

Comparative Treatment of Small Diameter ($\leq 400 \mu\text{m}$) Vascular Lesions Using Extended Pulse Dye Lasers

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Background and Objectives: Extended-pulse dye lasers (EPDL) are commonly used to treat a variety of vascular lesions. This study evaluated whether differences in pulse formats and cooling methods might affect outcome in the treatment of small facial telangiectasia.

Study Design/Materials and Methods: Ten subjects presenting with symmetric, bilateral facial telangiectasia were studied. Each side of the face was treated with either the V-StarTM smart-cool air cooling (Cynosure, Inc.) (VS) or V-beam DCD cooling (Candela, Inc.) (VB) EPDL treatments with both systems were undertaken with a 10-millisecond pulse duration, 1 J/cm² below the purpuric threshold, with up to three passes.

Results: Treatment clearance with the VS EPDL occurred with a lower fluence, using fewer passes than with the VB EPDL ($P < 0.05$).

Conclusions: Although both the currently popular EPDL systems are highly effective in the treatment of small facial telangiectasia, clinical differences can be seen between these two systems. *Lasers Surg. Med.* 38:106–111, 2006.

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Key words: telangiectasia; PDL; EPDL; pulsed dye lasers

BACKGROUND

The pulse dye laser (PDL) has become a mainstay for treatment of vascular lesions due to a high degree of both safety and efficacy. Since initial clinical introduction of the 577-nm, 350- μs PDL in the 1980's [1], better understanding of both vascular anatomy and laser technology have led to a series of enhancements. These include longer wavelengths allowing better targeting of deeper vascular structures [2]; longer pulse duration to more effectively heat larger vessels, based on selective photothermolysis [3]; higher energies allowing the use of larger spot sizes and/or higher fluences; and adjunctive cooling to improve treatment comfort and to allow the use of higher treatment fluences [4,5].

Most recently have been the introduction of two PDL systems, the PhotoGenica V-StarTM (Cynosure, Inc., Chelmsford, MA) (VS) and the VbeamTM (Candela Corp., Wayland, MA) (VB), which incorporate the above features with extended pulse durations up to 40-milliseconds, and output energies of eight and six joules, respectively. Both systems have proven effective in the treatment of a large

variety of applications including port wine stains (PWS) [6,7], rosacea [8,9], and a variety of vascular ectasia [10,11]. The two laser systems use different laser resonator designs, different extended pulse structures (six sub-pulses for VS, four sub-pulses for VB), different calibration and control systems, optical delivery systems and associated treatment cooling (cryogen spray cooling with VB; cold air cooling with VS).

These differences present an interesting question. How do the two system relate clinically? Are published parameters for one equivalent to the other; are there differences in outcome related to the differences in the two technologies? It is because of these questions that the two systems were tested on a group of subjects presenting with vascular ectasia on the face, using parameters suggested by the two manufacturers for minimal purpura treatment.

METHODS

Ten subjects (9 female, 1 male) were recruited upon presentation with similar, bilateral facial vascular ectasia. All subjects were provided with appropriate informed consent. The subject population included skin types I–III and lesions were measured with an optical loupe to estimate vessel diameters. Lesions with diameter less than 400 μm were treated using a 10-millisecond pulse duration from both lasers. Treatment was done with either laser randomly assigned to one half of the face. Vascular ectasia on the other side of the face were treated with the other laser. Study areas were labeled and photographed prior to initiation of treatment.

All treatments were conducted using the two currently most popular extended PDLs. The V-StarTM laser (Cynosure) is a 595-nm laser system with extended pulse durations consisting of a six-pulse burst. V-StarTM treatments were done in conjunction with cold air-cooling. The VbeamTM laser (Candela, Inc.) is also a 595-nm laser system with extended pulse durations consisting of a four-pulse burst. VbeamTM treatments were done in conjunction

The V-StarTM laser was provided on loan for this study.

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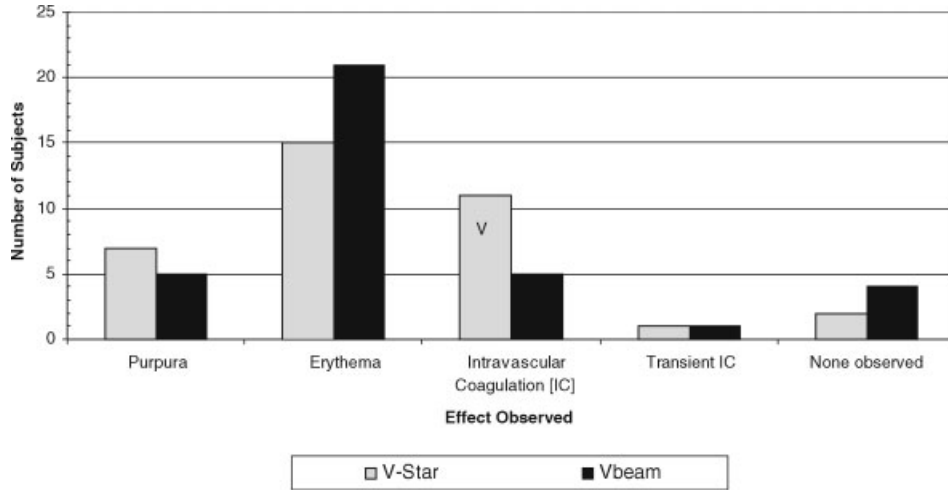


Fig. 1. Immediate effects of treatment observed over all treatments. Note more than one effect could be observed in a single subject treatment.

with cryogen spray cooling (DCD). All treatments were delivered using a 7 mm diameter hand piece based on respective manufacturer’s calibration of each device. An external meter was not available to compare device calibrations, however the use of purpuric threshold as a standard for treatment energy was chosen to eliminate calibration differences between devices.

Prior to treatment, subjects were tested to determine the purpuric threshold with the study lasers. Threshold testing was done on normal appearing skin, using a series of test spots behind the ear. Thresholds were determined for a single pulse and for up to a total of three passes. Threshold was determined by visual inspection of the test areas 1 hour following laser exposure. VS average purpura threshold was $9.8 \pm 1.0 \text{ J/cm}^2$, VB average purpura threshold was

$10.3 \pm 0.8 \text{ J/cm}^2$. Treatments were delivered by a single physician (EM) at a fluence $\sim 1 \text{ J/cm}^2$ below measured purpuric threshold (VS average $8.8 \pm 0.9 \text{ J/cm}^2$, VB average $9.3 \pm 0.7 \text{ J/cm}^2$), using technique as suggested by the device manufacturers. Up to three passes were delivered, separated by approximately 30 seconds between passes, (VS average 1.7 ± 0.7 passes, VB average 1.9 ± 0.6 passes), to each side by the appropriate laser per treatment session. Fewer passes were delivered if (a) there was obvious intravascular coagulation or vessel disappearance (b) treatment produced purpura (c) the patient was unable to tolerate additional passes. The air cooling associated with VS treatment was set to a fan speed of six for the first treatment, and was reduced to three for subsequent treatments. Air cooling was accomplished using the manufacturers

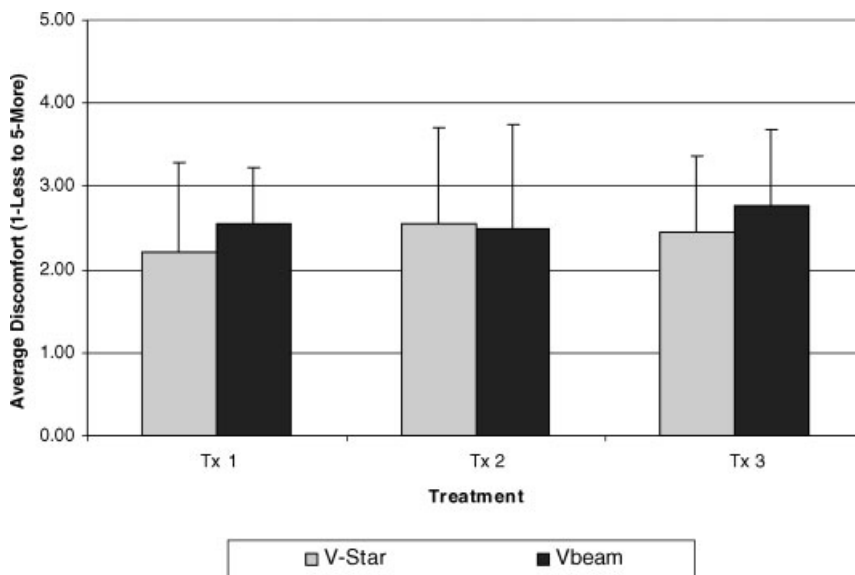


Fig. 2. Average discomfort reported by subjects on a scale of one (minimal) to five (worst imaginable).

handpiece mounted adaptor which placed the cooling nozzle approximately 37 mm from the treated skin. The DCD was set to a 30 milliseconds spray duration and a 30 milliseconds delay for all treatments.

Treatment areas were photographed immediately following treatment, and subjects were asked to rate treatment discomfort on a scale of 0–5 (0, none; 5, worst pain imaginable). Subjects were then provided a post-treatment log. Up to three treatments were provided at 4–6 week intervals. Treatment was not conducted if (a) there was complete resolution in fewer treatments or (b) the subject refused further treatment. Subjects returned for observation and photos 1 and 2 months following the final treatment.

Prior to each treatment and/or observation, the prior treatment log was collected and reviewed. Areas were photographed and evaluated by blinded observers to determine subjective improvement on an exact percent scale of 0%–100% (0=no improvement or worse to 100%=complete clearance of treated lesion). At the final follow-up visit, subjects were asked their preference of treatment side (device) and cooling method.

Due to the small sample size and the inability to assure a normal distribution of subjects, statistics were evaluated using the Wilcoxon signed rank test for significance. For statistical significance, the null hypothesis was disproved for $P < 0.05$.

RESULTS

The majority of lesions were nasolabial telangiectasia, although generalized facial telangiectasia were also treated.

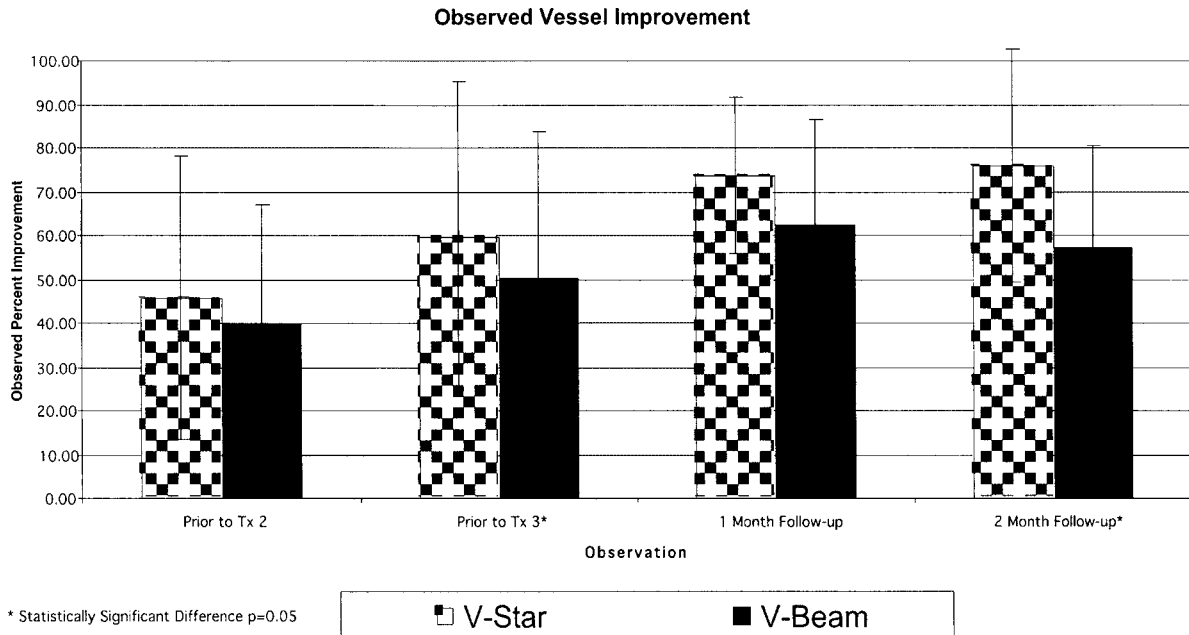
TABLE 1. Average Observer Graded Improvement at Each Evaluation Period

	Treatment improvement outcomes	
	Average	
	VS	VB
Prior to Tx 2	46% ± 32%	40% ± 27%
Prior to Tx 3*	59% ± 36%	50% ± 33%
1 month follow-up	73% ± 18%	62% ± 24%
2 month follow-up*	76% ± 27%	57% ± 24%

Asterisk denotes significant difference in outcomes at $P < 0.05$.

A total of 29 subject treatments were undertaken. Three treatments were completed in nine of ten subjects. One subject declined a third treatment for unspecified reasons, although she returned for follow-up visits. Treatments were completed without significant side effects (Fig. 1). With VS treatment typically resulted in immediate intravascular coagulation, although some treatments resulted in diffuse erythema. VB treatment typically resulted in immediate generalized erythema and/or intravascular coagulation. Transient side effects included swelling, crusting, purpura, and urticaria lasting for up to 7 days following treatment. There was no significant difference in transient side effects between the two devices.

On a scale of one–five (one minimal, five worst pain imaginable) treatment with VS was rated on average 2.2 ± 1.1 , 2.6 ± 1.2 , 2.4 ± 0.9 for treatments 1, 2, 3, respec-



* Statistically Significant Difference $p=0.05$

Fig. 3. Observed Improvement following treatment for bilateral, paired treatments compared to pre-treatment photographs. Asterisks* mark statistically significant ($P \leq 0.05$) measured using Wilcoxon signed rank test of significance.



Fig. 4. Before treatment with VS. [Figure can be viewed in color online via www.interscience.wiley.com.]

tively. Treatment with VB was rated on average 2.6 ± 0.7 , 2.5 ± 1.2 , 2.8 ± 0.9 for treatments 1, 2, 3, respectively. There was no significant difference in treatment discomfort between the two devices (Fig. 2).

Average observer graded improvement following each treatment with VS was $46\% \pm 32\%$, $59\% \pm 36\%$, $74\% \pm 18\%$, and $76\% \pm 27\%$ prior to treatments two and three, and at 1 and 2 months following the final treatment, respectively. Average observer graded improvement following each treatment with VB was $40\% \pm 27\%$, $50\% \pm 33\%$, $62\% \pm 24\%$, and $57\% \pm 24\%$ prior to treatments two and three, and at 1 and 2 months following the final treatment, respectively (Table 1). There was a consistent and statistically significant difference ($P \leq 0.05$) in outcomes prior to treatment three, and at the 2 month follow-up visit (Figs. 3–11). At all observation intervals, VS treatment exhibited superior outcomes in 8 of 10 subjects.



Fig. 5. Three months after treatment with VS. [Figure can be viewed in color online via www.interscience.wiley.com.]



Fig. 6. Before treatment with VB. [Figure can be viewed in color online via www.interscience.wiley.com.]

When queried regarding treatment preferences at the end of the study, four subjects stated a preference for treatment with VS, four with VB, and two did not state a preference. Two subjects preferred air cooling, four DCD, and four stated no preference. No device preferences were statistically significant. No reasons were stated by subjects regarding their reasons for device or cooling method preference.

DISCUSSION

All extended-pulse dye laser (EPDL) treatments were done using techniques to minimize purpura, including extended pulse durations, lower fluences, multiple passes, and adjunctive cooling methods. Clearly, purpurogenic treatment of ectasia is effective with both devices, and outcomes under those circumstances would likely prove similarly effective.

Interestingly, there was a significant difference in outcomes between these two devices. This was an unexpected result, as both devices are very similar in output. An attempt to cross-correlate treatment outcomes with side effects failed to show a clear trend. Subjects with a greater degree or duration of side effects did not necessarily achieve



Fig. 7. Three months after treatment with VB. [Figure can be viewed in color online via www.interscience.wiley.com.]



Fig. 8. Before treatment with VS. [Figure can be viewed in color online via www.interscience.wiley.com.]

greater improvement. There was a trend between exhibiting some treatment effect (intravascular coagulation, purpura, long lasting erythema) and greater improvement. Treatments resulting in no observable response exhibited little or no improvement.

Intra-treatment observation appears to provide a clue as to the difference between these two devices. Treatment with VS typically resulted in vessel darkening (intravascular coagulation) as an observable endpoint [12]. Treatment with VB, as reported by Rohrer [13], is often associated with a transient vessel darkening, followed by vessel disappearance. This outcome is often associated with erythema and/or edema lasting several days [14]. All of these effects were consistent with our experience, suggesting that the observed endpoints are predictable hallmarks of these comparative technologies.

While the wavelength, spot-size and fluence of these two devices is very similar or identical, there are two parameters of energy delivery, which are likely unique to each device: The extended pulse format and associated cooling method. It is likely that the combination of these two differences account for the differences in outcome between the two devices.



Fig. 9. Three months after treatment with VS. [Figure can be viewed in color online via www.interscience.wiley.com.]



Fig. 10. Before treatment with VB. [Figure can be viewed in color online via www.interscience.wiley.com.]

The VS 10-millisecond pulse duration consists of six 200-microsecond sub-pulses, separated to achieve the appropriate pulse duration. The similar VB pulse, in contrast, consists of four appropriately spaced sub-pulses. Studies have found that increasing pulse durations, with a larger number of sub-pulses provides better selectivity between large ($>100 \mu\text{m}$) and small ($<50 \mu\text{m}$) vessels, resulting in a higher purpura threshold. Tanghetti et al. [15] found that increasing the number of sub-pulses in an extended pulse format resulted in a monotonic increase in purpura threshold, allowing purpura-free treatment at higher fluences. Tanghetti has also found that this effect was more pronounced with longer pulse durations, such as



Fig. 11. Three months after treatment with VB. [Figure can be viewed in color online via www.interscience.wiley.com.]

20 and 40 milliseconds; and less pronounced at shorter pulse durations, such as 2–10 milliseconds [16]. In our study, we found that the VB exhibited a slight, but consistently higher purpura threshold, in contrast to the finding by Tanghetti.

Cooling methods used with the two lasers also differed considerably. Air cooling associated with VS treatment provides bulk cooling to the treated area. This method, when held in one location rapidly cools the tissue to 0°C [17]. Due to the duration of cooling, it is likely that the tissue is cooled considerably to some depth. The exact depth and degree of cooling is difficult to determine and varies from subject to subject, due to the nature of the device. This method can provide significant anesthesia and increase the purpuric threshold associated with EPDL laser treatment [6].

Cryogen spray cooling has been well studied both as a stand-alone device and in conjunction with EPDL's [18,19]. With cryogen spray cooling, a refrigerant is sprayed onto the skin, the evaporation of this compound quickly (millisecond time domain) and reliably cools a thin cross-section of the skin to well below 0°C. This method has been associated with the transient pooling of liquid cryogen, and the potential development of ice crystals associated with rapid freezing, which may interfere with the incoming laser pulse [20].

In the end, the following hypothesis may explain the noted differences between the two EPDL. The VS extended pulse combined with cold air cooling modestly increases the selectivity between large and small vessels at the 10-millisecond pulse duration allowing selective intravascular coagulation of target vessels. This effect is fairly uniform throughout the tissue, due to the bulk nature of air cooling, resulting in a visible "all or none" response.

In contrast, the VB pulse and associated cryogen spray cooling creates two zones of heating. Superficially, all vessels are "protected" by superficial cooling. Deep vessels are uniformly unprotected. This results in an appearance of erythema as deep, small vessel purpura is induced with overlying unaffected vessels. The transient darkening and disappearance of the target vessel are due to the transient development of methemoglobin at a temperature of ~60°C [21], followed by vasospasm. This may damage the vessel to a slightly lesser degree than the observed endpoint associated with VS, resulting in potential under treatment.

Finally, although there were observable differences in outcome, without significant differences in side effects or treatment discomfort, there was no clear patient preference for one device or the other. This suggests that both device and outcome are just two of many variables that go into patient satisfaction, which is highly subjective and personal.

CONCLUSIONS

Both EPDL devices provide acceptable treatment of vascular lesions less than 400 µm in diameter, when used with minimally purpuric techniques. There are, however, differences in both the subjective endpoint and final outcome between these devices.

Subtle differences between these two evaluated EPDL devices, and their application, may lead to differences in subjective treatment endpoints, accounting for the differences in clinical outcome.

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