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Multipass Treatment of Photodamage Using the Pulse Dye Laser

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BACKGROUND. Pulse dye lasers (PDLs) alter structural proteins in scars and photodamaged skin, in addition to their effects on dermal vasculature. The PDL has become an option in the treatment of photodamage. Although improvements to skin texture are generally modest when compared with ablative resurfacing, PDL offers a treatment with few side effects. A number of methods have been proposed in an effort to improve treatment outcomes. These range from single, low-fluence treatment with no purpura to multiple passes and treatment sessions as well as purpuric doses.

OBJECTIVE. To evaluate several of the PDL treatment methods to improve photorejuvenation outcomes while limiting the risk of side effects.

METHODS. Twenty patients with photodamage were separated into two groups. Each group received a series of four single-pass treatments or four double-pass treatments at 2-week intervals. Treatments were done using a 595-nm PDL (PhotoGenica V-Star) and a 585-nm PDL (PhotoGenica V) at a pulse duration of 0.5 ms and a 10-mm handpiece. Treatment fluences were maintained below the individual's purpuric threshold, ranging from 3 to 4 J/cm^2. Photos were taken before treatment and during follow-up. Efficacy of treatment was based on subjective grading of photos and by patient self-reporting.

RESULTS. Multiple treatments resulted in improvements to skin tone and texture, including a reduction in the appearance of rhytids and, in particular, improved pigmentary evenness. There was no significant difference between laser or treatment methods. No side effects were noted.

CONCLUSION. PDL treatments provide effective photorejuvenation with minimal risk of side effects.

EVAN SHERR IS AN EMPLOYEE OF CYNOSURE, INC., THE MANUFACTURER OF THE LASERS USED IN THIS STUDY.

ENVIRONMENTAL PHOTODAMAGE (EPD) typically manifests a number of observable changes to the affected tissue: (1) damage to dermal connective tissue, which manifests as textural changes and rhytids; (2) development of superficial melanin, resulting in uneven pigmentation and lentigines;[1] (3) development or increase in facial flushing and telangiectasias; and (4) epidermal abnormalities, such as actinic keratosis, which can eventually manifest in skin cancers. The totality of these changes is manifest in the appearance of premature aging.

Pulse dye lasers (PDLs) have been shown to alter the metabolism associated with structural proteins in scars and photodamaged skin, in addition to their effects on dermal vasculature.[2–8] A review of the wavelength absorption curves associated with dermal chromophores (Figure 1)[9] and their anatomic locations suggests that the PDL may be effective in selectively heating tissue at the level of the papillary dermis (via vascular absorption) as well as targeting superficial melanin. In this way, the PDL may provide substantial improvement to a number of signs of EPD.

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The PDL has a history of producing effective clearance of dermal vascular lesions with an exemplary safety history; however, treatment with moderate doses of PDL fluence can produce undesired purpura. In the case of vascular lesions, purpura is associated with effective treatment, leading to the question as to whether low dose (subpurpuric fluences) can lead to substantial improvement in any or all of the signs of EPD.[10]

In the treatment of hypertrophic scars, PDLs have been shown to modify structure of the scar tissue (primarily collagen), particularly when using short pulse durations and low fluences.[2,7,8,10–12] This results in reduction in scar redness and improvement in scar texture and elasticity. A clear mechanism of action for this improvement has not been determined. However, in the treatment of photodamaged skin, short-pulse, low-fluence PDL exposure has been shown to produce cytokines that stimulate the new production of collagen.[4] Clinically, this effect manifests as the improvement in the appearance of rhytides.[1,13]

PDL wavelengths (typically 585 to 600 nm) exhibit good absorption by melanin, the most superficial chromophore. This is the primary source of epidermal injury caused by high-fluence PDL exposures. In the case of low-fluence treatment, the preferential

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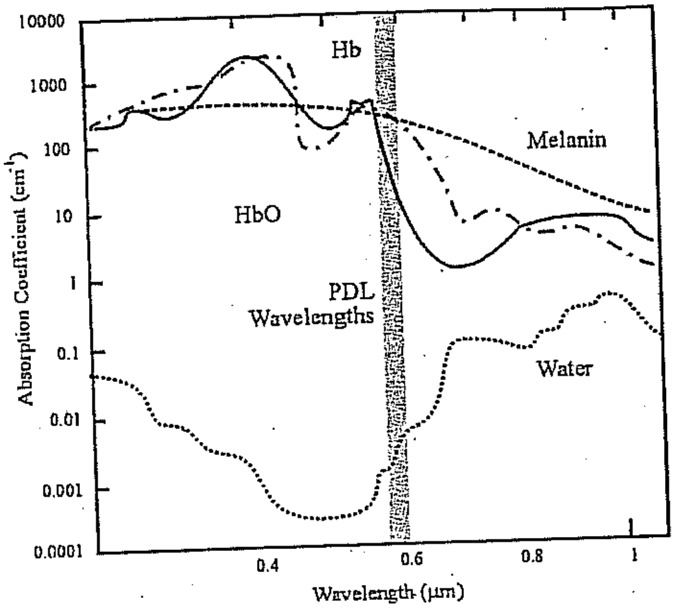

Figure 1. Absorption spectra of major skin chromophores and their relationship to PDL wavelengths (adapted from Goldman and Fitzpatrick9).

absorption by superficial melanin may result in melanin destruction or photobleaching, reducing or eliminating uneven pigmentation and lentigines.

In the treatment of vascular lesions, low-dose therapies produce less effect per exposure; thus, multiple treatments are typically required to achieve an optimal endpoint. Multipass, subpurpuric treatments have been shown to increase the depth of total tissue effect while reducing the risk of purpura.[14] Thus, multipass treatment may provide greater improvement over single-pass, low-fluence therapies. In addition, the tissue absorption effects between different PDL wavelengths (585 nm is preferentially absorbed by both melanin and hemoglobin vs. 595 nm) may alter the locations and degree of effect when using different PDL wavelengths.

Based on experience with scars, vascular lesions, and prior investigations of EPD treatment with the PDL, it appears that the use of the PDL may provide an effective, low-risk approach for treatment of EPD. Translating the experience of vascular and scar treatment to the treatment of EPD leads to several unanswered questions. First, does low-fluence, multiple-exposure treatment of EPD result in observable improvement? Second, do multipass procedures result in greater improvement? Third, is there a wavelength that may provide superior improvement?

The goal of this investigation was to evaluate systematically how treatment methods and laser parameters affect the outcome of PDL treatment of EPD. Specifically, this study addresses the questions of general observable improvement, single versus double-pass, and 585- versus 595-nm wavelength selection for treatment of EPD.

Methods

A total of 20 patients presenting with photodamage were recruited for the study. Consent was obtained, and the study protocol conformed to 1975 Declaration of Helsinki guidelines. All were female, with ages ranging between 34 and 72. Patients were recruited upon request for treatment of EPD. No effort was made to select for particular forms or grades of EPD. The subjects were randomized into two groups of 10. One group received a series of four single-pass treatments at 2-week intervals. The second group received a series of four double-pass treatments at similar intervals. Within each patient, one half of the face (left vs. right) was randomized and treated with either 585- or 595-nm wavelengths; 595-nm treatment was provided using the PhotoGenica V-Star laser, and a 585-nm PDL treatments were provided using the PhotoGenica V laser (Cynosure, Inc., Chelmsford, MA). All treatments were provided using a pulse duration of 0.5 ms, using a 10-mm handpiece. Treatment fluences were maintained just below the individual's purpuric threshold for the respective wavelength and ranged from 3 to 4 J/cm^2. Either side of the face did not necessarily receive the same fluence, as multipass and changes in wavelength alter the purpuric threshold. The goal was to provide a level of treatment with similar tissue effects, as determined by purpuric threshold. Purpuric thresholds were determined by threshold testing before treatment. Photos were taken before treatment and during follow-up. Photograph brightness and contract were manipulated where appropriate in an attempt to match better the quality of before and after images.

Blinded, subjective grading of before and final follow-up images (Figure 2) determined treatment efficacy. Five independent observers performed photographic evaluation. Observers independently graded changes in skin pigmentation, rhytids, and overall improvement on a scale of 0 to 5 (0 = no improvement or worse, 1 = minimal improvement, 2 = modest, 3 = good, and 4 = exceptional). In addition, observers were asked whether they had a preference for one side of the face (evaluating potential differences because of wavelength). Patients were also asked to provide their opinion as to their overall perceived improvement, first without and then with access to before treatment photos.

Statistical evaluation of the subjective observation was done using the Wilcoxon signed-ranks test. The

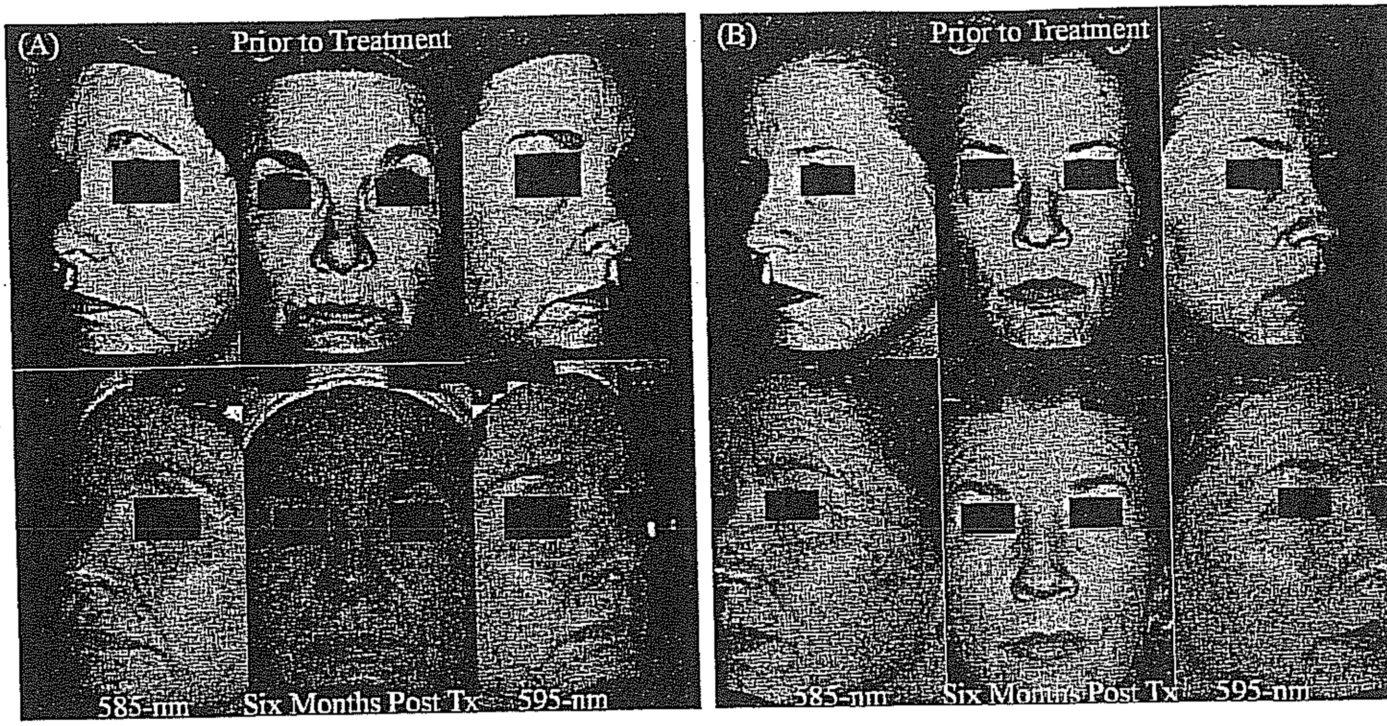

Figure 2. Representative examples of improvement achieved with this protocol. (A) Graded as achieving good pigment improvement, minimal rhyti improvement. (B) Graded as achieving good pigment improvement, moderate rhytid improvement.

threshold for statistical significance was set to be $P<0.05$.

Results

Of the 20 originally enrolled, 17 subjects completed the study through the final follow-up visit 6 months after the first treatment. Of the three lost to follow-up, none exhibited complications necessitating withdrawal from the study. Two of the three lost to follow-up were from the single-pass cohort, and one was from the double-pass cohort.

No subjects experienced side effects or complications caused by treatment other than a few who reported transient, localized purpura lasting less than 36 hours. The treatment did not interfere with normal activities.

The 10 of 17 subjects (59%) had photographs with clearly observable improvement in at least one parameter. Subjective grading of photos is summarized in Table 1.

Observers scored average pigment improvement of 1.5, or minimal to modest (Figure 3a). There was no observed preference for the 585- or 595-nm wavelength. Those treated with a series of single-pass treatments had greater average improvement, but not significantly so (2.2 vs. 0.9). If data are sorted according to those with and without obvious dyspigmentation before treatment, those with obvious dyspigmentation had greater average improvement, but not significantly so (2.3 vs. 0.8). The majority (fiv of seven) of those who began treatment with obviou dyspigmentation were in the single-pass cohort.

Observers scored an average rhytid improvement c 1.2, or minimal (Figure 3b). There was no observe preference for 585- or 595-nm wavelength. There wa no clear difference between single or double pas based on original pigment, or depth of rhytid.

Observers scored an average overall improvemei of 1.6, or minimal to moderate (Figure 3c). There wa no observed preference for the 585- or 595-n wavelength. Single- or double-pass and pigment-base improvements tracked the observed pigment improv ment closely.

Table 1. Average improvement, by condition, as grade by five blinded observers. Scores were evaluated for a subjects (Overall), those with and without significa superficial dyspigmentation at the start of the study, ar single and double pass treatments.

	All Scores	*Significant Pigment*	*Little Pigment Visible*	*1 Pass*	*2 P*
Average Pigment score	1.5	2.3	0.8	2.2	0.
Average Rhytid Score	1.2	1.1	1.2	1.1	1.
Average Overall Score	1.6	2.0	1.3	2.0	1.

Observer Grading Key: 0 = No Improvement or Worse, 1 = Minimal Improvem 2 = Moderate Improvement, 3 = Good Improvement, 4 = Exceptional Impr ment

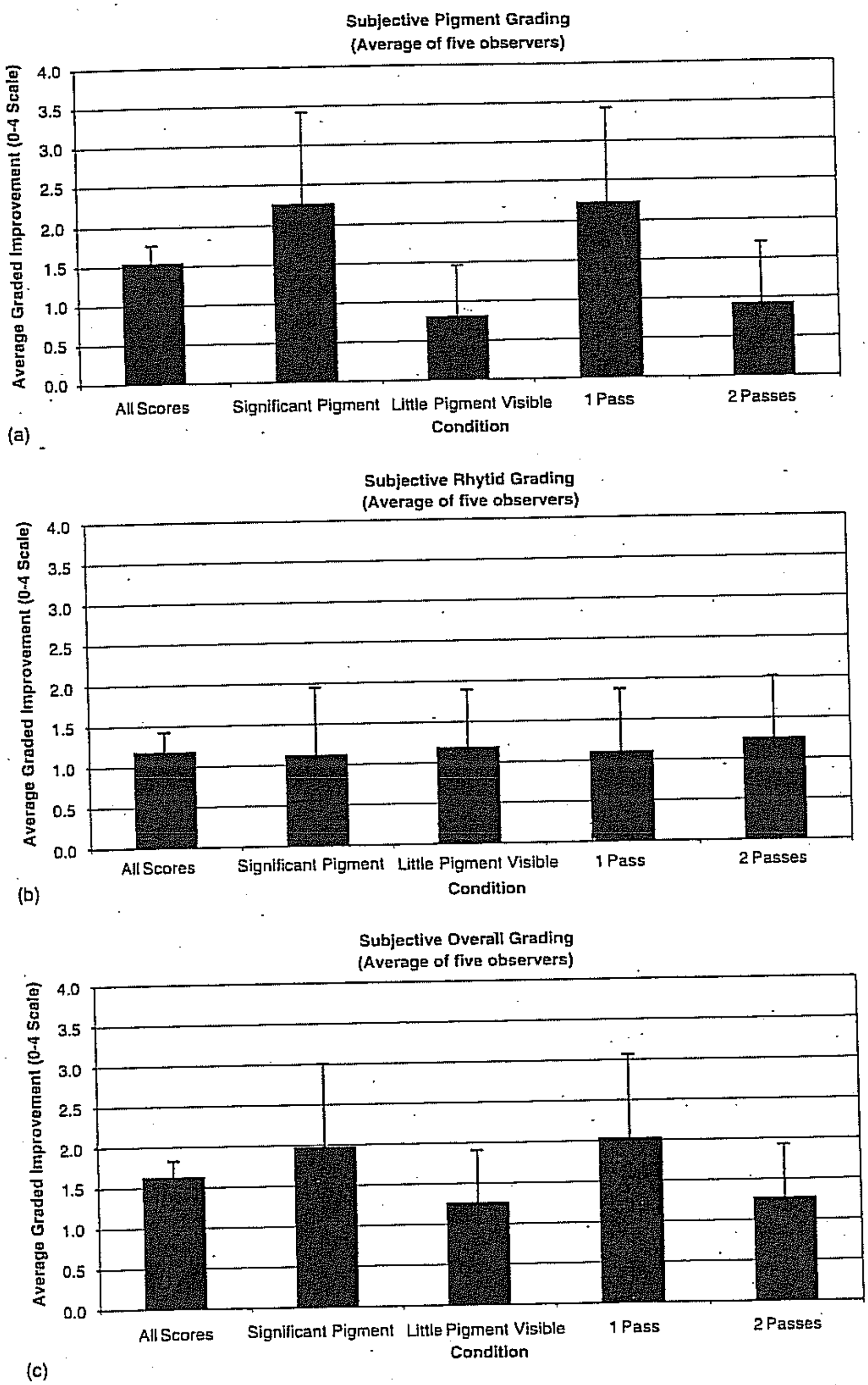

Figure 3. Graphical representation of observer graded improvement for (a) pigment, (b) rhytid, and (c) overall, respectively. Error bars represent 1 SD from the mean.

Although some subjects exhibited superior outcome to one side of the face, overall, there was no definitive preference based on treatment parameters. The subjects blindly self-reported a greater degree of satisfaction with wrinkle reduction than with pigment improvement, even in cases in which the pigment improvement was observer graded as good or where observer grading or overall improvement was minimal. Once shown before and after images, those with photographic pigment improvement noted the difference.

Discussion

The majority of those treated four times with the 0.5-ms PDL exhibited observable improvement in both reduction in dyspigmentation and reduction in rhytids, independent of the wavelength or the number of passes per treatment. The majority of the observed improvement is related to a reduction in superficial dyspigmentation.

Although the superficial location and preferential absorption of PDL wavelengths by melanin suggest that pigment improvement is a significant action of the PDL, this study provides the first systematic evaluation of this effect.

Interestingly, the original laser parameters under evaluation appear to be less important than the initial condition of the patient. Those with greater dyspigmentation before treatment were observed to have the greatest improvement. The imbalance of those with dyspigmentation in the populations of single versus double pass suggests that the single-pass data were tracking the pretreatment pigmentation rather than suggesting a preferred treatment method.

An attempt to correlate the observers grading with patient opinions of improvement yields a paradox. Those with the greatest observed improvement (pigment based) were typically unimpressed by the progress until shown before images. Those with minimal to no observed improvement were often the most enthusiastic about their progress and most often described improvement in skin texture rather than tone. This suggests that the improvements most obvious to the subjects are related to changes that are not easily photographed. Other methods, such as tissue elasticity, may be needed to better determine the nature of improvement important to the patient. It also suggests that keeping a photographic record of treatment progress is important to assist in gaugin observable improvement.

The use of the PDL at subpurpuric fluences for th treatment of EPD is a good option. It provides noninvasive treatment option with an exceptional side effects profile compared with other available treatmen options. A total of four subpurpuric PDL lase treatments provide improvement in the majority c patients. In many patients, the improvement caused b this treatment may be sufficient to avoid mo aggressive treatment options.

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Commentary

This study provides further evidence that the PDL may be used to improve the texture and rhytides of photodamaged skin. When we first investigated the use of the pulsed dye laser for reversal of wrinkling (1994, unpublished data), we found surprisingly good results but unacceptable purpura in achieving those results. We have subsequently found that subpurpuric fluences could achieve significant reversal of photodamage, and it is pleasing to see those results confirmed in this study. For this treatment to be clinically useful, it is necessary to use subpurpuric fluences. The authors studied a treat variable, that is, the use of double passes, that is a interesting approach to improving tissue response with adverse sequelae. Although their study did not find a signifi difference between single and double passes, I would encou further investigation in this direction. One advantag low-fluence, multiple passes is that it is possible to mai lower epidermal temperatures (especially with some ty epidermal cooling during treatment) because of epide cooling through thermal diffusion between pulses targeted vascular heat is accumulating (assuming a enough interval between pulses). To achieve these tissue effects, pulse stacking must be used. However, even if there is complete cooling of tissue between pulses, the second and subsequent passes encounter vessels with some degree of injury present, making them more susceptible to further injury. Because the fluences are not high, there is much less tendency toward purpura, as there is not the same rapid temperature increase resulting in boiling and vaporization of fluids with subsequent vessel rupture. Double passes may not be adequate to show significant tissue effects different from single-pass therapy, as it has been calculated that in order to have tissue effects equivalent to doubling the fluence, 14 separate but multiple passes must be used. Perhaps three or four passes would show a greater differential. One tissue effect shown in this study that has not been reported previously is the improvement in dyspigmentation. In fact, this aspect was the most visible improvement. It is surprising that patients did not notice this aspect until looking at before and after photos, as this is usually a primary concern of patients. Perhaps they did not notice because no one anticipated significant improvement, and therefore, they were not paying attention specifically to this aspect. It is also interesting that those patients with dyspigmentation did not have an enhanced response in rhytide improvement, as the epidermal pigment did absorb adequate laser energy for epidermal improvement and this often will trigger a secondary healing response in the dermis.

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