Modified Durham MPD tester (UVA-1 semi-automated skin tester)

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Abstract

Background: There are three MPD testing methods currently used in dermatology centers. These methods may expensive, fairly large device and time-consuming to use. In all of these techniques, the patients and the phototherapists are at risk of exposure to stray UVA and need to protect their skin.

Objective: As a new medical modified device, there was a need for a series of laboratory studies to establish its properties by: fully characterization of the device, establishing the optimum standard operating procedure and to identify potential health and safety issues relating to it's use in a clinical environment. Secondly, to proceed with *in-vivo* experimental work to determine how normal skin reacted to irradiation with this device to establish a normal range for systemic and bath PUVA for the MPD and a within-patient comparison of MPD testing with the conventional method versus the hand-held UVA-1 skin tester device.

Methods: The randomized, left-right, comparison study between MPD UVA-1 and MPD UVA panel PUVA was carried out on 22 patients. All volunteers recruited in this study received UVA1+psoralen irradiation on the lower back and UVA+psoralen (PUVA) irradiation on the contralateral side of the lower back. Allocation of these sites was randomly assigned to left or right.

Results: The UVA-1 lamp is still not a Philips Cleo PUVA lamp. In the application of MPD estimation, a known and robust relationship can be established between the erythemogenic potential of the UVA-1 lamp and the Cleo PUVA lamp because only psoralen is used as a sensitizer. This relation calculated by an equation:

MPD PUVA lamps = MPD UVA-1 X 0.40647 + 0.27448.

Conclusion: A method of "closed" UVA application (Durham tester) is quick (four minutes), safe (no unwanted radiation for the patient or phototherapist) and convenient (easy to use).

The combination of UVA (320-400nm) irradiation and 8-methoxypsoralen (systemic or topical) is known as photochemotherapy or (PUVA treatment). PUVA therapy is a frequently modality treatment in the management of psoriasis and a variety of other dermatoses. Systemic or oral 8-methoxypsoralen is associated with systemic adverse effects such as nausea, liver toxicity, cataract, squamous cell carcinoma and persistent photosensitivity of the whole body 12-24 hours. However, many of these adverse effects avoided or minimised by bath (topical) PUVA[3-6].

National guidelines for PUVA suggest that all patients referred for PUVA therapy should be tested to determine the minimal phototoxic dose (MPD)[7]. The definition of MPD is the smallest dose of UVA to result in a barely perceptible erythema after 120 hours[4]. The MPD does not inform on patient skin reaction to increased doses, and is currently used to set the start dose. It also has the important role of checking for unusual or unexpected sensitivity to PUVA in individual patients. The PUVA therapy start dose is 70% or 50% of MPD for each patient to avoid skin burning and erythema. There are three MPD testing methods currently used in dermatology centres (table 1). These methods usually involve a template to define several test areas plus a source of UVA. For example the Waldmann tester uses six areas and a UV canopy (the UV 800k). It is fairly large,

expensive, and time-consuming to use. Also plastic templates can be made on the phototherapy unit that stick to the patient's skin. The UVA source in this case is a hand/foot UVA panel or a PUVA cabin. In all of these techniques, the patients and the phototherapists are at risk of exposure to stray UVA and need to protect their skin.

Table 1: Methods of MPD tester

MPD method	Good points	problems
Hand-made templates	Cheap	Home made Adhesion to skin Time-consuming methodology Operator dependant
Waldmann skin tester	Semi-automated Once set up, can be turned on and left alone until completed	Expensive (£2000) Under-estimates MPD Inconvenient to use (couch) Patient needs to lie flat
Durham modified MPD tester (UVA1 Semi-automated skin tester)	Cheap (£400) Easy to use	UVA-1 not UVA

Patients and methods:

Before commencement of this study, ethical approval was obtained from the South East Wales Local Research Ethics Committee, Approval also be sought from Gwent Healthcare NHS Trust Scrutiny and Risk Review Committees. A randomized, left-right, comparison study between MPD UVA-1 and MPD UVA panel PUVA on the patients

was carried out on 22 patients. The sex distribution was 11 females and 11 males. The age range was between 18-61 years. Skin phototypes I, II, III and IV were assigned according to Fitzpatrick's classification[2]. All volunteers recruited in this study received UVA1+psoralen irradiation on the lower back and UVA+psoralen (PUVA) irradiation on the contralateral side of the lower back. Allocation of these sites was randomly assigned to left or right. Different doses of UVA-1 were applied to adjacent areas of skin by the use of modified Durham MPD tester (UVA-1 semi-automated skin tester) as in figure 1.

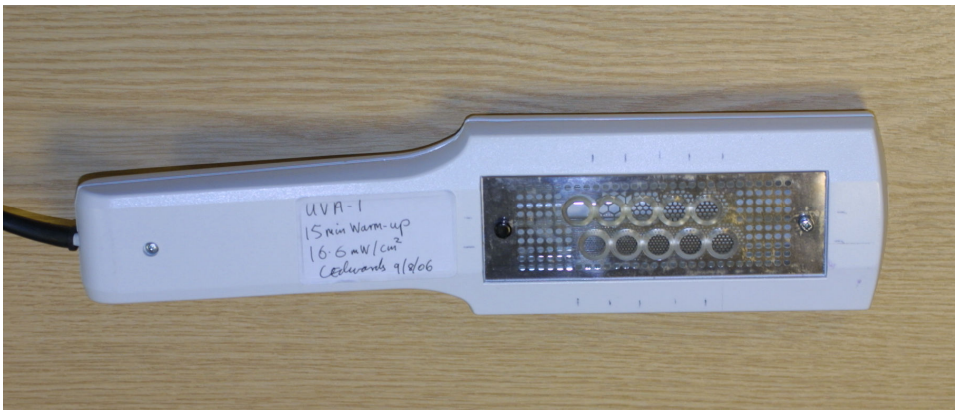


Figure 1: Modified Durham MPD tester (UVA1 Semi-automated skin tester).

Modified Durham MPD tester (UVA-1 semi-automated skin tester)

The Durham MED tester is a commercially available device found in most phototherapy units. It is a small hand-held unit containing low-pressure TL-01 (narrow-band UVB) fluorescent tubes[1]. In the medical physics department of the Royal Gwent Hospital in Newport (South Wales), the device was modified by replacing the TL-01 tubes with UVA-1 compact fluorescent tubes (340-400nm). The hand-held device consists of a plate with 10 apertures with metal foil attenuators. It is designed to administer a dose series increasing by a factor of 1.26 (this is the cube root of 2, so doses are double at every third

aperture). In other words, each dose is 1.26 times the previous dose[1]. Starting from the completely open aperture (100%) at dose 3 J/cm^2 ending to the maximum attenuating aperture (12.5%) at dose 0.36 J/cm^2. The dose sequence values for the device are given in table 3.1 and figure 3.2. All doses are given in three minutes. The dose sequence values for each aperture as shown in figure 2.

Electrical safety checks were done for the Durham modified MPD tester device before calibrating this device. This was to avoid electrical shock and involved checking earth leakage, earth current bouding resistance and applied part earth leakage. All tests were performed using a Seward Portable Appliance tester to IEC 6060-1-1 (2005). Medical device limits were applied. The modified Durham MPD tester was initially warmed-up for 15 minutes (Fig. 3). A Bentham DM150 spectroradiometer was used to calibrate the UVA-1 output of the Durham modified MPD tester. In addition the DM150 was itself calibrated against a standard tungsten lamp (Bentham CL6 NPL traceable tungsten lamp) calibrated by the National Physical Laboratory (NPL).

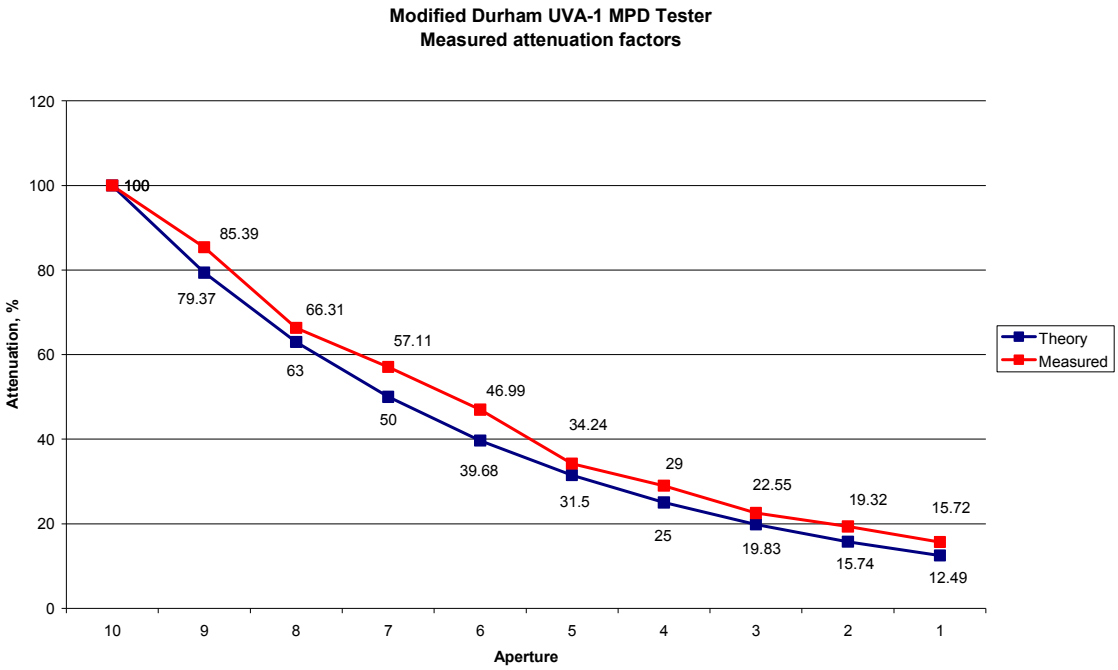


Figure 2: Two graphs show the attenuation factors for modified Durham UVA-1 MPD tester and the theoretical tester.

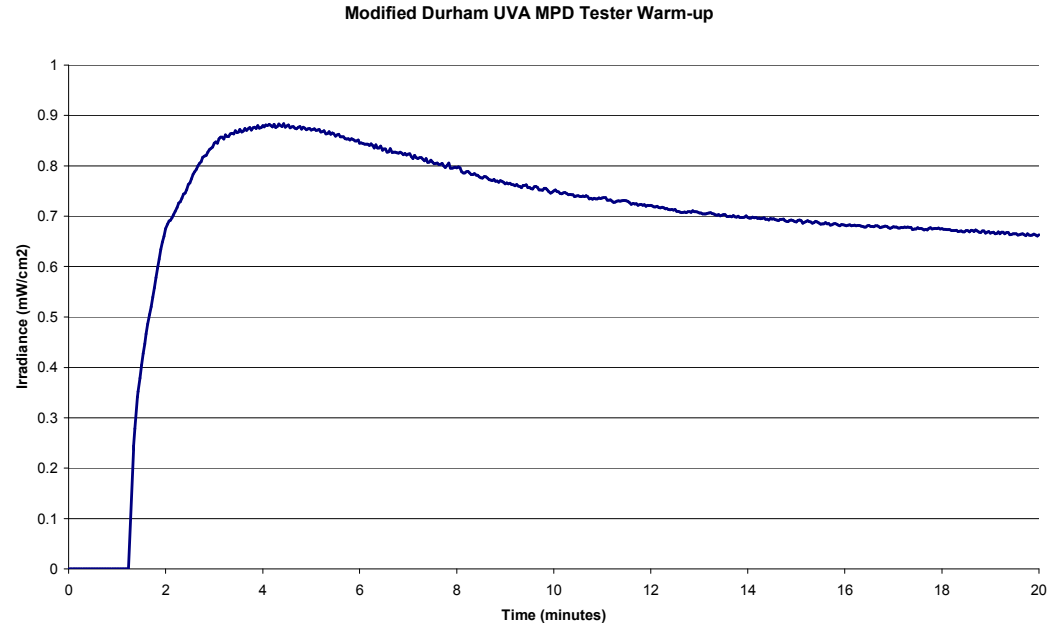
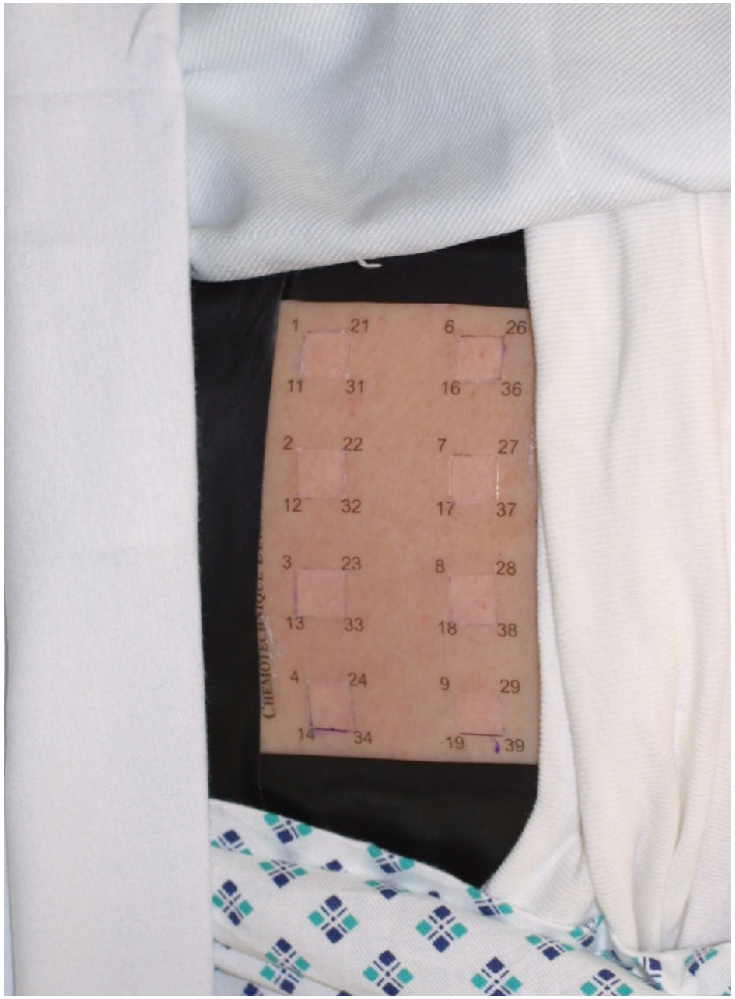


Figure 3: variation in irradiance with time following switch-on of device.

Panel PUVA tester

The modified Durham MPD tester was directly compared to the MPD method used in the phototherapy units. This "traditional" method is widely used elsewhere in the UK. It consists of irradiating eight squire apertures of psoralen-sensitized skin using a panel of PUVA lamps. The dose sequence consists of a maximum dose of 2.2 Joules, with a factor of $\sqrt{2}$ (1.42) between adjacent areas. Each dose is tabulated with the required time to administer the dose at a distance of 20 cm from the face of the panel at the calibrated output from that panel. The template is applied to the lower back and all other areas of the patient are protected. Seven of the eight apertures are covered with opaque tape (figure 4). The timer is set to the maximum time required, and started simultaneously with the UVA panel. Each aperture is uncovered at the time required to deliver its' appropriate dose. The dose sequence is given below:

2.2 J/cm^2, 1.55 J/cm^2, 1.10 J/cm^2, 0.78 J/cm^2, 0.55 J/cm^2, 0.39 J/cm^2, 0.28 J/cm^2 and 0.20 J/cm^2.


1 21
6 26
11 31
16 36
2 22
7 27
12 32
17 37
3 23
8 28
13 33
18 38
4 24
9 29
14 34
19 39

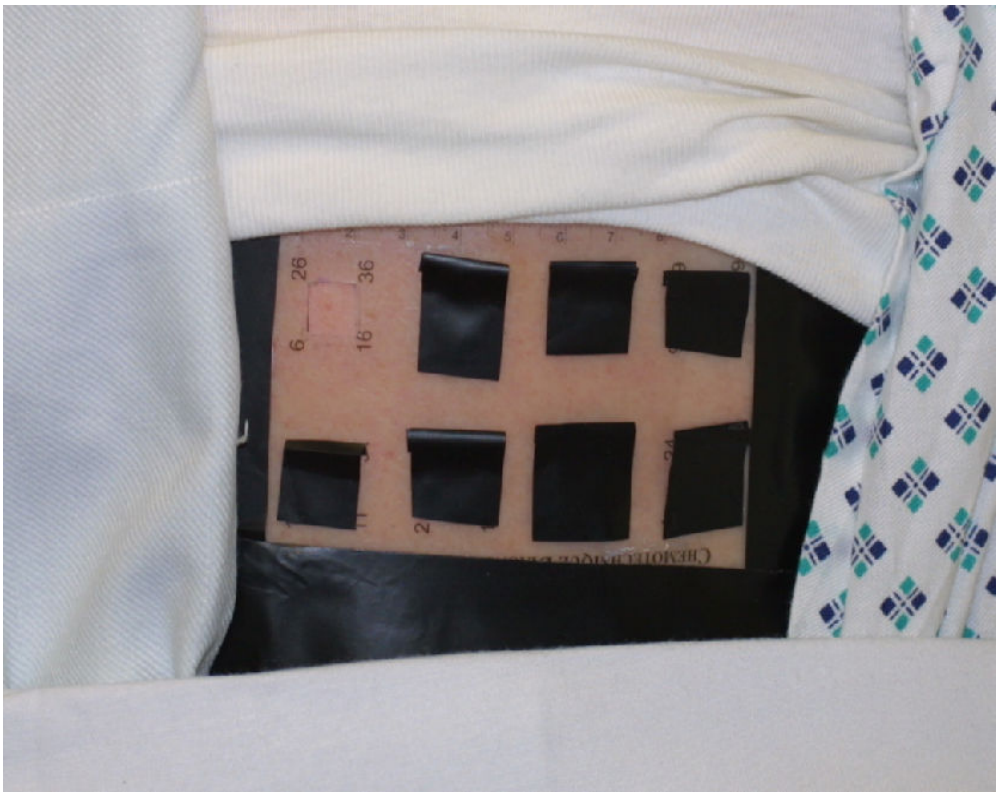


Figure 4: Hand made template with eight apertures in the above and while covered by opaque tape in the lower photography.

Statistical analysis

Statistica software version ??? was used to analyse the data and construct the graphs in this study.

Results

One side was exposed to UVA1, and UVA irradiation to the contralateral side of the lower back for all the 22 patients. The MPD was assessed visually and by erythema meter (mexameter from Courage and Kazaka Co.) for both sides. The assessment and measurement were made at day 5 (120 h) for each small square irradiated region on the lower back on the right and left side. All visual assessment were made with standard illumination at a colour temperature of 6500 K (CIE standared Iiiuminant D65)

All the 22 psoriasis patients' data entered a statistical computer program to analyze these data to estimate the modified Durham MPD tester (UVA-1) and MPD panel PUVA (UVA source). Figure 5 shows this relation. From this diagram we can calculate the relation through an equation:

MPD PUVA sources = MPD UVA-1 X 0.40647 + 0.27448

(0.40647 and 0.27448 both are fixed factors)

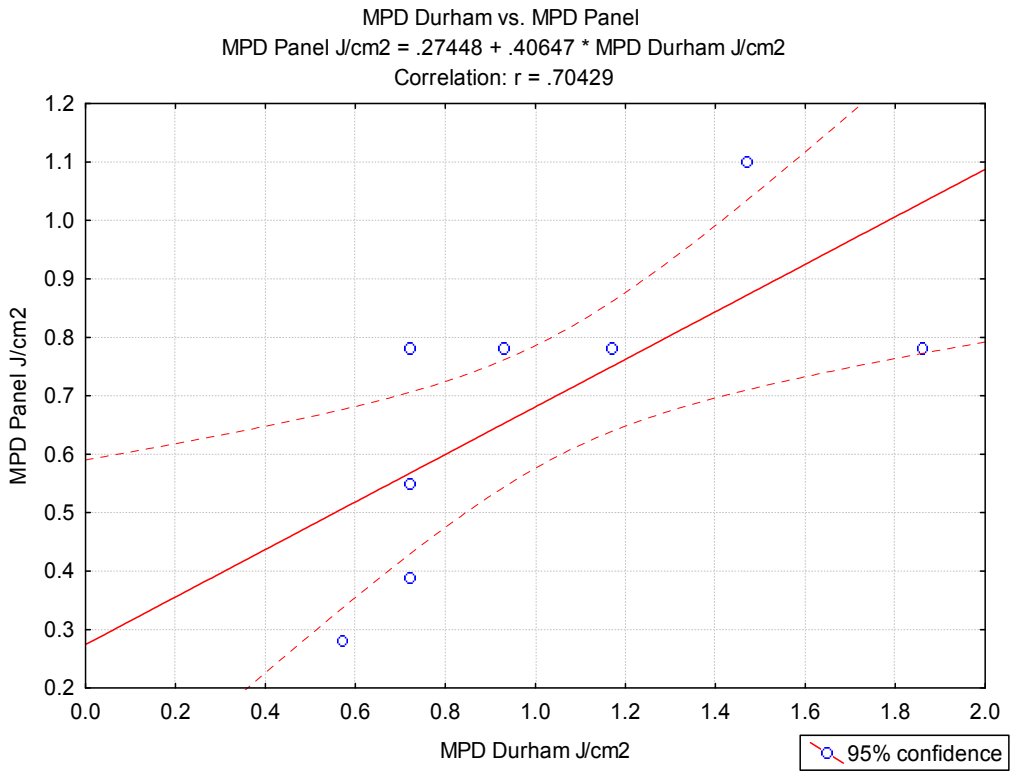


Figure 5: Comparison between MPD modified Durham tester and MPD panel PUVA.

Discussion

A method of “closed” UVA application such as the Durham tester is quick (four minutes), safe (no unwanted radiation for the patient or phototherapist) and convenient (easy to use). The problem with the use of a compact fluorescent lamp (CFL) as source of UVA in the Durham tester is that there is no compact lamp available with the same spectrum as a PUVA cabin fluorescent tubes. The UVA CFL is in fact a UVA-1 lamp. Therefore, an adjustment may be necessary to estimate a PUVA MPD from the MPD measured using the UVA-1 CFL in the Durham tester.

This study explored the use of the TL-09 CFL in a Durham tester for use as an MPD tester for PUVA treatments. The calibration, warm-up and attenuation characteristics were all measured. These factors were used to reconstruct a measurement protocol if the TL-09 CFL device is able to be used to estimate a PUVA-tube MPD. In order that the UVA-1 CFL can be used to estimate a PUVA MPD it has to be established that there is a consistent, preferably linear, correlation between measured values of MPD for both the UVA-1 and PUVA tube irradiation in each subject.

The results of this study show a linear relationship between the two UVA sources, although the number of subjects used to establish this relationship is relatively small. The recruitment of further volunteers is ongoing, and the exact relationship that has been established in this study will be updated with further data and adjusted if required. The method of comparing a running mean will be used. In this method, the average

correction factor for converting a UVA-1 MPD to a PUVA MPD will be plotted against the number of volunteers measured. When the variation of the running average becomes less than 10% of the average, then the number of subjects measured is considered sufficient.

Because the UVA-1 to PUVA MPD thus for established in this study has a significant intercept, a single multiplying factor will not convert from Durham MPD to a PUVA equivalent MPD. Therefore a conversion table is the best way to use the UVA-1 (Durham tester) MPD result to indicate the PUVA equivalent MPD. Form 1 overleaf is a form for use in a phototherapy unit where the Durham tester is used to establish a PUVA MPD. The phototherapiest applies the Durham tester to the psoralen-sensitized skin (bath PUVA in this example) for the stated time, four minutes. When, after the appropriate development time (five days) the MPD dose is visually assessed, the MPD sites is marked on the table, and the PUVA-equivalent MPD can then be read from the lower box. This is calculated by the equation given in the results:

In this study the Durham tester was applied to the skin for three minutes, delivering 3.0 J/cm^2 UVA-1. However, a significant number of patients failed to show any MPD reactions at this dose. Therefore, the Durham MPD form indicates an application time of four minutes (4.0 J/cm^2 UVA-1). This should ensure that all (or most) patients will show an MPD reaction.

In designing the does schedule for the UVA-1 CFL in the Durham tester an estimate of its erythemal effectiveness was made. The measured spectrum of the UVA-1 CFL was weighted with a PUVA erythema action spectrum published by Cripps *et al* [3]. This indicated that the UVA-1 lamp should be 15% as erythemally effective as a PUVA UVA lamp (Philips Cleo). In other words, it was expected that approximately 6.6 times the dose of UVA-1 would be needed to elicit erythema than a Philips Cleo on psoralen-

sensitized skin. However, the UVA-1 lamp used in this study was 45% as erythemally effective, which is three times as erythemogenic as the published PUVA action spectrum would predicted. It may, therefore, be informative to repeat a PUVA action spectrum study in order to establish the true wavelength dependence of PUVA erythema, and perhaps to further optimise PUVA treatments.

On a cautious note, it should not be forgotten the UVA-1 lamp is still not a Philips Cleo PUVA lamp. In the application of MPD estimation, a known and robust relationship can be established between the erythemogenic potential of the UVA-1 lamp and the Cleo PUVA lamp because only psoralen is used as a sensitizer. However, for the application of checking for unexpected sensitivity, other considerations must be taken into account. If a patient has a photosensitivity caused by an expected agents, such as a prescription drug, and the action spectrum of that photosensitivity lies outside the irradiation spectrum of the UVA-1 lamp, then it may not be detected. In practice this is unlikely, as the PUVA treatment spectrum has a considerable overlap into the UVA-1 spectrum.

Form 1: Durham Bath PUVA MPD Test Record Sheet

10min warm-up

Open aperture output- 16.6 mW/cm^2

All Skin Types:

Max PUVA dose 2.31 J/cm^2 MPD tester time = **4 minutes 0 seconds**

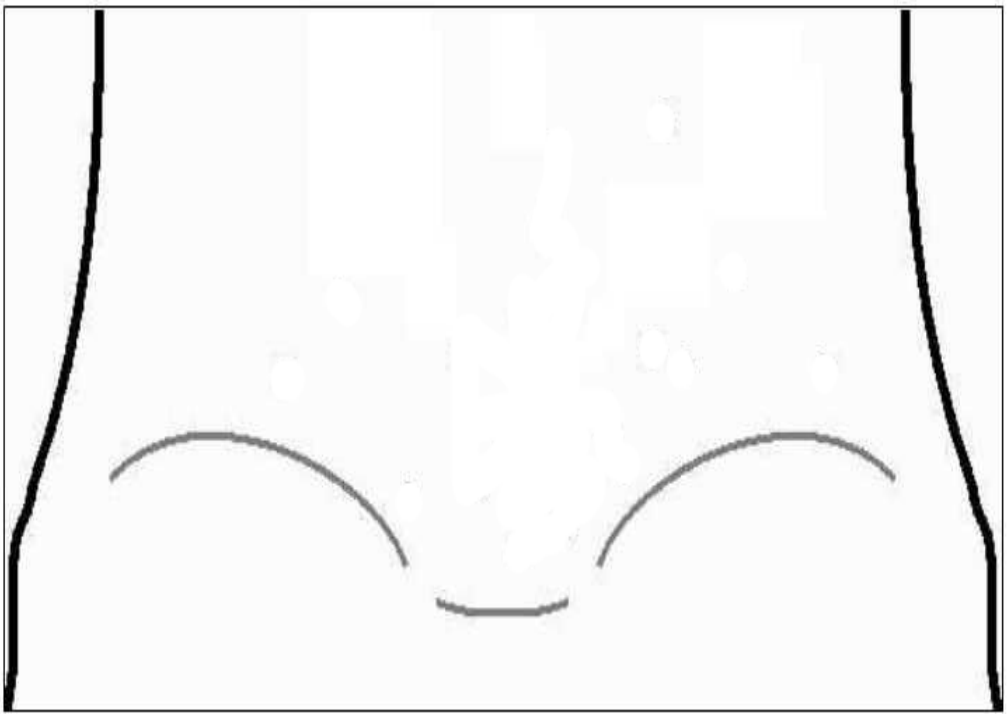
Aperture	10	9	8	7	6	5	4	3	2	1
Attenuation	1.00	0.79	0.63	0.50	0.40	0.31	0.25	0.20	0.16	0.13
PUVA Dose J/cm^2	2.31	1.80	1.40	1.08	0.82	0.62	0.46	0.34	0.23	0.15
Erythema120 h										

PUVA equivalent MPD _____ J/cm^2

Signed: _____

Date: _____

Site: _____



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