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# PDT in dermatology: quantification, relevance and comparison of light sources within a few clicks

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## ABSTRACT

Photodynamic therapy (PDT) for dermatological conditions relies on the photoactivation of the photosensitizer protoporphyrin IX (PpIX). Many light sources have been or are being investigated. The stronger the overlap of the spectral irradiance of the light source with the absorption spectrum of PpIX is, the more powerful to photoactivate PpIX is the light source. This overlap can be quantified using the PpIX-weighted irradiance, which results from the weighting of the spectral irradiance of the light source by the normalized PpIX absorption spectrum.

We have previously developed a freely available website (<http://www.oncothai.fr/light-efficiency-calculator/>), which aims to compute the PpIX-weighted irradiance of any uploaded spectral irradiance.

Through this website, we have assessed a variety of light sources proposed for use in dermatological PDT. The spectral irradiances of these light sources were collected either by extraction from the literature or request to manufacturers.

Due to the variations in position, shape, and amplitude of the spectral irradiances with regard to the PpIX normalized absorption spectrum, a wide range of PpIX-weighted irradiances has been obtained. The maximal PpIX-weighted irradiance was achieved with daylight on a clear sunny day.

## Keywords

Photodynamic therapy, light sources, actinic keratoses, protoporphyrin IX, PpIX-weighted irradiance, website

## INTRODUCTION

Photodynamic therapy (PDT) is a well-established treatment for various dermatological diseases including actinic keratoses (AK) [1, 2]. Although the clinically approved protocols for PDT of AK require photoactivation with red light or daylight in Europe and with blue light in USA, there is a growing interest in other lights particularly in white lights [3-5]...

To evaluate and compare the relevance of light sources for PDT for AK, the protoporphyrin IX (PpIX)-weighted irradiance ( $\text{mW}/\text{cm}^2$ ) and the PpIX-weighted light dose ( $\text{J}/\text{cm}^2$ ) are more suitable than the more widely available irradiance ( $\text{mW}/\text{cm}^2$ ) and light dose ( $\text{J}/\text{cm}^2$ ). In fact, the PpIX-weighted quantities, which derive from the weighting of the spectral irradiance of the light source by the normalized PpIX absorption spectrum, take into account the power of the light source to photoactivate PpIX.

We have therefore previously developed a freely available website [6, 7] (<http://www.oncothai.fr/light-efficiency-calculator/>) that, from any uploaded spectral irradiance, automatically and instantly displays the value of the PpIX-weighted irradiance. The irradiance and illuminance are also displayed. Furthermore, according to the user-specified photoactivation time, the light dose and the PpIX-weighted light dose can also be determined. At the end of the process, a PDF file with all the results can be downloaded by the user.

We have collected the spectral irradiances of more than 20 light sources either by extraction from the literature [4, 8-12] or request to manufacturers. Among these light sources are several currently marketed products (e.g., the Aktelite CL 128 lamp, Galderma SA, Switzerland; the Blu-U illuminator, DUSA, USA; the Dermaris lamp, Surgeris, France), some devices under development and the naturally available daylight solution. Uploading these spectral irradiances to the website (regardless of the sampling scheme) allows to obtain the corresponding PpIX-weighted irradiances and other above-mentioned quantities.

As expected regarding the variations in position, shape, and amplitude of the spectral irradiances with regard to the PpIX normalized absorption spectrum, a wide range of PpIX-weighted irradiances has been obtained. The daylight provided the maximal PpIX-weighted irradiance when on a clear sunny day and a considerably reduced PpIX-weighted irradiance when on an overcast day. The minimum PpIX-weighted irradiance was achieved using the Phosistos device.

## MATERIALS AND METHODS

### The freely available website

Developed in 2017, the freely available “Light Efficiency Calculator for PpIX PDT” website [6, 7] (<http://www.oncothai.fr/light-efficiency-calculator/>) allows to quantify the relevance of any light source for PDT for AK. This quantification is performed in terms of five physical quantities. These quantities, computed from the spectral irradiance of the light source that the user uploaded, are as follows:

- The irradiance ( $\text{mW}/\text{cm}^2$ ), which is the result of integrating the spectral irradiance over the wavelength,
- The light dose ( $\text{J}/\text{cm}^2$ ), which is the result of multiplying the irradiance by the photoactivation time,
- The illuminance (Lux), which is the result of integrating the spectral irradiance weighted by the luminous efficiency function over the wavelength,
- The PpIX-weighted irradiance ( $\text{mW}/\text{cm}^2$ ), which is the result of integrating the spectral irradiance weighted the normalized absorption spectrum for PpIX over the wavelength,
- The PpIX-weighted light dose ( $\text{J}/\text{cm}^2$ ), which is the result of multiplying the PpIX-weighted irradiance by the photoactivation time.

Derived from the normalized absorption spectrum for PpIX, the PpIX-weighted irradiance and the PpIX-weighted light dose take into account the power of the light source to photoactivate PpIX and are therefore more suitable to evaluate and compare the relevance of light sources for PDT for AK.

Once the Compute button is clicked, the five physical quantities are automatically computed and instantly displayed on the screen (Figure 1). The user can export the results as a PDF file.

Note that this software has been registered in December 2017 at the French agency for software protection (<https://www.app.asso.fr/>) with the Inter Deposit Digital Number: IDDN.FR.001.520002.000.S.P.2017.000.31230.

### The light sources

A variety of light sources proposed for use in dermatological PDT were assessed through the website. Among these light sources are:

- The Aktelite CL 128 lamp (Galderma SA, Lausanne, Switzerland) – the spectral irradiance we used was that measured at a distance of 8 cm from the lamp by O'Gorman et al. [4],
- The Blu-U illuminator (DUSA, Wilmington, MA) – the spectral irradiance was obtained by weighting the spectral irradiance extracted from <https://www.physiciansofficersource.com/resources/pdf/2099-8132-learn-more.pdf> to achieve the recommended 10 mW/cm<sup>2</sup> for irradiance [13],
- The Waldmann PDT 1200L (Waldmann Medizintechnik, VS-Schwennigen, Germany) – the spectral was derived by weighting the relative spectral irradiance provided by the manufacturer to obtain the recommended 160 mW/cm<sup>2</sup> for irradiance [10],



**Figure 1.** Example of results obtained with the freely available “Light Efficiency Calculator for PpIX PDT” website.

- The Omnilux lamp (PhotoTherapeutics Inc., Carlsbad, CA) – the spectral irradiance we used was that recorded at 3.5 cm from the front of the lamp by O'Gorman et al. [4],
- The Ambulight PDT (Ambicare Health Ltd, St Andrews, United Kingdom) – the spectral irradiance was extracted from a figure in [11],
- The Phosistos device (ONCO-THAI INSERM U1189, Lille, France) – the spectral irradiance was that we measured inside the light-emitting fabric-based cap [14],
- The Dermaris lamp (Surgeris, Croix, France) – the spectral was provided by the manufacturer [5],
- The daylight on a clear sunny day at 10h28 – the spectral irradiance we used was that recorded by O'Gorman et al. [4],
- The daylight on an overcast day at 13h45 – the spectral irradiance we used was that recorded by O'Gorman et al. [4].

## RESULTS

The illuminances, irradiances and PpIX-weighted irradiances obtained through the “Light Efficiency Calculator for PpIX PDT” website for the above-mentioned light sources are reported in Table 1.

The light dose and the PpIX-weighted light dose do not only depend on the spectral irradiance of the light source but also vary according to the photoactivation time. For the sake of clarity and to prevent an excessive amount of results (several photoactivation times can be used for a given light source), these two physical quantities are not reported here. The values obtained for 10 efficient protocols (with specific well-defined photoactivation times) for PDT of AK can be found in a recent paper [12].

**Table 1.** The illuminance, irradiance and PpIX-weighted irradiance (columns 2 to 4) obtained through the “Light Efficiency Calculator for PpIX PDT” website for the light sources reported in column 1.

Light source	Illuminance	Irradiance	PpIX-weighted irradiance
Aktelite CL 128 lamp	199,981	85.4	1.44
Blu-U illuminator	709	10.0	4.12
Waldmann PDT 1200L	186,820	160.0	0.93
Omnilux lamp	120,726	59.5	0.95

Ambulight PDT	13,375	7.0	0.12
Phosistos device	1,678	1.33	0.01
Dermaris lamp	199,980	70.4	2.01
Daylight on a clear sunny day at 10h28	105,958	55.2	5.08
Daylight on an overcast day at 13h45	14,242	7.8	0.79

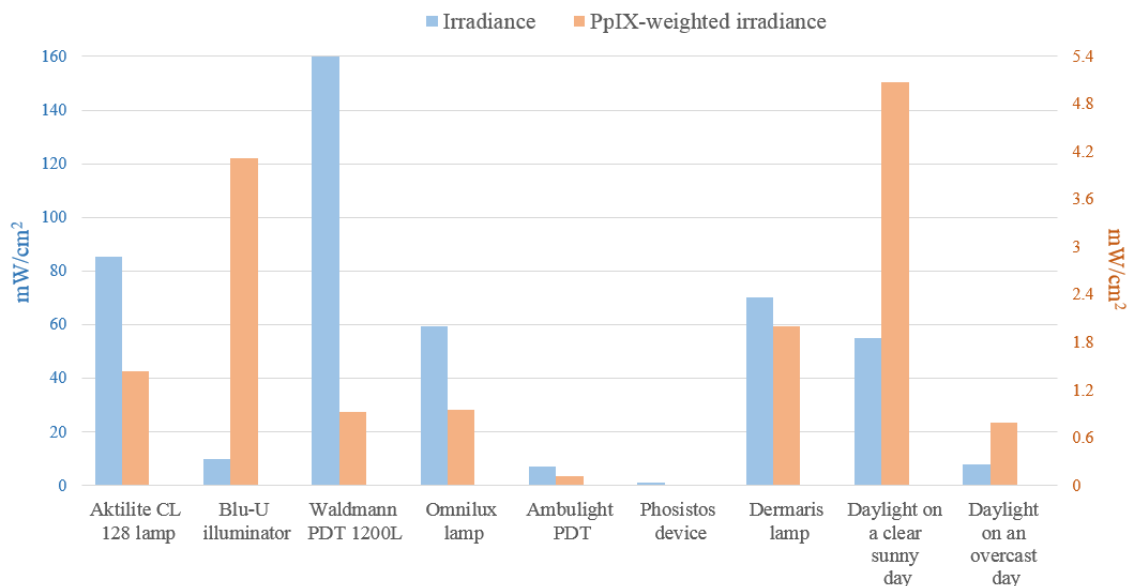
Table 1 (column 4) and Figure 2 (orange bars) indicate a wide range of PpIX-weighted irradiances, from 0.01 mW/cm<sup>2</sup> for the Phosistos device to 5.08 mW/cm<sup>2</sup> for the daylight on a clear sunny day. This wide range results from the variations in position, shape, and amplitude of the spectral irradiances with regard to the PpIX normalized absorption spectrum.

The daylight on a clear sunny day provides the highest PpIX-weighted irradiance and is therefore the most powerful light source to photoactivate PpIX. The Blu-U illuminator takes second place, followed by the Dermaris lamp. With the two highest irradiances in Table 1, the Aktelite CL 128 lamp and the Waldmann PDT 1200L are only ranked as the fourth and sixth most powerful light source to photoactivate PpIX, respectively. This is due to the poor overlap of their spectral irradiances with the PpIX absorption spectrum. With substantially the same shape but an amplitude approximately seven times lower for the spectral irradiance than that of the daylight on a clear sunny day, the daylight on an overcast day provides the seventh highest PpIX-weighted irradiance. Finally, with the two lowest irradiances in Table 1 and a poor overlap of their spectral irradiances with the PpIX absorption spectrum, the Ambulight PDT and the Phosistos device are, predictably, the two least powerful light sources to photoactivate PpIX.

## DISCUSSION & CONCLUSION

In this paper, a variety of light sources proposed for use in dermatological PDT were assessed through a freely available website we have previously developed.

This assessment is performed in terms of the PpIX-weighted irradiance, which results from integrating the spectral irradiance weighted by the normalized absorption spectrum for PpIX over the wavelength. The better the combination of a suitable irradiance with a relevant overlap of the spectral irradiance with the PpIX normalized absorption spectrum is, the higher is the PpIX-weighted irradiance and the more powerful to photoactivate PpIX the light source is.



**Figure 2.** Irradiance and PpIX-weighted irradiance obtained through the “Light Efficiency Calculator for PpIX PDT” website for the light sources shown on the X-axis.

Among the assessed light sources, the daylight on a clear sunny day was found to be the most powerful to photoactivate PpIX. Unfortunately, every day is not a clear sunny day and the power to photoactivate PpIX was strongly reduced in case of an overcast day. Preference should therefore be given to a light source equally powerful to photoactivate PpIX irrespective of the weather and the time of the year.

Although the PpIX-weighted irradiance allows to quantify the power to photoactivate PpIX, it is insufficient to draw conclusions about the efficacy of the treatment. Other factors including the photoactivation time also influence the efficacy of the treatment. Thus, although the Phosistos device was found to be the least powerful light source to photoactivate PpIX, the manufacturer-recommended protocol for the Phosistos device has recently been demonstrated to be non-inferior in efficacy than the conventional protocol for the Aktilite CL 128 lamp [14]. The manufacturer-recommended protocol for the Phosistos device has led to a lesion complete response rate at six months following the treatment of about 94% [14]. This complete response rate suggests that even if the Phosistos device is the least powerful light source to photoactivate PpIX, it is an efficient light source to photoactivate PpIX. The other light sources may therefore involve unnecessary effort and lead to over-treatment... This potential over-treatment has been addressed and discussed in a recent paper on comparison of the efficacy of 10 protocols for PDT of AK [12] that we invite you to discover.



We also invite you to visit our “Light Efficiency Calculator for PpIX PDT” website at <http://www.oncothai.fr/light-efficiency-calculator/>

## REFERENCES

- [1] C. Morton, R. M. Szeimies, A. Sidoroff *et al.*, “European Dermatology Forum Guidelines on topical photodynamic therapy,” *Eur J Dermatol*, 25(4), 296-311 (2015).
- [2] S. R. Wiegell, “Update on photodynamic treatment for actinic keratosis,” *Curr Probl Dermatol*, 46, 122-8 (2015).
- [3] C. M. Lerche, I. M. Heerfordt, J. Heydenreich *et al.*, “Alternatives to Outdoor Daylight Illumination for Photodynamic Therapy--Use of Greenhouses and Artificial Light Sources,” *Int J Mol Sci*, 17(3), 309 (2016).
- [4] S. M. O’Gorman, J. Clowry, M. Manley *et al.*, “Artificial White Light vs Daylight Photodynamic Therapy for Actinic Keratoses: A Randomized Clinical Trial,” *JAMA Dermatol*, 152(6), 638-44 (2016).
- [5] S. Mordon, A. S. Vignion-Dewalle, E. Thecuia *et al.*, “Can daylight-PDT be performed indoor?,” *G Ital Dermatol Venereol*, 153(6), 811-816 (2018).
- [6] A. S. Vignion-Dewalle, G. Baert, E. Thecuia *et al.*, “A software for analyzing and comparing the light sources available for PDT in dermatology.,” *EuroPDT Munich*, (2017).
- [7] A. S. Vignion-Dewalle, G. Baert, E. Thecuia *et al.*, “Light efficiency calculator for PpIX-PDT,” *IPA 2017 World Congress Coimbra, Portugal*, (2017).
- [8] C. Clark, A. Bryden, R. Dawe *et al.*, “Topical 5-aminolaevulinic acid photodynamic therapy for cutaneous lesions: outcome and comparison of light sources,” *Photodermatol Photoimmunol Photomed*, 19(3), 134-41 (2003).
- [9] A. Juzeniene, P. Juzenas, L. W. Ma *et al.*, “Effectiveness of different light sources for 5-aminolevulinic acid photodynamic therapy,” *Lasers Med Sci*, 19(3), 139-49 (2004).
- [10] P. Babilas, E. Kohl, T. Maisch *et al.*, “In vitro and in vivo comparison of two different light sources for topical photodynamic therapy,” *Br J Dermatol*, 154(4), 712-8 (2006).
- [11] S. H. Ibbotson, and J. Ferguson, “Ambulatory photodynamic therapy using low irradiance inorganic light-emitting diodes for the treatment of non-melanoma skin cancer: an open study,” *Photodermatol Photoimmunol Photomed*, 28(5), 235-9 (2012).

- [12] A. S. Vignion-Dewalle, G. Baert, E. Thecuia *et al.*, "Comparison of 10 efficient protocols for photodynamic therapy of actinic keratosis: How relevant are effective light dose and local damage in predicting the complete response rate at 3 months?," *Lasers Surg Med*, 50(5), 576-589 (2018).
- [13] E. W. Jeffes, J. L. McCullough, G. D. Weinstein *et al.*, "Photodynamic therapy of actinic keratoses with topical aminolevulinic acid hydrochloride and fluorescent blue light," *J Am Acad Dermatol*, 45(1), 96-104 (2001).
- [14] S. Mordon, A. S. Vignion-Dewalle, H. Abi-Rached *et al.*, "The conventional protocol versus a protocol including illumination with a fabric-based biophotonic device (the Phosistos protocol) in photodynamic therapy for actinic keratosis: a randomized, controlled, non-inferiority clinical study," *Br J Dermatol*, (2019).