Light-Based Treatment of Pigmented Lesions

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Pigmented lesions are common among patients presenting to dermatologists. Fortunately, a large arsenal of light-based technology is available for the reduction and removal of these lesions. By developing a comprehensive understanding of the microanatomy of dyschromia, physicians can optimize protocols based on principles of laser-tissue interactions and reports in the literature. This article will examine the author's experience and preferences in treating specific types of pigmented lesions with various lasers and light devices.

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Dermatologists commonly treat patients with pigmented lesions. A large arsenal of light-based devices are available for the reduction and removal of these lesions. The most important factor to consider when choosing the best light source for the treatment of pigmented lesions is the microanatomy of the dyschromia. A crucial factor in treatment of excessive pigment is having an understanding of the pigment distribution with the lesion. Lesion microanatomy should be considered when strategizing for optimal removal. It also is important to consider certain types of dyschromia, such as melasma, postinflammatory hyperpigmentation (PIH), and Hori nevus, as inflamed "dynamic" types of pigmented lesions. In contrast, lentigines and freckles typically are stable and noninflamed. Multiple types of laser and nonlaser devices can be employed, sometimes with different wavelengths, spot sizes, and pulse widths, but still achieve similar results.[1]

Chemical peels and cryotherapy at one time were worthy opponents of the laser but can present challenges related to damage confinement. For generalized superficial pigment reduction, chemical peeling in experienced hands is quite sufficient. However, in focal destruction, the agent often will extend beyond the perimeter of the lesion, even with careful application. Cryotherapy also is notoriously challenging to control. The best success usually is achieved with a cotton swab, copper tip attached to a sprayer, or cone (such as an ear speculum) to confine the spray to a particular treatment spot; however, the chance of temporary PIH and possibly even long-term hypopigmentation still is high. Although an accomplished peeler or cryotherapist might perform admirably and competitively in a laser duel, reaching that level of experience would require much practice, and similar to dermabrasion, the number of residents being trained to treat pigmented lesions with peels and advanced cryotherapy is declining.

An exceptional review of laser treatment of pigmented lesions recently was published in the literature.[2] In contrast to that review, this article will examine the author's experience and preferences in treating specific types of pigmented lesions with various lasers and light devices.

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A series of key pearls will be presented as well as practical and realistic approaches for treating pigmented lesions that are typically seen in a dermatology practice.

PRINCIPLES IN LIGHT-BASED PIGMENT REDUCTION

The basis for pigment reduction in most laser and light applications is selective targeting of the 1-µm diameter melanosome.[1] Melanin absorption scales as $\frac{1}{\lambda^2}$. It follows that the threshold for epidermal damage in surface pigmented lesions increases by the same scale of relative absorption versus λ. For example, a typical ratio for pigment damage threshold fluence at 504 and 750 nm in pigmented lesions was shown to be approximately 1 to 1.7, indicating that almost twice the fluence is needed to heat a lesion at 750 nm versus 504 nm.[1] Therefore, if a lentigo is treated with 10 J/cm^2 at 532 nm for immediate graying or darkening, a fluence of 18 J/cm^2 would be required at 750 nm for the same lesion. These calculations assume similar pulse durations. For shorter pulses with the same wavelength, smaller fluences are required for selective melanosome heating; for instance, although a fluence of 8 J/cm^2 might be required to treat a typical lentigo with a Q-switched alexandrite laser, 20 to 35 J/cm^2 might be required for a 3-millisecond pulse. Thus pulse duration and wavelength are the 2 most important factors in selective epidermal heating of pigmented lesions.

Physicians can optimize a particular device for selective heating of pigmented lesions versus vascular lesions by manipulating the laser parameters. For example, by applying a compression handpiece without cooling with 595 nm, blood is depleted as a target and pigment is preferentially heated.[3] Also, some intense pulsed light (IPL) devices allow the user to increase or decrease the sapphire window temperature to enhance epidermal versus vascular heating.

When the pulse width is reduced to the nanosecond range, melanosomes are preferentially heated instead of vessels. Extremely short Q-switched 532-nm pulses will cause fine vessels to rupture, and inadequate heat diffusion to the vessel walls precludes long-term vessel destruction.[4] On the other hand, melanosomes are sufficiently heated for single-session lentigo destruction.

Nonbulk skin heating is based on selective absorption by discrete chromophores of relatively low concentration (ie, melanin, hemoglobin). Anderson and Parrish[5] described the concept of selective photothermolysis, a process that offers a mathematically rigorous rationale for tissue-selective lasers. They explained that extreme localized heating relies on a wavelength that reaches and is preferentially absorbed by the target, an exposure duration that is less than or equal to the time necessary for cooling of the target structures, and sufficient energy to damage the target. The heterogeneity of the skin allows for selective injury in microscopic targets, and the focal nature of heating decreases the likelihood of widespread thermal damage.[5]

Thermal relaxation time (τ) is the interval necessary for a target to cool to a certain percentage of its peak temperature. The larger the area, the longer it takes to cool. When defining thermal relaxation time, the target size and geometry are important. Normally, the value for τ is expressed as $\delta^2/g\kappa$, where δ indicates the diameter of the particle; κ, the thermal diffusivity (a measure of heat capacity and conductivity [for tissue, $\kappa \sim 1.3 \cdot 10^{-3}$ cm^2/s]); and g, a constant based on the shape of the target (ie, slab, cylinder, sphere).

A simple rule for most targets is that the thermal relaxation time in seconds is approximately equal to the square of the target dimension in millimeters. Thus a 0.5-µm melanosome (5×10^{-4} mm) should cool in approximately 25×10^{-8} seconds or 250 nanoseconds. Recall that τ is derived from a solution of a differential equation and does not represent an absolute cooling time but rather provides approximate pulse widths for varying degrees of thermal confinement.[4]

The geometry and therefore the microscopic characteristics of the lesion also is important. For example, nevi are composed of melanocytes in aggregates; collectively, the nodules often are several hundred micrometers in diameter. In contrast, lentigos are comprised of a thin sheet of melanocytes, some 10-µm thick. When treating a nevus with a long-pulsed alexandrite laser at a high fluence, the thermal relaxation time will approach 1 second. According to the previous equation, it follows that thermal confinement will be high, and the peak temperature will rise accordingly. More importantly, the thick slab of melanocytes will take longer to cool, so there will be considerable heat diffusion away from the target. On the other hand, the lentigo represents a slab only tens of microns thick; there will be heat diffusion during the long pulse and rapid cooling after the pulse. Thus, with millisecond-domain fluences, the nevus case might result in scarring, whereas a lighter lentigo (so-called low contrast lesion) might not become hot enough for clearance. If nanosecond pulses are applied to both types of lesions, the lentigo shows a good response with a possibility for complete clearing, whereas the nevus will require multiple sessions, as each laser application will result in confinement of heat to the most superficial part of the lesion.

Most pigment-specific lasers rely on selective absorption of light. In another category, there are devices (ie, CO_2 and erbium:YAG [Er:YAG] lasers) in which water is the

chromophore and the pigment just happens to be in the way. These lasers require a more skilled operator because, whether in continuous-wave or pulsed mode, the ablation/heating must be confined to the level of the lesion and not proceed deep into the dermis.

GENERAL GUIDELINES AND SCENARIOS

In my practice, if a lighter-skinned white patient presents with a few discrete lentigines, the Q-switched alexandrite laser is used and has minimal risk for PIH (Figure 1). The endpoints are frosty and white (Figure 2). Q-switched lasers also carry little risk for PIH in lighter-skinned Asian and Hispanic patients as well as tanned white patients with Fitzpatrick skin types II and III.[4]

In darker-skinned Asians and other populations with olive complexions, some persistence of pigmented lesions is observed after Q-switched 532-nm, 755-nm, and 694-nm laser applications. In these scenarios, it is difficult to determine after a short interval if residual pigment represents persistent melanin in the treated lesion or PIH. Patients usually report almost complete clearance of the lesions after 3 to 7 days, and most of this pigmentation is postinflammatory, at least for thinner lentigines. Patients are started on triple-bleaching cream and steroid creams as early as 7 days after treatment. Repeat treatments are delayed for 8 to 12 weeks, allowing for at least partial resolution of any PIH. Unfortunately, patients often react unfavorably to this PIH period, with the exception of those with exophytic seborrheic keratoses (SKs), because they are disappointed that the lesions are darker than their initial presentation.[4] One article suggested that longer-pulse visible-light technologies are less likely to cause PIH in patients with darker skin types[6]; however, for lighter lentigines, whether a pulsed dye laser (PDL) with compression, IPL, or potassium titanyl phosphate (KTP) laser is applied, clearance is challenging because there often is insufficient color contrast for safe lightening of the lesions. It follows that once the darker lesions are reduced using longer-pulse strategies, lighter lesions must be addressed with either Q-switched lasers or ablative approaches.

For diffuse hyperpigmentation (actinic bronzing), the long-pulsed variable-spot KTP laser (Gemini, Iridex Corporation) or IPL (both with contact cooling) can be applied as first choices. These approaches are associated with a low incidence of side effects and combine a good ease of use with a high rate of patient satisfaction. When treating combinations of darker and lighter lentigines in

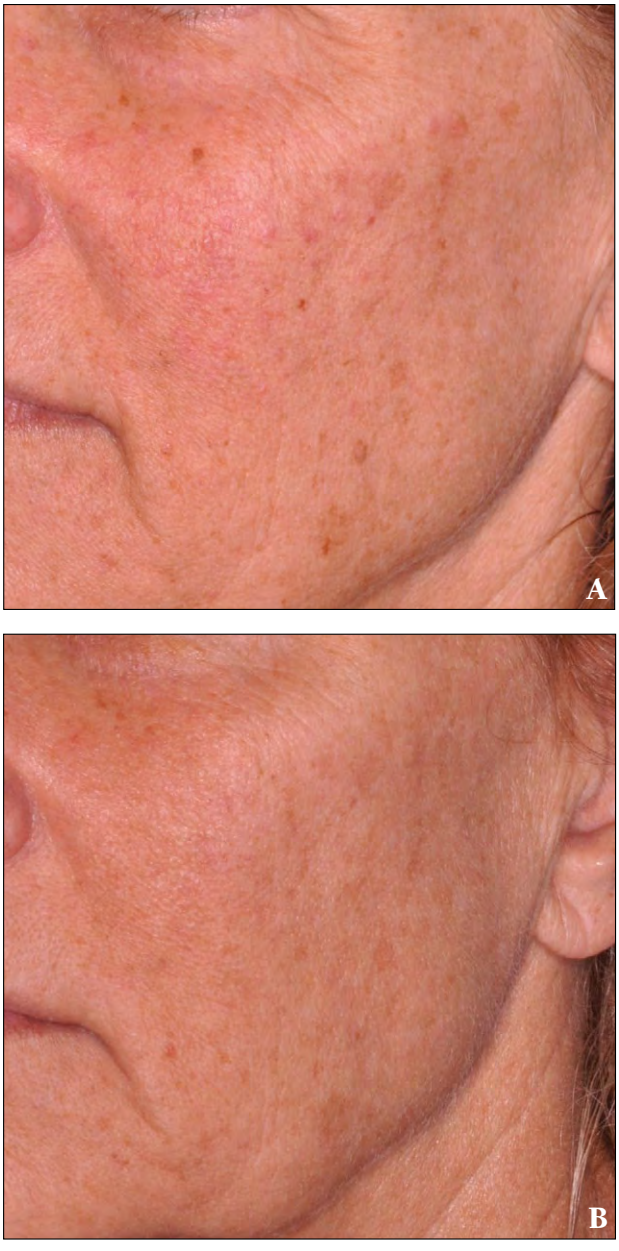

Figure 1. Lentigines and flat seborrheic keratoses before (A) and 2 months after the first session with a Q-switched alexandrite laser (B).

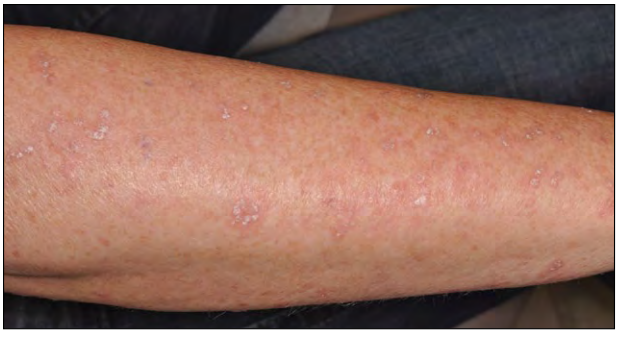

Figure 2. Frosty white endpoints shown immediately after Q-switched alexandrite laser therapy.

white patients, use the Q-switched alexandrite laser for the lighter lentigines followed by a panfacial treatment with IPL or KTP laser in the same session (for darker lesions and redness). Patients might be disappointed with the results if only long-pulsed strategies are applied, as the lighter lentigines will persist. Another strategy is to employ increasingly higher fluences with IPL or KTP in serial sessions; however, as the contrast diminishes between the pigmented lesions and background skin, safety is compromised as normal skin might be damaged. Background pigmentation tends to vary from region to region, and the practitioner can easily wander from a less-pigmented area (ie, central face) to the lateral cheek (more pigmented) and observe focal crusting where the background pigmentation is greatest.

Pigment meters and test spots can optimize treatment. Pigment meters are becoming more widely available, and at least one company is finalizing plans to integrate a pigment meter (SkinTel, Palomar Medical Technologies, Inc) into its latest IPL platform. The need for test spots is somewhat controversial. In my practice, test spots are used in 2 ways: (1) to demonstrate the healing sequence and possible efficacy to patients, and (2) to test for the maximum fluence that is tolerated by the background skin, particularly when treating large areas with diffuse dyschromia. Ideally, when the patient arrives, small test spots are performed with a masked plastic piece or small spot over a range of "best guess" safe and effective fluences. While numbing cream is applied over approximately 1 hour, these test spots are evaluated, and the best fluence is chosen for the remainder of the treatment session.

Poikiloderma is a hybrid lesion, composed of vascular and melanocytic components. However, the vascular contribution is probably greatest, as I have noted good reduction in severity of poikiloderma even when a PDL is used with cryogen spray cooling (dynamic cooling device), where epidermal pigment is protected by extreme surface cooling.

Poikiloderma is best treated with IPL, large-spot KTP laser therapy, or an extended-pulse PDL. Multiple sessions are necessary, and some cases are quite resistant to treatment. Interestingly, treatment of the ectatic vessels alone will achieve marked clearance, even in cases in which both melanin and telangiectasia appear to be in excess. Application of hydroquinone cream and sunscreen will expedite treatment by reducing background pigment and allowing for higher fluence settings.

PEARLS

One advantage of a variable-spot KTP laser (1–5 mm) is that higher fluence pulses can be used and confine potential overtreatment to the lesion alone. For example, for a lighter lentigo, one can apply a 14 J/cm^2 fluence and 5-millisecond pulse with a 2-mm spot and carefully trace over the entire lentigo in a pixilated fashion. This approach minimizes the risk for collateral damage while still avoiding PIH associated with Q-switched lasers. Likewise Cutera manufactures a small-spot IPL (AcuTip, Cutera, Inc). Another way to increase efficacy of millisecond technologies is to use a mask. Other IPLs such as the BroadBand Light laser (Sciton, Inc) use special adapters to reduce the spot size as necessary. External masking (ie, using a piece of white plastic with precut holes) reduces the risk for epidermal damage when treating smaller lesions in darker or slightly tanned skin.[7]

The pulsed CO_2 laser or Er:YAG laser is used in my practice to treat lighter lentigines, particularly if they are evolving into SKs. Exophytic SKs must be treated with ablative lasers, a Q-switched alexandrite or ruby laser, or a high-fluence long-pulsed alexandrite laser. In one application, the Q-switched alexandrite beam is focused to a small spot to vaporize smaller flatter SKs using repeated pulses. Sometimes slight bleeding is observed, but this technique generally is well-tolerated by the patient and is associated with rapid scarless wound healing. More recently, I have used the long-pulsed alexandrite laser with a 6-mm spot, higher fluences (40–70 J/cm^2), and 3-millisecond pulse duration to treat thicker SKs (Figure 3).

For larger areas of lentigines over the arms or legs, a combination of both IPL (or a large-spot long-pulsed alexandrite laser) for the entire region and the Q-switched alexandrite laser for discrete lighter lesions can be used. With this approach, much of the background pigment is reduced by the large-spot IPL/laser and more resistant lesions can be treated with the Q-switched alexandrite laser. Another approach for diffuse, low-contrast, pigmented lesions is to add a series of fractional ablative or semiablative treatments.

For flashlamp systems, filters placed between the lamp and skin are configured to optimize heating of specific targets. These filters transmit wavelength ranges as labeled on the crystal. I use IPL without reservation in appropriate female candidates; however, reservations that often preclude treatment of males include temporary hair reduction, particularly in the preauricular area where many telangiectases are observed.

If the patient presents exclusively with melasma and no discrete static pigmented lesions (ie, lentigines), treatment is started with topical hydroquinone and retinoids before pursuing interventional therapy. Melasma represents the most common pigmentation disorder, but light-based technologies routinely underachieve or fail. When I evaluate a new melasma patient, I explain that light is not a first-line treatment of melasma, melasma is a chronic

condition, and absolute UV protection and bleaching creams can play positive roles in treatment. Patients are instructed to avoid or eliminate as many contributing factors as possible (eg, UV exposure, exogenous estrogen, heat). If all of these conditions are met and the patient agrees to the terms of light treatment, combinations of fractional nonablative and visible light approaches are initiated. My most recent approach is a combination of millisecond 532-nm light and low-energy fractional nonablative lasers in the same session, coupled with application of an opaque sunblock and triple-bleaching cream (Figure 4). Patients receive treatment every 2 to 4 weeks for 4 to 6 sessions and then every 3 months thereafter. An alternative approach is a low-fluence Q-switched

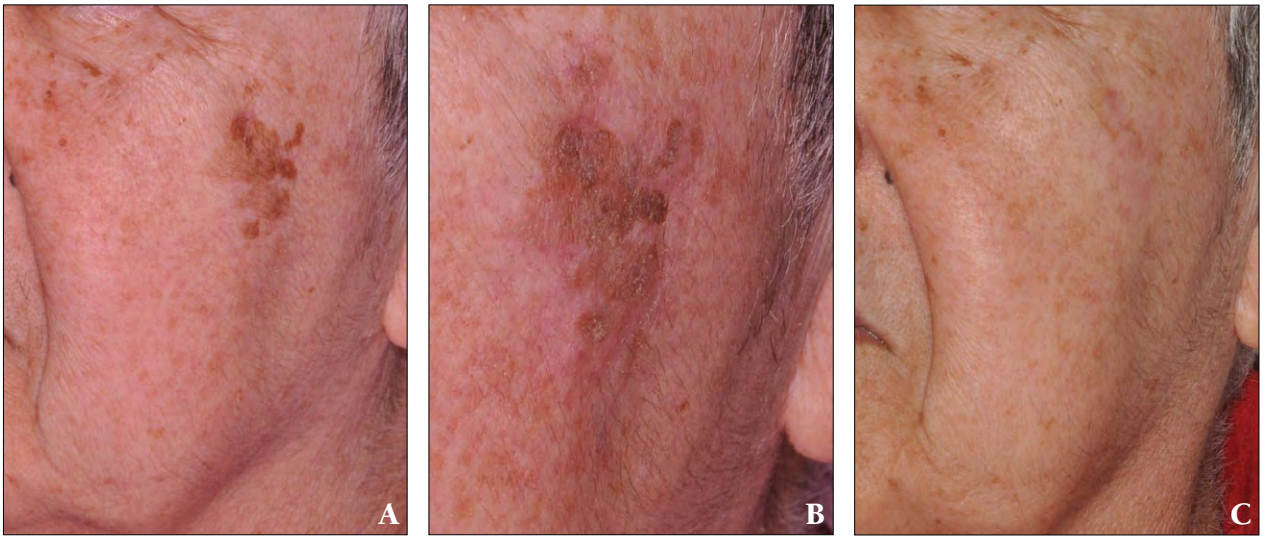

Figure 3. Seborrheic keratosis before (A), immediately after (B), and 2 months after treatment with the long-pulsed alexandrite laser (60-J/cm^2 fluence; 3-millisecond pulse; 6-mm spot; 755 nm; no cooling)(C).

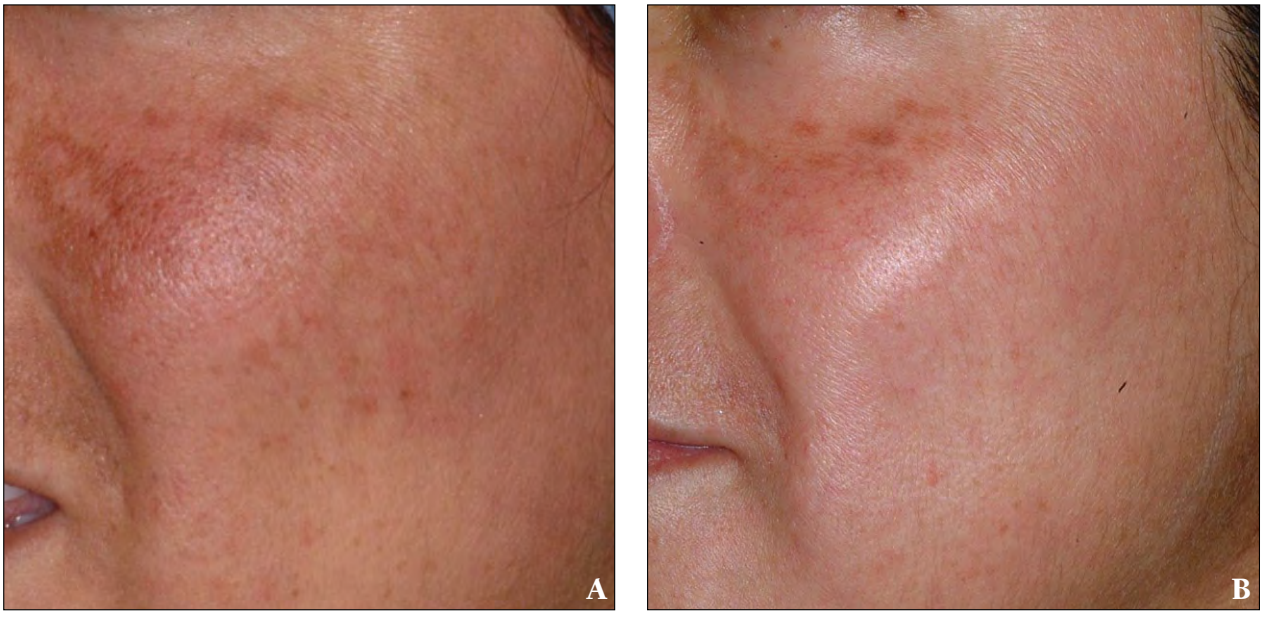

Figure 4. A melasma patient before (A) and after 3 sessions with a fractional 1540-nm laser (120 µm; 5 mJ; 10% total coverage per session) and a long-pulsed potassium titanyl phosphate laser (6-J/cm^2 fluence; 15-millisecond pulse; 10-mm spot; contact cooling)(B). Both lasers were applied in the same treatment session.

Nd:YAG laser (2-J/cm^2 fluence; 10 Hz; 6-mm spot; 3 passes). Although good results can be achieved with the Q-switched Nd:YAG laser, higher rates of recurrence have been observed as well as occasional confettilike hypopigmentation. I have not found Q-switched alexandrite, ruby, or 532-nm lasers helpful in the treatment of melasma; in nearly all cases, despite visible resolution within 4 to 5 days, worsening of the melasma ultimately follows.

Laser treatment of pigmented lesions can be enhanced using a polarizing lamp during procedures. The lamp (v600, Syris Scientific, LLC) enhances the contrast between the background skin and the affected areas. The only drawback is the sheer weight of the device on the physician's head, which can lead to fatigue with prolonged wearing. In some cases, the enhancement provided by the polarizing light source is so effective that lesions that are not troublesome to the patient appear conspicuous enough to treat.

COMMON PIGMENTED LESIONS

Nevi

Patients often struggle to differentiate dark spots (lentigos or freckles) from nevi, particularly when, as in many cases, both types of lesions are present in the same area. When a patient presents with nevi, I draw a small picture to show how the nevus is similar to the tip of an iceberg and how surgical approaches offer the only definitive, one-time removal technique. We also discuss risks for malignancy in certain types of nevi and biopsy of these lesions prior to any laser approach. If the patient still desires removal and the lesion appears completely benign and flesh colored, the Er:YAG or CO_2 laser can be used with a 1- to 2-mm spot size to vaporize the lesion until it is flush with the surrounding skin. Depending on the elevation of the lesion, multiple passes are delivered in a stacking fashion. If the lesion presents with even the slightest atypical features, a shave biopsy precedes the laser ablation. One particular concern regarding treatment of nevi is the possibility of pigment recurrence at the base of the site. Even in lesions in which no clinical preexistence of pigment is noted, brown-black pigmentation has been observed in scars 3 to 6 months after treatment. In these cases, Q-switched or long-pulsed alexandrite lasers can be applied to remove the remaining melanin; however, the patient may require more than 8 sessions administered 6 to 8 weeks apart to produce a durable response.

Another approach for treating pigmented nevi is the use of Q-switched or long-pulsed 532-nm, 755-nm, and/or 1064-nm lasers (without prior ablation with an Er:YAG or CO_2 laser). I normally start with a long-pulsed alexandrite laser at approximately 50 J/cm^2 with a 6-mm spot and no cooling. Lesions will demonstrate a grayed appearance immediately after treatment. Using this technique, darker lesions require smaller fluences and lighter lesions require greater fluences. One risk for long-pulsed technologies is scarring; therefore, it is prudent to use test spots or begin with a lower range of fluences. Although safer in lightening nevi, Q-switched lasers will require more treatments versus their long-pulsed counterparts.

Somewhat unpredictable responses to lasers for café au lait spots have been reported.[8-10] Similarly, I have observed variable responses with Q-switched 532-nm, 755-nm, and 1064-nm lasers. In general, lesions in lighter-skinned patients respond more favorably than those in darker-skinned patients. Often, a test spot is performed to show the patient both the short-term wound healing sequence and the overall response to treatment. Responses range from PIH, clearance after only 2 to 3 treatments, to brief clearing and early persistence/recurrence. Hydroquinone cream and sun avoidance aid in positive outcomes.[11] Nevus spilus can be similarly treated, with the caveat being that even more sessions will be required for the stippled components of the lesion. In one case of nevus spilus on the face, I treated the patient every 8 weeks for 2 years before establishing long-term remission (>3 years).

Becker nevus[12] presents a great challenge. Unlike café au lait spots, the hamartomatous component of Becker nevus contributes to its resistance to clearance. In my practice, I have tried IPL, long-pulsed KTP lasers, and the full range of Q-switched technologies and found all to be unpredictable insofar as achieving durable responses free of side effects. I have achieved more success with hair reduction within the lesions, thereby enhancing the appearance. In one case, I used the 810-nm diode laser for hair reduction and observed partial pigment clearing. If a patient insists on treatment in a smaller lesion, test spots can be performed.

Epidermal nevi are best treated with either an Er:YAG or CO_2 laser equipped with a small spot. First, the physician should completely ablate the exophytic portion of the lesion. At the base of the lesion, an additional 50 µm of the dermis should be removed to reduce the likelihood of rapid recurrence. No matter how deeply the physician proceeds, there is a long-term risk for recurrence; however, this possibility is an acceptable concession versus excessive ablation and the associated risk for severe scarring.

Dermatosis papulosa nigra lesions respond best to hyfrecation, especially small lesions (<1 mm). For some larger darker lesions, the 1- or 2-mm spot KTP laser achieves impressive results. A light graying effect is the desirable end point.

Postinflammatory Hyperpigmentation

Long-standing PIH following trauma, sclerotherapy, and some infections responds well to the Q-switched alexandrite or ruby lasers. In darker-skinned patients, a series of low-fluence Q-switched Nd:YAG or long-pulsed Nd:YAG lasers can be applied. Hemosiderin staining also responds well to the Q-switched alexandrite laser. The end point should be slight epidermal whitening. Fractional lasers can augment pigment clearance achieved by pigment-specific lasers.[13]

Exogenous Ochronosis

In my experience, the Q-switched Nd:YAG and alexandrite lasers have yielded disappointing results when treating exogenous ochronosis. Part of the challenge is that patients cannot use hydroquinone to reduce any PIH from the treatment itself.

Minocycline-Induced Pigmentation

By far, the Q-switched alexandrite laser has yielded the greatest results for minocycline-induced cutaneous pigmentation.[14] During treatment, lightening of the gray-blue pigment can be observed in real time. Although the Q-switched Nd:YAG laser is less likely to cause PIH, results have been more modest.

Ota and Ito Nevi

In lighter-skinned patients, the Q-switched alexandrite laser shows predictable improvement of Ota and Ito nevi and results in minimal PIH. In patients with Fitzpatrick skin types V and VI, the greater epidermal preservation rate of the Q-switched Nd:YAG laser and low risk for PIH make it preferable to its shorter-wavelength counterparts (ie, ruby and alexandrite lasers). It should be explained to patients that multiple treatments will be necessary to achieve a 50% to 80% reduction in pigment. Treatments should be administered approximately 3 to 4 months apart. Patients also should know that recurrence is possible.[15-23] In some cases, even longer intervals between treatments have been proposed for Ota nevi.[20,21] A Hori nevus, or acquired Ota nevus, is best treated with a combination of Q-switched alexandrite and Q-switched Nd:YAG lasers in the same session.

PITFALLS

Potential risks for treatment include bluing of the skin in patients with a history of parenteral gold therapy. This reaction exclusively occurs when undergoing treatment with Q-switched lasers. In the treatment of larger areas with long-pulsed, pigment-specific lasers and light sources, fluences might have to be changed when moving to and from different subunits of the same anatomic area. For example, in evaluating test spots, the site with the most pigmentation should be chosen (ie, dorsal versus volar forearm). Another pitfall is the risk for confettilike hypopigmentation in treating melasma with a low-fluence Q-switched Nd:YAG laser. I have observed this phenomenon in patients who have received multiple treatments for bilateral Ota nevi. Finally, acne associated with PIH in women is common; the first step in reducing PIH is clearing the acne. Once accomplished, the work of reducing PIH can begin using a combination of laser and light therapy and topical agents.

CONCLUSION

Pigmented lesions represent one of the most common concerns in the standard cosmetic practice; therefore, physicians must be well-versed in the nature of pigmented lesions to optimize treatment outcomes. The physician first must know what is being treated. If the lesion does not respond in a conventional fashion, the pigmented area should be reassessed. In patients with recurring lesions, a biopsy might be indicated. The most common scenario is the lentigo that resists Q-switched laser therapy or recurs as a nonhomogenously colored macule or patch. Either a shave biopsy or a sampling of punch biopsies is helpful when evaluating these lesions. The first rule of cosmetic dermatology is to insure that the lesion is truly only "cosmetic."

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