MS ISLA ROSE MARY BARNARD (Orcid ID : 0000-0002-9390-0969)
MR EWAN EADIE (Orcid ID : 0000-0002-7824-5580)

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# Could psoralen plus ultraviolet A1 ("PUVA1") work? Depth penetration achieved by phototherapy lamps

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I. R. M. Barnard*[1], E. Eadie[2], L. McMillan[1], H. Moseley[2], T. Brown[1], K. Wood[1], R. Dawe[2]
[1] SUPA, School of Physics and Astronomy, University of St Andrews, St Andrews, UK
[2] Photobiology Unit, NHS Tayside, Ninewells Hospital, Dundee, UK
* Corresponding Author: irmb@st-andrews.ac.uk, 01334 46(3091)

Psoralen and ultraviolet A (PUVA) is useful in treating various hand and foot skin diseases.[1] Most cases of psoriasis respond well to phototherapy or PUVA. However, for some diseases, such as palmoplantar pustular psoriasis, PUVA is not always sufficient to produce therapeutic effect. If PUVA fails, it is sometimes necessary to progress to other treatments such as Grenz ray therapy (where available),[2] systemic retinoid or systemic immunosuppression. Could "PUVA1" (psoralen combined with ultraviolet A1 long wavelength ultraviolet A [UVA]) work in cases where conventional PUVA (psoralen plus broadband UVA) has been inadequate?

Previous *in-vitro* and *in-vivo* work has indicated that longer UVA wavelengths can activate Psoralen and induce erythema[3,4]. Combine this with the fact that longer UV wavelengths penetrate deeper into tissue (and this is probably why UVA1 monotherapy might work in palmoplantar pustulosis[5]), and a potential result is that psoralen plus a UVA1 source might be more effective than the standard broadband UVA source in treating conditions that affect sites with a thick epidermis, such as palms and soles of

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feet.

We wanted to determine if PUVA1 might be a useful treatment, before deciding whether or not a pilot clinical study would be appropriate.

Monte Carlo radiative transfer (MCRT) methods use localised scattering and absorption probabilities to describe the path of photon packets through a medium, and are ideally suited to modelling a complex structure such as the upper layers of the skin[6]. These computationally intensive methods rely on repeated random sampling to form predictive models of radiation transport through a scattering medium, such as the skin[7]. MCRT methods are widely used and rely upon published optical properties of the tissue. Using a modified version of a previously published 5 layered MCRT skin model,[8] irradiation by several phototherapy light sources (metal halide UVA1, fluorescent lamp UVA1, broadband UVA ("PUVA tubes") and narrowband ultraviolet B (a standard phototherapy) was simulated. Four simulations were performed, one for each light source, and each simulation was run with 100 million photon packets, to achieve statistically significant results. The total fluence, at depth, achieved by each light source is recovered. The four simulations were repeated for psoriatic skin, achieved by thickening the modelled stratum corneum (keratin layer of epidermis) by a factor of two.

The results of our simulations quantify the depth penetration advantage achieved by UVA1 (both fluorescent and metal halide lamps) over that achieved by broadband UVA and narrowband UVB. The advantage is smaller at 50% of incident fluence, but larger when considering the depth of 10% of the fluence (**Table 1**). In addition, we found that psoriatic tissue greatly reduced the depth achieved by all lamps - the stratum corneum strongly scatters and absorbs UV radiation, so thickening of this, by psoriatic scales, will greatly reduce the UV radiation reaching deeper layers of the skin. Given that the absorption spectrum of psoralen overlaps with the emission spectrum of UVA1 and the clinical evidence demonstrating the efficiency of longer wavelengths[4] it may be possible to combine the two and achieve greater depth effect than with standard PUVA therapy. However as longer, less psoralen-effective wavelengths, reach the deeper depths, it is still not clear whether there will be enough activation of psoralen at deeper depths.

Following the example of Al-Ismail et al.[4], at depth of 250 μm in healthy tissue, the Metal halide UVA1 source has a PUVA effective ratio of 0.207.

In conclusion, our results suggest that UVA1 radiation may be suitable for combination with psoralen in cases where deeper depth penetration is required than with conventional PUVA. However, this is dependent on how the penetrating UV radiation actually interacts with psoralen treated cells at depth within the skin and requires further investigation. We are planning a pilot study of PUVA1 in palmoplantar pustulosis.

**Table 1**. The results in Table 1 present the depth, measured from the surface of the skin, that 50% and 10% of the total integrated incident radiation has reached. **In addition, for the Metal Halide UVA1 lamp, we present the depths reached by 50% and 10% of the radiation in the wavelength bands comprising the lamp's output.**

| Lamp | Healthy Skin | | Psoriatic Skin | |
|---|---|---|---|---|
| | Depth Of 50% Incident | Depth Of 10% Incident | Depth Of 50% Incident | Depth Of 10% Incident |
| Broadband UVA (PUVA) | 37 μm | 215 μm | 16 μm | 65 μm |
| Narrowband UVB | 17 μm | 124 μm | 14 μm | 41 μm |
| Fluorescent UVA1 | 45 μm | 254 μm | 18 μm | 83 μm |
| Metal Halide UVA1 | 46 μm | 251 μm | 19 μm | 85 μm |
| 340nm-350nm | 33 μm | 192 μm | 16 μm | 57 μm |
| 350nm-360nm | 39 μm | 220 μm | 17 μm | 66 μm |
| 360nm-370nm | 43 μm | 247 μm | 18 μm | 75 μm |
| 370nm-380nm | 47 μm | 264 μm | 19 μm | 88 μm |
| 380nm-390nm | 49 μm | 262 μm | 20 μm | 101μm |

| | | | | |
|---|---|---|---|---|
| 390nm-400nm | 51 μm | 257 μm | 20 μm | 102 μm |

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