Flash-lamp pulsed-dye laser treatment of port-wine stains in childhood. A case of technology assessment

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The introduction of the flash-lamp pulsed dye-laser treatment of facial port-wine stains in childhood

A case of Health Care Technology Assessment

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A case of health care technology assessment

Abstract

Background — Lasers have been used in the treatment of port-wine stains (PWS) for over 30 years. With the introduction of the flash-lamp pulsed-dye laser (FPDL) it was assumed that infants could be treated safely, effectively and probably more efficiently. Nowadays FPDL treatment is an established form of treatment of port-wine stains (PWS) in childhood.

Methods — Based on the iterative Health Care Technology Assessment (HCTA) loop, we examined whether sufficient evidence from evaluations has been present to support the introduction of FPDL treatment for facial PWS at an early age. Such an assessment requires an interdisciplinary approach focusing on aspects of safety, efficacy, effectiveness, quality of life, costs, as well as the ethical issues of treatment.

Results — Assessment of the FPDL in PWS treatment of children did not follow the model of medical innovation and evaluation. Most assessments have been focused on laser applications that were already in clinical use. Efficacy and effectiveness of laser treatment have been the major concern in most assessments. Only a few studies have looked at costs and ethical aspects of treating children.

Conclusions — We believe that this non-adherence to the iterative model reflects the gradual way by which innovations find their way into clinical practice.
**Introduction**

Port-wine stains (PWS) are congenital vascular malformations of the superficial dermis which affect 3 to 5 children per 1000 births. The skin discoloration usually is seen at birth as a faint pink macule that progresses over time and darkens to a deep red or purple. Nodularity of PWS may occur as the patient reaches middle age. Most (90%) of PWS occur on the head and neck, at equal rates in males and females. There is no spontaneous regression of PWS at any time of life.

Lasers have been used in the treatment of PWS for over 30 years. The use of laser light introduced a degree of selectivity that was unachievable with conventional therapeutic modalities, such as surgical excision, ionizing radiation, tattooing with skin-tone colors, cryosurgery and dermabrasion.

Initially argon and ruby lasers were used in the treatment of PWS. Positive results were reported for argon laser treatment in 60 to 85% of selected adult patients, usually after puberty. Unfortunately, this treatment resulted in cosmetically unacceptable outcomes in approximately 40% of the treated children, mostly due to scarring. Treatment with the argon laser was therefore not selected for the treatment of facial PWS in childhood. In the absence of effective treatment alternatives, patients depended on camouflage as the only possibility to cover their facial PWS at any age.

With the introduction of the flash-lamp pumped pulsed-dye Laser (FPDL) in 1985 clinicians assumed that infants and children could be treated safely and effectively and, probably, also more efficiently. Nowadays FPDL treatment (450 microseconds, 585-nm) has become the treatment of choice for facial PWS in children and most adults.

Although there is increasing awareness that the introduction of any new technology should be founded evidence-based, many new therapeutic strategies ‘emerge’ without a systematic evaluation of the associated costs and benefits at any time during the development. Health Care Technology Assessment (HCTA) is a system for the structural evaluation of new medical techniques or strategies, including procedures, equipment and drugs. Such an assessment requires an interdisciplinary approach focusing on aspects of safety, efficacy, effectiveness, quality of life, costs, as well as the ethical issues of treatment.
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This paper discusses the introduction and dissemination of the FPDL and the corresponding evidence base for treating facial PWS at an early age. Based on the HCTA loop, we will examine whether sufficient evidence from evaluations has been present to support the introduction of FPDL treatment for facial PWS in children.

The first section describes Health Care Technology Assessment in more detail. Subsequent sections address specific issues in the HCTA loop of laser treatment of PWS in children: (1) the need of treating PWS in childhood (burden of illness), (2) the use of the FPDL in PWS treatment (safety, efficacy), (3) documentation of improved patient outcomes (effectiveness, quality of life measures, patient preferences), (4) societal impact (costs, and ethical issues) and finally (5) the implementation of the FPDL into medical practice (monitoring, reassessment). We will show that the introduction of FPDL treatment did not exactly follow the steps prescribed in the HCTA loop. The paper closes with a discussion of likely explanations for this discrepancy between the proclaimed need for data to support evidence-based decisions in clinical practice and in policy areas and the absence of such relevant information in this particular application.

Health Care Technology Assessment

Several authors have described a framework to assess medical innovations from a societal point of view, to support rational decision-making. These authors were primarily interested in the evaluative strategies used during the evolution of a medical technology, rather than setting out the mere technical evolution of these technologies. To be fair, one must admit no standard methodological approach for conducting such HCTAs has been developed. More and more HCTA is considered to be an iterative process rather than a one-time analysis. In general the following four actions can be distinguished in HCTA studies: identification, testing, synthesis, and dissemination.

Feeny et al. described a more specific model for the assessment of a new medical technology on the basis of what they called a Technology Assessment Iterative Loop (TAIL, Figure 1). Within this loop 7 steps are identified, each covering a specific part of the evaluation. Each step should be concluded with the overall judgement before continuation of the cycle is justified. Drummond and Davies pointed out that these different types of measures complement
Chapter 7

Synthesis and dissemination

Figure 1. Health Care Technology Assessment Iterative Loop (TAIL).

Each other, each one adding important information about the consequences of introducing a new medical intervention or strategy. If the effectiveness of the new treatment modality is proven, that is if the benefits are clear and if only less effective alternative treatments are available, it is likely that a positive societal recommendation will be given, encouraging the acceptance and implementation of the new treatment into everyday practice.

The following sections describe to what level such required information was and is nowadays available for laser treatment of facial PWS in children.

1. Burden of illness

Before the introduction and the use of the FPDL as a therapeutic modality, for (facial) PWS at an early age, it is important to appraise the potential for the development of medical complications and psychological problems over time.
Having a PWS is in itself not a life-threatening condition. In fact, PWS are often perceived as a “cosmetic problem”. Most observers will admit that a visible PWS is responsible for a certain degree of disfigurement. It is this disfigurement that can cause a negative impact on emotional and psychological well being. For this reason, treatment can be regarded as a reconstructive rather than a pure cosmetic procedure.

Several studies have tried to assess the burden of having a PWS for the individual as well as for society in terms of the associated psychological morbidity. Kalick, Goldwyn and Noe examined the psychological status of 82 patients with PWS. The mean age of these patients was 24 year during the early stages of treatment. Lanigan and Cotterill studied the psychological morbidity of 71 PWS adult patients before they had applied for laser treatment. In both studies the standard generic psychological screening tests used did not display emotional disturbance or psychiatric morbidity in PWS patients compared to “normal” controls or other patient groups. However, based on qualitative information Lanigan concluded that patients with a facial PWS suffer a significant degree of social stigmatization. He concluded that these patients have lowered levels of self-esteem, which has an adverse effect on social development. Van der Horst et al., using a generic quality of life measure, reported little effect on role and social functioning in adolescents and adults (13-31 years) with a PWS. Nevertheless, these same patients reported low scores on mental health, self-perceived health and vitality/energy.

In a comparative analysis of the specific consequences of having a PWS, adolescents and adults (13-31 years) showed significantly more negative consequences of their PWS in social contacts compared to children, aged 0-13 years. Troilius et al. confirmed these results, reporting most disturbances of the PWS during the age period 10-20 years.

Since the introduction of the FPDL two studies have been published that looked at the psychosocial adjustment of children with a PWS. Both studies did not report malfunctioning of children with PWS compared to non-disfigured peers on measures of psychosocial adjustment using standardized instruments (Child Behavior Check List).

In summary, we can say that FPDL treatment of facial PWS is warranted based on two health care purposes: the prevention of psychological morbidity in the long term, by treating children as young as possible, and medical treatment, aimed at improving the current health status of a patient.
the natural progression of PWS may lead to medical complications, the major morbidity is most likely psychosocial.

So far such morbidity has not consistently been identified in adults or children, when compared to a general or comparable patient population. A possible explanation for this absence can be the fact that most studies designed to assess the burden of having a PWS at any age have used general psychological or psychiatric screening tests. Such tests may not be sensitive enough to detect the presupposed psychosocial morbidity. Standardized instruments that focus on children, skin diseases or more specifically having a PWS, are still under development.

It is safe to conclude that the development of laser treatment for PWS in childhood has been based on an intuitively plausible yet empirically not confirmed (future) burden of disease: an apparent stain, associated with disfigurement, presumed to lead to psychosocial maladjustment.

2. The use of the FPDL in PWS treatment during childhood

If subjects with a PWS qualify for treatment, there is supposed to be a clear advantage in treating patients with a (facial) PWS as young as possible. In order to substantiate this claim, it is essential to assess the safety and efficacy of using the FPDL at any age. Efficacy refers to the benefit of using the FPDL under ideal conditions.

Within this HCTA step studies are undertaken to outline the specific conditions and patients for which the tentative, preliminary use of the FPDL is suitable. Discussing these issues does not give an immediate answer on whether FPDL treatment is effective. The data at this step allow identification of the conditions and patients in which the treatment is promising enough to make further studies on effectiveness suitable.

The clinical use and safety of using the FPDL in the treatment of PWS at any age was based on the evidence that selective photothermolysis could result in ablation of vascular lesions with minimal scarring. Since the introduction of the FPDL the efficacy of treatment in childhood is reported to be associated with a number of prognostic criteria: including anatomical site, age of the patient, color of the PWS, the varying mean depth of vessels and different skin types. On the basis of these observations, it was expected that (very young) children could be treated more successfully, as they have a thinner skin, a smaller PWS surface area and less ectatic structure of the abnormal bloodvessels in the superficial dermis.
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While the clinical efficacy of the FPDL is considered to be proven from clinical experience, there are still no conclusive data on optimal parameters of treating PWS during childhood.

3. Patient outcomes

To show that FPDL treatment actually improves patient's health status, or prevents deterioration, one must provide data on health gains compared to the best available alternative strategy. The basic question is whether any such improvement in patient outcome outweighs the burden of reported side effects and discomfort.

From a medical point of view, patient outcomes can be operationalized into clinical effectiveness, health-related quality of life, and disease specific health status.

Effectiveness

During the last fifteen years many clinical reports on PWS treatment using the FPDL in childhood have been published. The evaluation of treatment outcome and adverse effects has traditionally been based on subjective clinical scoring systems. Effectiveness studies concentrated on proximal criteria as skin texture, color and scarring. There are no standard criteria so far.

In early studies patient outcome was reported in qualitative, rather subjective terms, like poor or excellent clearance, favorable or unfavorable outcome. On some occasions outcome was assessed in terms of the percentage reduction in color, compared with pre-treatment photographs.

Although it is generally considered that younger children require fewer treatments than adults, Alster en Wilson have reported that younger children may require even more treatments, due to rapid growth of the residual blood vessels between consecutive treatments. Significantly better results were reported in patients who commenced treatment before 1 year of age. PWS less than 20 cm² at initial examination also showed better clearance. The overall percentage of children achieving complete clearance is considerably less than initially reported. Treatment outcome for the individual child is still rather unpredictable, also due to the fact that an indefinable subgroup of children responds slowly and with poor outcome. The results of several published studies specifically concerning the effectiveness of FPDL treatment during childhood are outlined in Table 1.
summarized studies looked at the hypothesized correlation of outcome of FPDL treatment with the age of the patient.

More recent studies introduced objective outcome-measures, such as colorimeters and reflectance spectrophotometry.\textsuperscript{34} Diverging results have been published about the importance of color of the PWS.\textsuperscript{37-39} Controversies have been described concerning the importance of lesional color before onset of treatment for the treatment outcome.\textsuperscript{39,40} Some report better clearing in light lesions (pink), while others demonstrate poor results in pink lesions. In a study of 261 patients treated over a five-year period\textsuperscript{41} color of the PWS was not found to be of prognostic value. Orten et al. experienced that PWS show a tendency to recur at a rate approaching 50\% between 3 and 4 years post-treatment.\textsuperscript{42}

As the experience of treating PWS with the FPDL increases, the interest grows in attempting to measure clinical features (anatomical site\textsuperscript{42} vessel location or vessel diameter) that beyond age, may be of prognostic importance for the outcome of treatment. Negative outcomes were associated with increasing size (diameter), depth and location of the involved vessels. The wide variation in treatment response poses a profound need for objective devices to measure treatment outcomes. Non-invasive methods of investigating PWS such as reflectance spectrophotometry, videomicroscopy, infra-red tomodiography and pulsed photothermal radiometry are suggested to be of value in predicting the outcome and assessing whether different laser parameters may be more appropriate for individual patients.\textsuperscript{43}

Reported medical complications with the FPDL in adults and children are rare. The incidence of adverse effects is considered low for patients with PWS.\textsuperscript{7,10,11,32,44} FPDL treatment causes few adverse changes to skin colour and texture, irrespective of age, anatomical site, number of treatments and type of lesion. Scars have occurred in areas accidently traumatised soon after laser therapy. Nevertheless, it has been suggested that the incidence of side effects and complications produced by the FPDL may be higher than stated in previous investigations.\textsuperscript{45} Hyperpigmentation, usually transient and resolved in 2 to 3 months, is the most common side effect after FPDL treatment of PWS.\textsuperscript{39,46}

The establishment of clinical effectiveness of FPDL treatment has concentrated on retrospective cohort studies or follow-up. Most of these studies did not include appropriate controls, nor did they report on unselected series of consecutive patients. Until recently little attempt has been made to standardize the criteria by which treatment results are assessed.
Table 1. Evidence table for treatment of facial PWS with FPDL in childhood.

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Age range (mean)</th>
<th>Treatment % patients / % clearing</th>
<th>Average treatments</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garden et al. 1989</td>
<td>52</td>
<td>(29)</td>
<td>44% / &gt;75%</td>
<td>2.4</td>
<td>Less clearing with dark nodular PWS.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>29% / 50-74%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>19% / 25-49%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>8% / &lt;25%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tan et al. 1989</td>
<td>35</td>
<td>3 mths-14 years</td>
<td>100% / 100%</td>
<td>6.5</td>
<td>Best response on neck, nose and forehead. All children receive complete</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(7.2 years)</td>
<td></td>
<td></td>
<td>clearance. Children &lt; 7 years needed fewer treatments than older children.</td>
</tr>
<tr>
<td>Reyes et al. 1990</td>
<td>73</td>
<td>3 mths-14 years</td>
<td>45% / &gt;75%</td>
<td>2.5</td>
<td>Best response: neck/eye region, pale flat PWS and younger children (3 mth-6 years). Least response: purple PWS.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(6.2 years)</td>
<td>42% / 50-74%</td>
<td>1.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>7% / 26-49%</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5% / &lt;25%</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Ashinoff et al. 1991</td>
<td>12</td>
<td>6 wks-30 wks</td>
<td>83% / &gt;50%</td>
<td>2.9</td>
<td>FPDL safe in infancy.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(14.9 wks)</td>
<td>45% / &gt;75%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>n</td>
<td>Age range</td>
<td>Treatment % patients / % clearing</td>
<td>Average treatments</td>
<td>Comments</td>
</tr>
<tr>
<td>------------------------</td>
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<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Morelli et al. 1992</td>
<td>134</td>
<td>0-12 years</td>
<td></td>
<td>7.0</td>
<td>More complete clearance with younger children.</td>
</tr>
<tr>
<td>Goldman et al. 1993</td>
<td>43</td>
<td>0-4 years</td>
<td>49% / 70%</td>
<td>3.4</td>
<td>Best response (better clearance and fewer treatments) in lesions in patients less than 4 years of age. Best response on face, neck and torso.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.5-14 years</td>
<td>51% / 68%</td>
<td>4.0</td>
<td></td>
</tr>
<tr>
<td>Alster et al. 1994</td>
<td>76</td>
<td>0-2 years</td>
<td>29% / 87.3%</td>
<td>9.1</td>
<td>Better results at younger ages, however number of treatments is greater than previously reported.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-8 years</td>
<td>26% / 78.5%</td>
<td>10.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>9-15 years</td>
<td>14% / 77.3%</td>
<td>8.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;=16 years</td>
<td>31% / 73.5%</td>
<td>5.7</td>
<td></td>
</tr>
<tr>
<td>Morelli et al. 1995</td>
<td>83</td>
<td>&lt; 1 year</td>
<td>27% / 65%</td>
<td>8.1</td>
<td>Best clearance with very young children. Initial size of the lesion is also important to consider. Smaller PWS (&lt;20 cm) better clearance.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1-2 years</td>
<td>16% / 62%</td>
<td>7.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2-6 years</td>
<td>22% / 54%</td>
<td>9.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>6-12 years</td>
<td>22% / 45%</td>
<td>7.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt; 12 years</td>
<td>13% / 58%</td>
<td>6.3</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>n</td>
<td>Age range (mean)</td>
<td>Treatment % patients / % clearing</td>
<td>Average treatments</td>
<td>Comments</td>
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<td>---------------------</td>
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<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Van der Horst et al. 1998</td>
<td>89</td>
<td>0-5 years</td>
<td>24% / 33%±26</td>
<td>10.0 (±4)</td>
<td>Objective assessment of clearance. Effect of treatment not related to age/timing.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6-11 years</td>
<td>26% / 43%±17</td>
<td>11.0 (±5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>12-17 years</td>
<td>24% / 45%±20</td>
<td>10.0 (±6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>18-31 years</td>
<td>26% / 37%±23</td>
<td>9.0 (±5)</td>
<td></td>
</tr>
<tr>
<td>Nguyen et al. 1998</td>
<td>91</td>
<td>&lt; 1 year</td>
<td>33% / 48%</td>
<td>10.0</td>
<td>Most successful in young patients with small PWS (&lt;20 cm) located over bony areas of the face.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1-6 years</td>
<td>37% / 32%</td>
<td>10.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt; 6 years</td>
<td>30% / 32%</td>
<td>10.0</td>
<td></td>
</tr>
</tbody>
</table>
Health related Quality of life

Health related quality of life (HRQOL) measures are increasingly used along with traditional outcome measures to assess health care technologies. They provide a more complete picture of the ways in which health care affects patient outcome. HRQOL can be a useful method of measuring benefit in aesthetic surgery of low-priority plastic surgery patients.\textsuperscript{47,48} HRQOL measures can thus be used to determine the effects, of the FPDL treatment on (young) patients with a PWS.

Former studies\textsuperscript{9} have suggested that improvement in HRQOL can be realised by PWS treatment, but so far a formal HRQOL measurement is often not included in effectiveness studies of FPDL. If present, HRQOL is narrowed to the presence of psychological morbidity and behavioural problems.

Recently Troilus et al. showed significant differences in 231 patients (aged 0 to 80 years) before and after FPDL treatment on several issues concerning socio-psychological distress of having a PWS.\textsuperscript{23} It is thought that PWS treatment at young age, before formal education begins and the child interacts with many other children, could prevent considerable psychological impairment.\textsuperscript{10}

Wagner and Wagner used anecdotal interview data to describe ways in which parents and the parent-child relationship may be impacted by the presence of a PWS.\textsuperscript{49} In a recent study Miller et al. explored the psychological experiences of parents of children with a facial PWS undergoing laser treatment.\textsuperscript{50} They found four variables associated with lower parenting stress: child's age, parents degree of family satisfaction, the level of parental concern regarding the child's facial PWS, and the parents satisfaction with staff communication. Their results support the need for treatment of the PWS at an early age.

Patient preferences

Few authors so far have looked at patients' assessment of laser surgery. In those that were performed, the design is a reflection of the assessment by adult patients,\textsuperscript{51} not children, of the results of older laser types,\textsuperscript{52,53} not the FLPLD, in different anatomical sites,\textsuperscript{54} not facial PWS, in most cases after a short treatment period, not the full length of treatment. There is a growing appreciation of the need to incorporate patients' preferences and satisfaction into the decision whether to treat PWS at any age.
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We found a wide variation in the basic assessment of patient outcome variables used in the reviewed FPDL studies. Methods for assessments were far from standardised and often biased, the use of independent blind comparisons was rare. Early reports concluded that treatment at an early age was associated with better clearance rates, and that fewer treatments were needed, compared to older patients. More recent and better-controlled studies reported no significant differences in the number of patients attaining complete clearance, nor in the percentage of lesional lightening or the number of treatment required when patients were compared by age. The assessment of general HRQOL is usually not included in evaluative reports. Outcomes research was often based on expert opinion without explicit critical appraisal. Notable variations in methodological approach make a comparison of overall outcome difficult.

4. Costs

After establishing an improvement in patient outcome, there is a need to document costs and related economic implications of new technologies.

Costs considerations are an important part of HCTA. An economic evaluation of a clinical strategy serves two objectives. The first is to introduce resource considerations into the analysis through an assessment of the opportunity costs of the new technology. The second objective is the development of a framework within which the incremental costs of the new technology can be compared with the improved benefits if both are positive.

The additional resources associated with laser treatment of PWS are best justified when they are spent when the anticipated benefits are highest. Although this is an interesting theme, no studies to date have systematically estimated the cost-effectiveness of FPDL treatment. Cost-effectiveness of the use of the FPDL in childhood cannot be established until effectiveness is known. For this reason, cost-effectiveness studies have tended to come rather late in the life-cycle of any technology.

So far one study addressed cost information of PWS treatment in relation to age (Chapter 3). Besides the issue of earlier versus later treatment, one could also think of evaluating FPDL treatment versus alternative treatment options (the use of camouflage or other types of lasers) or comparing a short treatment period versus a long treatment period (finished treatment).
The isolated use of clinical outcome within the economic evaluation is difficult. Most PWS patients, even in childhood, did not finish therapy when assessment was performed. Patients who did finish treatment received optimal clearing, not necessarily leading to complete clearance of their PWS. Ideally the time span for evaluation should be long enough to include the total costs of initial and further treatment. This is not always feasible. An evaluation based on a short duration can lead to erroneous conclusions.

From the available literature it would seem that the number of treatments required for clearance of PWS varies greatly between patients, depending on the position and color of the birthmark. Nobody has as yet established the point at which no further improvement of PWS clearance is to be expected from FPDL treatment. The majority of patients require from 1 to 20 therapy sessions, spread out over many months or even a few years, to obtain optimal fading in a single area. This observation holds for all age groups.

The length of a single therapy session depends primarily on the individual pain threshold level and the use of general anaesthesia. The time per visit may last from 5 minutes to four hours (Chapter 4). In contrast with other lasers the FPDL is relatively painless. Yet despite advances in pain therapy, many children tolerate laser sessions poorly.\(^{55}\) While general anaesthesia is not a requirement for all young patients, its use with those who are highly anxious or pain-sensitive allows a more effective use of treatment session time.\(^ {56,57}\) Some proponents have argued that treatment can be performed without the repetitive use of general anaesthesia, avoiding the expense of staff and equipment and possible complications, especially to very young children, of this procedure.

The need of general anaesthesia brings an element of risk into the treatment procedure. It also increases the costs of the procedure considerably. One must wonder whether the risks of early treatment of PWS then outweigh the benefits, especially when multiple laser sessions have to be used. Therefore it should not be falsely accepted that treatment is painless and psychologically atraumatic.

The possibility of treatment during childhood raises some social and ethical concerns. Treating PWS at early ages affects patients, family members, providers and employers in several ways that are not reflected in morbidity rates (Chapter 4).
5. Synthesis and implementation

FPDL treatment has changed during the last decade. Like many technologies FPDL therapy underwent multiple innovative improvements after the initial acceptance into general practice. The assessment of the use of lasers in PWS treatment has followed more or less a common pattern. Most assessments have been focused on a selection of the laser application that was already in clinical use. In most early assessments safety and efficacy of medical lasers have been the major concern. Only a few studies have identified costs and ethical aspects of treating children.

Traditional mechanisms of assessing port-wine stain response to laser therapy have rested mainly on subjective determinations by physicians and patients. However, the wide variation in treatment response poses a profound need for objective devices to measure treatment outcomes so that maximum effectiveness can be achieved without unnecessary repeat of treatments.

Were technology is fast changing, reassessment should take place from time to time. The problem then becomes to decide when a technology has changed enough to warrant reassessment. The choice of time scale depends both on the natural history of the disease and on the timing and pattern of treatment distinction between curative and palliative treatment modalities. Although it is obvious that FPDL treatment has presented a significant and substantial advance in the treatment of PWS in childhood, this laser may not be the treatment of choice for all PWS at any age. New lasers with larger spot sizes and faster repetition rates may enable new possibilities within laser treatment. Longer wavelengths penetrate deeper into the dermis, but are absorbed less by oxyhemoglobin, and require higher fluences. 585 nm remains the wavelength of choice in treatment of PWS with the FPDL.

Discussion

The efficacy and effectiveness of the use of the FPDL in the treatment of PWS can in principle be determined along a chain of inquiries that lead from technical capacity of technology to changes in patient health outcomes to cost-effectiveness (TAIL). As summarized in this paper, the evaluation of the FPDL in PWS treatment of children is in contrast with such an iterative model of medical innovation and evaluation. The diffusion of the use of the FPDL in the treatment of PWS is not cyclic but gradual. Systematic information evaluating the use of the FPDL at any age was not at any practical stage available.
We believe that this non-adherence to the TAIL for development and evaluation is typical for this type of technology, fast changing and rapid diffusion, reflecting the ad-hoc way by which medical technical innovations find their way into clinical practice. The diffusion of the FPDL into childhood has little relation to proven effectiveness and cost-effectiveness.

Product champions and opinion leaders have pioneered the introduction of the FPDL into clinical practice. Their enthusiastic reports may have lead to rapid diffusion of this technology treating children before adequate evaluation was performed. There is still no planning or regulation of medical lasers. In general, they can be freely purchased from available funds. It is therefore important to exchange information developed by technology assessments (effectiveness, cost-effectiveness and life cycle studies) to encourage appropriate diffusion.

The introduction of the FPDL has been influenced by policy initiatives to limit costs. In particular, fixed health care budgets and global budgeting for hospitals make capital investments in a technology such as the laser difficult, given its relatively high capital costs. Patient demand and prestige reasons of the (specialized) centers might have stimulated the fast diffusion of using the FPDL in the treatment of PWS in childhood, without much thought for utility and cost-effectiveness.

In a health care environment that increasingly realizes the need for sound data to support rational decision making, the situation will change. Future years will most likely show a discrepancy between the traditional mode of gradual innovation, sometimes based on notions with high intuitive appeal, and more formal evaluations before these innovations are incorporated into clinical practice and into reimbursement systems. Before this will happen, researchers have to recognize the need to discuss the methods for conducting and reporting evaluation studies.
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References

17. Drummond and Davies 1991
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