Assessment of Pulsed-Dye Laser Therapy for Pediatric Cutaneous Vascular Anomalies

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C utaneous vascular anomalies, such as hemangiomas of infancy (HOIs), are prevalent in 5% to 10% of children and are the most common tumors of infancy.1 Approximately 20% of these vascular anomalies result in pain, bleeding, ulceration, infection, or functional impairment with vision, feeding, or breathing necessitating medical or surgical treatment.2 Complications from these lesions include painful ulceration, infection, bleeding, and occlusion or obstruction of vital structures such as the eyes, nose, mouth, and auditory canal.3 Facial lesions especially can cause great cosmetic disfigurement and psychosocial morbidity, affecting the child and the parent. Fifty percent of vascular lesions are still present when the child starts primary school. Although involution can be complete in up to 50% of children by the start of school, 15% to 40% of children are left with permanent skin changes,4 including pigment alteration, telangiectasia, atrophy, and fibrofatty residuum.5

Port-wine stains are benign congenital vascular anomalies that are localized in the dermis and affect 0.3% to 0.5% of infants.6 In contrast to HOIs, port-wine stains do not spontaneously involute. These lesions are characterized by an abnormal dermal plexus of layers of dilated blood vessels that increase in size with age.7 Although port-wine stains can occur anywhere in the body, about 83% are seen in the head and
When located on the face, these lesions can be psychologically devastating. Multiple studies have been performed examining different types of laser therapy applied to port-wine stains; however, none have shown a validated tool with high interrater reliability. Furthermore, because many of these studies involve subjective evaluation of pretreatment and posttreatment lesions, a validated assessment tool is especially important.9

The pulsed-dye laser (PDL) with the addition of dynamic epidermal cooling has gained popularity for treating vascular anomalies. The addition of epidermal cooling has been demonstrated to decrease the frequency of adverse events when used in combination with the PDL. The laser produces short pulses of yellow light at a wavelength that is absorbed by oxy-hemoglobin. This causes selective thermal destruction of abnormally dilated blood vessels with minimal to no damage to surrounding skin structures.10 It can improve residual telangiectasias left after involution of some childhood HOIs, reduce pain, and speed healing in ulcerated lesions.11 Although the PDL can prevent vascular proliferation, improve cosmetic outcome, and reduce complications in the treatment of HOIs and port-wine stains, published studies have not shown consistent benefits, and laser therapy is controversial.1,10-15 To date, no validated assessment tools exist to analyze results from PDL therapy. Such a validated assessment tool must have high interrater reliability and the ability to detect significance between groups. The goal of this article is to present this type of tool.

Methods

This was a retrospective medical chart review performed at a tertiary care hospital. The medical records of all consecutive patients treated with the cool-tip PDL from January 2005 to March 2011 were screened against eligibility criteria. Inclusion required the treatment of an HOI or port-wine stain with the 595-nm cool-tip PDL (Candela Corp). Exclusion criteria were a lack of photographic documentation of both the pretreatment and posttreatment state. Patients who underwent surgical reconstruction after laser therapy needed to have post-surgical photographic data in the electronic medical record to be included in the study. The institutional review board at Children's Hospital and Clinics of Minnesota approved the study protocol.

Lesions were treated until a purpuric skin point was reached. Pretreatment and posttreatment photographs were assessed independently by 3 pediatric otolaryngologists and facial plastic surgeons (R.T., T.L., and J.S.) using an assessment tool developed by our group (Figure 1). This assessment tool asked the reviewers to quantify the change in size, color, thickness, scaring, hypopigmentation, and atrophy when comparing preoperative and postoperative pictures. The reviewers were blinded to the treatment and type of lesion present. In addition, the reviewers were nontreating surgeons for these patients. Standardized lighting and specialty photography were not performed, and all images were obtained from our electronic medical records (EMRs). Change in lesion color, thickness, and size was graded as 1 (0%), 2 (1%-24%), 3 (50%-75%), 4 (76%-99%), and 5 (100%). The presence or absence of scarring, atrophy, and hypopigmentation were noted by each reviewer. Average values for each question (Q1-Q6) were calculated. The nonparametric Mann-Whitney test was used to compare the aggregated scores between patients with port-wine stains and those with HOIs for Q1 to Q3. Fisher exact test was used to compare the score between patients with port-wine stains and those with HOIs for Q4 to Q6. Intraclass correlation was reported for the interrater reliability between 3 raters with the assumption of a 2-way mixed model. Interrater reliability is the degree of agreement among 2 or more individual raters. It addresses the consistency of the implementation of a rating system. A score higher than 0.7 is usually considered acceptable. Some authors accept a score lower than 0.6 for exploratory purposes, but there is a lack of substantial mutual agreement (Table 1).16 We used the following guide to analyze our interreliability. P < .05 was considered to be statistically significant.

Results

Medical records of 43 pediatric patients with facial vascular anomalies were reviewed. Twenty-one patients were excluded because adequate photographic data were not available. Twenty-two patients met the study criteria. Five patients had port-wine stains, and 19 had HOIs. One of the 5
patients with a port-wine stain was diagnosed as having Sturge-Weber syndrome. Eight of the 17 patients with HOIs underwent surgical reconstruction after PDL therapy. Patients were treated with the 595-nm cool-tip PDL with the following parameters: energy fluence of 4.0 to 7 J/cm², spot size 7 to 10 mm, and a pulse width of 0.45 milliseconds. The dynamic cooling device settings consisted of a 30-millisecond cryogen spray with a 20-millisecond delay. Each patient was placed in the supine position under general anesthesia. An external metal eye shield was used to protect both eyes.

The 22 patients underwent a total of 79 laser treatments. The average age at the start of treatment was 10 months. Pulsed-dye laser therapy was applied to the upper lip, lower lip, nasal tip, nasal ala, upper eyelid, cheek, forehead, and the temple. Interrater reliability of our assessment to detect change in color was 0.92; thickness, 0.92; size, 0.92; and scarring, 0.90. This translates to excellent agreement among raters and a consistent rating system.16 Interrater reliability was acceptable (0.70) in detecting atrophy; however, interrater reliability was unacceptable in detecting hypopigmentation (0.10).

On average, patients with HOIs treated only by PDL showed a 50% to 75% improvement in color, 1% to 24% improvement in thickness, and 1% to 24% improvement in size of the lesion. Figure 2 demonstrates how the reviewers rated each patient. Eight patients with HOIs did not achieve satisfactory results from PDL therapy and elected to undergo surgical reconstruction. These lesions were in the upper lip (2 lesions), lower lip and cheek (2 lesions in each location), and the nasal tip, upper eyelid, and forehead (1 lesion in each of these locations). These patients were noted to have 100% improvement in color, thickness, and size of the HOIs after surgical reconstruction. Patients who underwent only PDL therapy did not show any scarring; however, patients who underwent surgery did show scarring. In contrast to HOIs, patients with port-wine stains showed a 1% to 24% improvement in color and no improvement in thickness or size. Because HOIs and port-wine stains are unique anomalies, we performed a comparison between groups. Owing to the small sample size, the non-parametric Mann-Whitney test was used to compare the aggregated scores between patients with port-wine stains and those with HOIs for Q1 to Q3. Fisher exact test was used to compare the score between patients with port-wine stain and those with HOIs for Q4 to Q6. From this statistical analysis, significant differences were noted between the groups (Table 2).

### Table 1. Interpretation of the Interrater Reliability Results

<table>
<thead>
<tr>
<th>Score</th>
<th>Internal Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥0.90</td>
<td>Excellent</td>
</tr>
<tr>
<td>0.80 to &lt;0.90</td>
<td>Good</td>
</tr>
<tr>
<td>0.70 to &lt;0.80</td>
<td>Acceptable</td>
</tr>
<tr>
<td>0.60 to &lt;0.70</td>
<td>Questionable</td>
</tr>
<tr>
<td>0.50 to &lt;0.60</td>
<td>Poor</td>
</tr>
<tr>
<td>&lt;0.50</td>
<td>Unacceptable</td>
</tr>
</tbody>
</table>

*See LeBreton and Senter.16*

### Table 2. Average Values of Reviewer Answers for Questions 1 to 6

<table>
<thead>
<tr>
<th>Assessment, Question (Aspect of Improvement)</th>
<th>By Diagnosis, % of Improvement</th>
<th>Surgical Reconstruction for Patients With HOIs, % of Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Port-Wine Stain</td>
<td>Hemangioma</td>
</tr>
<tr>
<td>Q1 (Color)</td>
<td>1-24</td>
<td>50-75</td>
</tr>
<tr>
<td>Q2 (Thickness)</td>
<td>0</td>
<td>1-24</td>
</tr>
<tr>
<td>Q3 (Size)</td>
<td>0</td>
<td>1-24</td>
</tr>
<tr>
<td>Q4 (Scarring)</td>
<td>1-24</td>
<td>1-24</td>
</tr>
<tr>
<td>Q5 (Atrophy)</td>
<td>1-24</td>
<td>1-24</td>
</tr>
<tr>
<td>Q6 (Hypopigmentation)</td>
<td>1-24</td>
<td>1-24</td>
</tr>
</tbody>
</table>

Abbreviations: HOI, hemangioma of infancy; NA, not available (P value not determined owing to lack of interrater reliability for assessing).

### Discussion

Our assessment tool is a valid analysis to detect change in color, size, thickness, scarring, and atrophy to HOIs and port-wine stains treated with a cool-tip PDL. Interrater reliability was ex-

Figure 2. A Patient With a Hemangioma of Infancy

cellent for Q1 to Q4 and acceptable for Q5 of our tool. In addition to being a consistent rating system, our assessment tool detected clinically significant differences in the response of HOIs and port-wine stains to PDL. The Table shows that patients with HOIs had a more significant change in color (P = .03) and thickness (P = .004) when compared with those with port-wine stains. Although patients with HOIs on average had a better response to change in size, this was not significantly different than the change in size in those with port-wine stains (P = .18). Because PDL therapy does not have an impact on the size of these lesions, this is a clinically expected finding that our assessment tool also found. Furthermore, our assessment tool agreed with the clinical finding that surgical reconstruction leads to resolution of HOIs. Eight patients with HOIs did not achieve satisfactory results with PDL therapy and chose to have surgical reconstruction. Surgical reconstruction resulted in complete resolution of color (P = .03), thickness (P < .001), and size (P < .001) of the lesion when compared with laser therapy. Surgery did result in significant scarring (P = .008).

Patients with port-wine stains responded less well than did patients with HOIs. The literature is ambiguous regarding the resolution of port-wine stains treated with PDL. A study of 30 patients by Hennedige et al.17 and a study of 8 patients by Léauté-Labrèze et al18 also showed 50% reduction in color of port-wine stains. None of these patients achieved complete clearance. In contrast, Garden et al19 achieved at least 75% clearance in 44% of patients, with another 29% having 50% to 75% clearance. Garden et al18 did not separate patients and looked at all patients, whereas Hennedige et al17 and Léauté-Labrèze et al18 reviewed only patients with port-wine stains who also had Sturge-Weber syndrome. Patients with port-wine stain in our study showed a 1% to 24% improvement in color and no improvement in thickness or size. One of our 5 patients with port-wine stains also had Sturge-Weber syndrome. The pathophysiologic characteristics of port-wine stains do not change in syndromic children, and one would expect similar results across institutions that are using a similar technique. The lack of a standardized and validated assessment tool can contribute to this variability in results. Our tool aims to fill this gap in the literature.

Since the discovery of the use of propranolol in treating HOIs by Léauté-Labrèze et al.,20 several groups have reported good, yet variable results; however, no standardized assessment tool exists to evaluate treatment.21-24 The medication is given at high doses of up to 2 to 3 mg/kg per day and is typically administered for 9 months to treat head and neck HOIs. Continuation of treatment is often based on clinical results. Adverse effects of therapy include sleep disturbance, memory loss, lethargy, exacerbation of asthma, hypoglycemia, gastrointestinal discomfort, and mood changes. Fuchsmann et al.,25 in a retrospective study in which propranolol was the first-line treatment for 33 pediatric patients with HOIs, noted improvement in the color of the lesion; however, they had no means of quantifying their response to treatment. Forty percent of the patients in that study received adjuvant therapy, including laser, corticosteroids, and surgery. Use of our tool in such treatments can help measure response to treatment and set benchmarks of when to administer adjuvant or alternative therapy.

Hypopigmentation is a relatively common complication seen with PDL therapy; it can be seen in up to 14% of patients.14,15 Other, more rare complications include burns, scars, and blisters. Our assessment tool was not able to reliably assess which patients had hypopigmentation (intrarater reliability = 0.10). We did not include other complications in our study because they were not seen in our patients and are rare. To determine if hypopigmentation was present in our patients, we assessed photographs directly from the EMRs that were taken without standard lighting or photography. Some of the pictures were mailed to us by parents owing to their distances from our facility. These factors likely contributed to inconsistent responses from our reviewers. However, many clinics are not equipped with professional lighting and photography to take pictures of pediatric patients with vascular lesions. The ability of our assessment tool to be reliable in these circumstances enhances its ability to function well in routine clinical practice where professional photography may not be available. Furthermore, our assessment tool does not rely on the use of expensive and professional software to perform analysis. To our knowledge, no other such assessment tool exists in the literature.

In conclusion, currently no standardized or validated methods exist to evaluate results from intervention. Our assessment tool is reliable to assess HOIs and port-wine stains in patients who undergo PDL therapy. Our tool is a consistent rating system that shows agreement among raters to detect change in color, size, thickness, scarring, and atrophy in HOIs and port-wine stains treated with PDL.