Use of a Long-Pulse Alexandrite Laser in the Treatment of Superficial Pigmented Lesions

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BACKGROUND/OBJECTIVE Although the alexandrite 755-nm-wavelength laser is effective in the treatment of unwanted hair, there are no published studies gauging the efficacy of the variable long-pulse alexandrite laser in the treatment of superficial pigmented lesions.

STUDY DESIGN/METHODS Eighteen patients underwent a single treatment session using a variable pulse-width alexandrite laser. Test sites were performed using a 10-mm spot size and up to four pulse widths (3, 20, 40, 60 ms) with and without epidermal cooling. Full treatments were performed 3 weeks later using optimum test parameters. The patients were evaluated at 3 and 6 weeks.

RESULTS Patients with darker lentigines had greater lesion clearance than those patients with lighter colored lentigines. Shorter pulse widths and treatment without cryogen cooling both, independently, lowered the fluence threshold for lentigo clearance.

CONCLUSION A long-pulse alexandrite laser is effective in clearing solar lentigines in a single pass with minimal adverse effects.

Candela Corporation loaned the alexandrite 755-nm long-pulse prototype. Yacov Domankevitz, PhD, is a full-time employee of Candela Corporation.

Continuing advances in technology have expanded the dermatologist's armamentarium for treatment of solar lentigines. Light-based options include the erbium:yttrium aluminum garnet (Er:YAG) laser; the carbon dioxide (CO_2) laser; the Q-switched alexandrite, ruby, neodymium-doped yttrium aluminum garnet (Nd:YAG; 1,064-nm),[1] and frequency-doubled Nd:YAG (532-nm)[2] lasers; the 595-nm flash-pumped dye laser; the long-pulsed 532-nm Nd:YAG laser; and intense pulsed light.

Anderson and Parrish[3] demonstrated that melanosomes were the primary sites of injury during laser therapy of epidermal pigmented lesions. Based on this theory of selective photothermolysis, the Q-switched lasers were the initial choice to treat solar lentigines. The Q-switched lasers' high energy and short pulse widths permit less heat diffusion from the target melanosomes, resulting in precise, spatially confined heating of epidermal pigmented lesions.

Although the Q-switched alexandrite laser is effective for discrete solar lentigines, the "violent" destruction of the melanosomes can be associated with significant postinflammatory pigmentation[4] in darker patients.[5,6] For patients with diffuse dyschromias and/or actinic bronzing, treatment of the entire face with the typical 3- to 4-mm spot using a Q-switched alexandrite laser can be labor- and time-intensive.

The efficacy of the long-pulse alexandrite laser with a fixed pulse duration in the treatment of solar lentigines has been reported.[7] We present data that demonstrate the efficacy and safety of the variable

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long-pulse alexandrite laser in the treatment of superficial pigmented lesions.

Methods

Patients

Eighteen volunteers were evaluated in this prospective study conducted with the approval of the Naval Medical Center San Diego Institutional Review Board. After demonstrating understanding of the risks and benefits of this procedure, each patient signed an informed consent form before enrollment. The study protocol conformed to the guidelines of the 1975 Declaration of Helsinki. The mean age of the patients was 53.8 years (range, 36–78 years). All patients were Fitzpatrick skin types I to III with the majority (77.8%) being Type II, and all had clinically diagnosed lentigines on their faces, chest, shoulders, arms, or hands. Exclusion criteria included the inability to read and comprehend English, age less than 18 years, known photosensitivity, pregnancy, recent tan, history of poor wound healing, scarring in the treatment area, and history of keloid formation. Additionally, patients could not be taking concurrent iron supplementation or nonaspirin anticoagulants and could not have used isotretinoin within the preceding 6 months.

Procedure

The study was divided into two components: a test site phase and a "full treatment" phase. Sites were photographed using a digital camera (Nikon D70, Nikon, Melville, NY), both with and without a cross-polarizing filter (Canfield Imaging Systems, Fairfield, NJ). In the test phase, up to six square or rectangular small test sites were marked. Topical anesthetic (LMX4, Ferndale Laboratories, Ferndale, MI) was applied to test sites for 30 minutes, after which the sites were treated using a 10-mm spot size with different pulse durations (3, 20, 40, or 60 ms) and fluences. Fluences were determined by patient Fitzpatrick skin type, pigmentation of lesions, and background skin color. Test areas were treated both with and without the dynamic cooling device (DCD). Single test laser pulses were performed followed by a 10-minute wait period. At the end of this period, satisfactory treatment end points included darkening of the lentigo and/or perilesional erythema. Overtreatment was diagnosed by diffuse bright red erythema in the normal background skin. Patients returned the following day for photographs of the test sites.

At 3 weeks, the patients followed-up for additional photos. Investigators scored the efficacy at each test site and determined the best treatment parameters based on clearance and safety. Up to three selected body areas of similar background skin color to that of the test spots were photographed and treated with the laser using the optimal treatment parameters. Posttreatment skin received one application of 0.5% clobetasol ointment. Patients with a more robust erythema response also had ice packs applied to the treated area for 15 minutes. Patients returned for evaluation 3 and 6 weeks after the full-treatment session. All patients wore appropriate laser wavelength–specific eye protection while receiving treatment on nonfacial body areas and wore laser opaque eye shields during facial treatment.

Evaluation

Photographs were taken at the initial visit and at the 3- and 6-week full-treatment follow-up visits. Ten staff and resident dermatologists, not associated with the study, evaluated the percentage of lesion clearance by comparing the pretreatment and 6-week follow-up polarized images. The grading system was as follows: 0 = no improvement, 1 = 1% to 25% improvement, 2 = 26% to 50% improvement, 3 = 51% to 75% improvement, 4 = 76% to 99% improvement, and 5 = complete removal. These scores were averaged for each individual body treatment area. Based on these data, we calculated the mean fluence for 50% reduction in lentigos as a function of pulse width and the presence or absence of DCD.

TABLE 1. Treatment Parameters for Test Spot Areas

No. of areas treated	Pulse duration (ms)	Fluence (J/cm^2), mean (range)	Spot size (mm)	DCD spray (ms)	DCD delay (ms)	Pain, mean (range)
28	3	42.2 (16–76.5)	10	20, 30, 40	10, 20	2.0 (0–9)
8	3	17 (9–28)	10	none	none	1.6 (0–8)
22	20	41.2 (18–75)	10	20, 30, 40	10, 20	1.7 (0–6)
10	20	18.4 (12.8–26)	10	none	none	1.1 (0–5)
22	40	48.1 (18.5–88)	10	20, 30, 40	10, 20	2.1 (0–9)
8	40	19.8 (10–35)	10	none	none	1.5 (0–5)
21	60	40.9 (21–75)	10	20, 30, 40	10, 20	2.1 (0–8)
10	60	17.3 (9–26)	10	none	none	1.7 (0–8)

DCD, dynamic cooling device.

At the final visit, the patients rated their overall satisfaction with the procedure (1 = not satisfied, 2 = little satisfied, 3 = somewhat satisfied, 4 = satisfied, 5 = very satisfied) as well as their perception of improvement in the treatment area (1 = no improvement, 2 = little improvement, 3 = some improvement, 4 = significant improvement, 5 = complete improvement).

Results

Of the original 18 patients, only 16 patients were included in the photographic pre/post evaluation. One patient relocated and was unable to attend the 6-week follow-up. The other patient's pretreatment photographs were unavailable. Fluences used in test spot treatments ranged from 16 to 88 J/cm^2 with cryogen cooling and 9–35 J/cm^2 without cryogen cooling (Table 1). Based on the results of the initial test spots, 5 body areas were treated with the alexandrite laser using a 40-ms pulse width, 13 body areas were treated using the 20-ms pulse width, and 3 body areas were treated with the 3-ms pulse width. No body areas were treated with the 60-ms pulse width.

The relationship between pulse width, fluence, and DCD is shown in Figure 1. Some lesion clearance was obtained at all pulse widths, but there were subtle differences among the three pulse durations. Notably, at the 3-ms pulse width, lower fluences achieved results comparable to those attained with higher fluences at the 20- and 40-ms pulse widths (Figure 1). Treatment without DCD also required lower fluences (Figure 1). For example, at the 20-ms pulse width, the mean fluence of 23.9 J/cm^2 without DCD is much lower than the mean fluence of 41 J/cm^2 needed with DCD at the same pulse width.

Six weeks after the full treatment, all patients showed some improvement in their lentigines. Both the physicians' and the patients' perceptions of efficacy closely mirrored one another. Patients with darker lentigines achieved the greatest lesion clearance. In fact, the patient with the darkest lentigines had the best response to treatment, experiencing a 76% to 99% lesion clearance overall (Figure 2). Ideal skin conditions (dark lentigines and relatively light background skin) were conducive to the best responses to therapy.

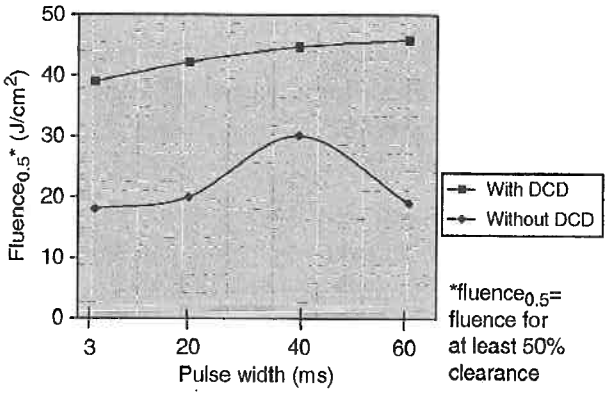

Figure 1. The test spot data show that the fluence threshold increases with pulse width and that in the absence of dynamic cooling, lower fluence is required for lesion clearance.

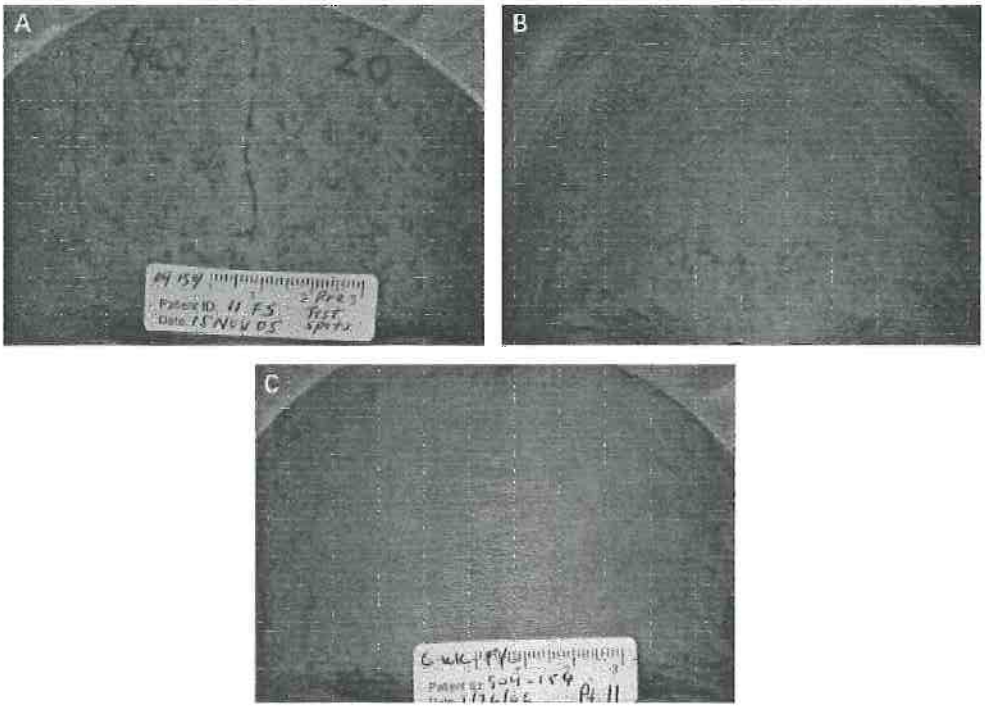

Figure 2. (A) Before test spot treatment. (B) After test spot treatment with long-pulse alexandrite laser (20 ms, 40 ms in the marked areas; fluence, 42 J/cm^2), there is remarkable lesion clearance. (C) After full treatment of this patient's entire face, including her forehead, there is virtually complete clearance of the remainder of her dark lentigos (3 ms; fluence, 34 J/cm^2).

Fifty-six percent of patients were very satisfied with the procedure and 87% reported either some, significant, or complete improvement. Only one patient noted little to no improvement and expressed overall dissatisfaction with the procedure. Her pretreatment lentigines, however, were much lighter than those of our other subjects.

Neither the patients nor the evaluators commented on any side effects at the treated skin sites at the 6-week follow-up visit. There were no instances of postinflammatory hyperpigmentation. Erythema, which was mainly perilesional, was noted in patients 1 to 2 minutes immediately after treatment. Some patients also experienced mild perilesional edema. Both the erythema and the edema reportedly resolved after 2 days. Patients also commented that pigmented lesions that responded well to treatment would darken, crust, and flake off within 10 days of treatment. Two small erosions occurred at the darkest lesions (superficial seborrheic keratosis) on one patient's chest, but healed well, leaving only a small erythematous macule at the 6-week follow-up.

One test spot performed with DCD resulted in an annular ring of hypopigmentation encircling a normally pigmented, presumably "DCD-protected" center, giving the appearance of a donut. Purpura, graying, blistering, or scarring did not occur in any test subject at any time.

Most patients noted mild, but tolerable pain during the procedure with a mean pain rating of 2.9 $\pm$ 2.3, on a scale of 0 to 10 where 0 = no pain and 10 = severe pain (Tables 1 and 2). The level of pain did not correlate with the erythema response or with topical anesthetic use; some patients reported little or no pain without anesthetics whereas others reported moderate pain even with anesthetics. In both the test and the full treatment phases, however, pain was noticeably lower in those patients treated without DCD (Tables 1 and 2).

Discussion

Among alexandrite lasers, the Q-switched class has traditionally been used to treat solar lentigines. In a

TABLE 2. Treatment Parameters for Full Body Areas

No. of areas treated	Pulse duration (ms)	Fluence (J/cm^2), mean (range)	Spot size (mm)	DCD spray (ms)	DCD delay (ms)	Pain, mean (range)
2	3	36 (34–40)	10	30	10	3.8 (2–7.5)
1	3	22.7	10	none		2
9	20	41.7 (37–45)	10	30	10	2.9 (0–6)
2	20	41 (40–42)	10	40	20	2.5 (2–3)
2	20	23.6 (22.7–25)	10	none		1 (0–2)
3	40	40.0 (36.1–48.4)	10	30	10	4.4 (0–8)
2	40	41.1 (38.0–41.9)	10	40	20	2 (0–4)

DCD, dynamic cooling device.

typical application, individual lesions are targeted, and the desired end point is an immediate whitish crust associated with localized vacuolization surrounding pigment-containing cells. Although the Q-switched alexandrite laser is capable of efficiently treating large numbers of discrete lentigines, the smaller spot sizes and the time constraints of targeting individual lesions can become cumbersome, especially when treating very light or very numerous lesions as illustrated by Figure 2A. In addition, as the Q-switched laser treats individual lentigines by causing instant melanocyte destruction, it may be more likely to damage normally pigmented epidermis contained within a larger treatment area. Conversely, the long-pulse laser achieves less spatially selective but more gentle heating and thus can cover a much larger area at a time without causing undue damage to normal skin.

During the course of this study, we noted several key elements that contributed to the success of the long-pulse alexandrite laser in treating superficial pigmented lesions. The degree of lesion lightening was a function of the fluence, the darkness of the lesion compared to background skin, and surface cooling. We found that test spots, with a minimum of a 10-minute wait, should be used to select the optimal fluence. Unlike the immediate white-colored crusting noted with the use of the Q-switched laser, changes were often not apparent in the pigmented lesions for up to 10 minutes after treatment with the long-pulse alexandrite laser.

Fluence and lesion darkness were the most important factors influencing outcome. A wider range of fluences was used in earlier test spots. As the study progressed, however, the range of optimal settings became more predictable and reproducible. Fair-skinned patients with light lentigines required higher fluences for equivalent clearances versus patients with darker lesions. In fact, one of our more fair-skinned patients with very faint lentigines showed little improvement of her lesions despite receiving the highest treatment fluence of any patient. Moderate lesion darkening and perilesional erythema foreshadowed a good outcome.

Another important consideration in the treatment of diffuse solar lentigines is the uniformity of color in the treatment field. Sprinkles of darker lesions within a field of otherwise homogenously shaded lesions can lead to unwanted erosion formation at the site of the darker lentigines if the laser parameters are optimized for treatment of the lighter lesions. For example, we treated the chest of one patient who had two thin dark seborrheic keratoses embedded within a field of numerous diffuse lighter colored lentigines. Although there was an overall great improvement of the lighter lesions, treatment of these seborrheic keratoses caused robust erythema, resulting in two superficial erosions. Close inspection revealed that the tops of these darker colored lesions had immediately peeled after treatment. A more prudent strategy would have been to treat this patient's

lesions in stages. First, the lesions that are darker than the background should be selectively lightened to match their neighboring lighter lentigines. Then, at a follow-up visit, a higher overall fluence should be used to treat a field of now more uniformly colored lesions. Alternatively, one could avoid treatment of darker lesions within a field altogether or individually treat those lesions at a lower fluence during the same visit.

We found little difference in overall efficacy among the 3-, 20-, or 40-ms pulse widths. The lower threshold fluence for lentigo reduction at the 3-ms pulse width is likely due to less diffusion of heat from the melanosome during the shorter pulse width. In other words, there is more spatially confined heating of the melanosomes and basal cell layer using the shorter pulse width. The erythema and edema responses were also more confluent at the 3-ms pulse width, extending somewhat outside of the immediate perilesional field, but did not appear to cause any additional pain compared to other pulse widths.

As the study progressed, we believed that DCD might have been causing too much cooling centrally compared to the beam perimeter. This might have resulted in overcooling of the spot center and undercooling of the perimeter. Subsequently, at times there was a lack of lentigo lightening at the center of the spot and overheating of normal background skin at the perimeter, resulting in peripheral normal skin lightening. Although the DCD is advantageous for epidermal preservation when treating deep targets with a large spot size (i.e., telangiectasias or hair), the ratio of epidermal to dermal cooling is not optimal when treating superficial pigmented lesions. Because our use of DCD did not improve efficacy or mitigate pain, we suggest that the DCD be "disarmed" when treating epidermal pigmented lesions. The reason that DCD use did not always improve pain tolerance may be related to mild stinging caused by the DCD itself.[8] The overall higher fluences used in DCD-treated skin also likely contributed to additional discomfort.

The variable-long-pulse alexandrite laser proved effective in field reduction of superficial pigmented lesions if perilesional erythema and near-immediate pigment darkening were achieved. The majority of patients expressed satisfaction. Treatment was well tolerated with few side effects, only mild pain, and minimal downtime. Outcomes were predictable and treatment was rapid.

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[Correction added after online publication Sep 10, 2007: Figure 3 deleted]