficacy

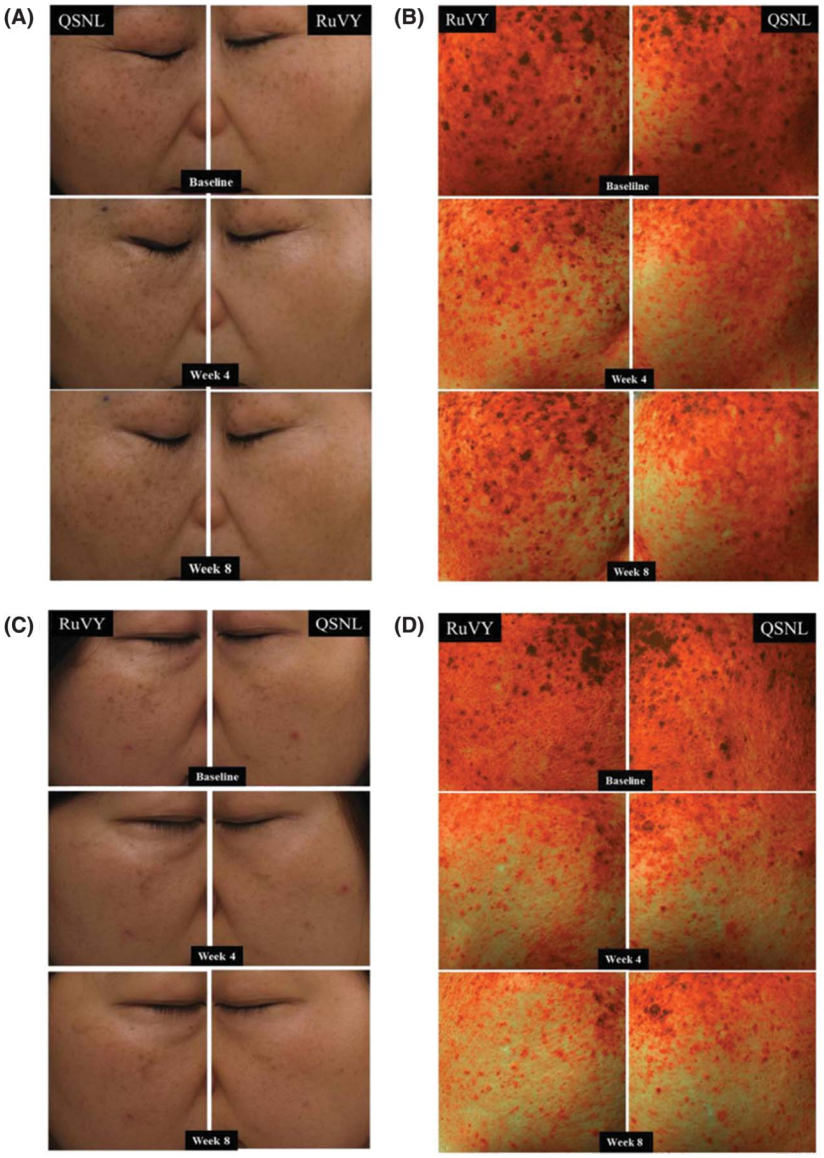


**Figure 3.** Standard digital photography (A and C) and profilometry using Antera 3D (B and D) images of Patients 1 and 7 at baseline, 4 weeks, and 8 weeks after 660-nm and 532-nm laser treatment.

only between baseline and Week 8 in the 660-nm group ($p < .05$). This result might be related to the differences in the incidence of PIH between the 2 groups. Hence, the author would argue that the efficacy of the 660-nm laser is as high as that of the 532-nm Nd:YAG laser for the treatment for lentigines in patients with darker skin types.

To provide a more objective evaluation of the clinical efficacy of the laser treatments under analysis in their this study, the authors used several objective assessment tools, including a profilometric skin analysis tool that calculates the overall melanin average and distribution within a captured area of an image. This is a new and reliable evaluation tool because the present rating systems, such as the GAIS and patient satisfaction score, are necessarily subjective, even if the study in question is designed to ensure the independence of the evaluators.

The authors' present study was limited by its small sample size and brief follow-up period. After an additional 4 months of follow-up, the participants showed a similar tendency in the GAIS and patient satisfaction score compared with 8 weeks of follow-up in the 2 treatment groups. There were no significant

differences found between the 2 laser devices. Although all of the scores generally tended to decrease slightly in both groups, 4 months of follow-up revealed similar levels of satisfaction to those recorded after 8 weeks of follow-up. Further studies of larger cohorts over a longer follow-up period are needed to determine the optimal treatment modalities and settings, such as fluence and pulse duration, for pigmented lesions in patients with darker skin types.

## Summary

Both 660-nm and 532-nm lasers effectively treat lentigines in patients with darker skin types. The treatment efficacy is not significantly different between these 2 devices, but the objective melanin average was significantly reduced by the 660-nm but not the 532-nm treatment at Week 8 compared with baseline. This difference could be related to the occurrence of PIH at 8 weeks after treatment. Although there are many factors related to the occurrence of PIH, the laser wavelength may be one of the most important.

## References


1. Ezzedine K, Mauger E, Latreille J, Jdid R, et al. Freckles and solar lentigines have different risk factors in Caucasian women. J Eur Acad Dermatol Venereol 2013;27:e345–56.
2. Anderson RR, Margolis RJ, Watenabe S, Flotte T, et al. Selective photothermolysis of cutaneous pigmentation by Q-switched Nd: YAG laser pulses at 1064, 532, and 355 nm. J Invest Dermatol 1989; 93:28–32.
3. Wang CC, Sue YM, Yang CH, Chen CK. A comparison of Q-switched alexandrite laser and intense pulsed light for the treatment of freckles and lentigines in Asian persons: a randomized, physician-blinded, split-face comparative trial. J Am Acad Dermatol 2006;54:804–10.
4. Kono T, Manstein D, Chan HH, Nozaki M, et al. Q-switched ruby versus long-pulsed dye laser delivered with compression for treatment of facial lentigines in Asians. Lasers Surg Med 2006;38:94–7.
5. Chan HH, Fung WK, Ying SY, Kono T. An in vivo trial comparing the use of different types of 532 nm Nd:YAG lasers in the treatment of facial lentigines in Oriental patients. Dermatol Surg 2000;26:743–9.
6. Negishi K, Akita H, Tanaka S, Yokoyama Y, et al. Comparative study of treatment efficacy and the incidence of post-inflammatory hyperpigmentation with different degrees of irradiation using two different quality-switched lasers for removing solar lentigines on Asian skin. J Eur Acad Dermatol Venereol 2013;27:307–12.
7. Chan HH, Alam M, Kono T, Dover JS. Clinical application of lasers in Asians. Dermatol Surg 2002;28:556–63.
8. Ho SG, Chan HH. The Asian dermatologic patient: review of common pigmentary disorders and cutaneous diseases. Am J Clin Dermatol 2009;10:153–68.
9. Margolis RJ, Dover JS, Polla LL, Watanabe S, et al. Visible action spectrum for melanin-specific selective photothermolysis. Lasers Surg Med 1989;9:389–97.
10. Nanni CA, Alster TS. Complications of cutaneous laser surgery. A review. Dermatol Surg 1998;24:209–19.
11. Sadighha A, Saatee S, Muhaghegh-Zahed G. Efficacy and adverse effects of Q-switched ruby laser on solar lentigines: a prospective study of 91 patients with Fitzpatrick skin type II, III, and IV. Dermatol Surg 2008;34:1465–8.
12. Yamashita T, Negishi K, Hariya T, Yanai M, et al. In vivo microscopic approaches for facial melanocytic lesions after quality-switched ruby laser therapy: time-sequential imaging of melanin and melanocytes of solar lentigo in Asian skin. Dermatol Surg 2010;36:1138–47.
13. Jang WS, Lee CK, Kim BJ, Kim MN. Efficacy of 694-nm Q-switched ruby fractional laser treatment of melasma in female Korean patients. Dermatol Surg 2011;37:1133–40.
14. Kimbrough-Green CK, Griffiths CE, Finkel LJ, Hamilton TA, et al. Topical retinoic acid (tretinoin) for melasma in black patients. A vehicle-controlled clinical trial. Arch Dermatol 1994;130:727–33.
15. Clementoni MT, Lavagno R, Catenacci M, Kantor R, et al. 3D in vivo optical skin imaging for intense pulsed light and fractional ablative resurfacing of photodamaged skin. Facial Plast Surg Clin North Am 2011;19:737–57, x.
16. Anderson RR, Parrish JA. The optics of human skin. J Invest Dermatol 1981;77:13–9.
17. Ara G, Anderson RR, Mandel KG, Ottesen M, et al. Irradiation of pigmented melanoma cells with high intensity pulsed radiation generates acoustic waves and kills cells. Lasers Surg Med 1990;10: 52–9.
18. Tomita Y, Maeda K, Tagami H. Melanocyte-stimulating properties of arachidonic acid metabolites: possible role in postinflammatory pigmentation. Pigment Cell Res 1992;5:357–61.
19. Bastiaens M, Hoefnagel J, Westendorp R, Vermeer BJ, et al. Solar lentigines are strongly related to sun exposure in contrast to ephelides. Pigment Cell Res 2004;17:225–9.


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