OPEN ACCESS

University of Dundee

University of Dundee

Global verification of a model for determining daylight photodynamic therapy dose

O'Mahoney, Paul; Khazova, Marina; LaRochelle, Ethan; Pogue, Brian; Ibbotson, Sally H.; Eadie, Ewan

Published in:
Photodiagnosis and Photodynamic Therapy

DOI:
10.1016/j.pdpdt.2021.102260

Publication date:
2021

Licence:
CC BY-NC-ND

Document Version
Peer reviewed version

Link to publication in Discovery Research Portal

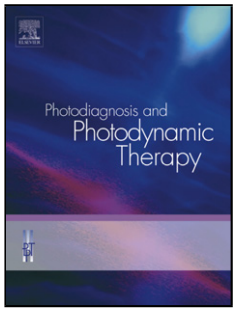
Citation for published version (APA):
O'Mahoney, P., Khazova, M., LaRochelle, E., Pogue, B., Ibbotson, S. H., & Eadie, E. (2021). Global verification of a model for determining daylight photodynamic therapy dose. *Photodiagnosis and Photodynamic Therapy*, *34*, Article 102260. https://doi.org/10.1016/j.pdpdt.2021.102260

General rights
Copyright and moral rights for the publications made accessible in Discovery Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Download date: 16. Sep. 2025

Journal Pre-proof



Global verification of a model for determining daylight photodynamic therapy dose

Paul O'Mahoney, Marina Khazova, Ethan LaRochelle, Brian Pogue, Sally H. Ibbotson, Ewan Eadie

PII: S1572-1000(21)00086-7

DOI: https://doi.org/10.1016/j.pdpdt.2021.102260

Reference: PDPDT 102260

To appear in: *Photodiagnosis and Photodynamic Therapy*

Received Date: 17 February 2021

Revised Date: 15 March 2021

Accepted Date: 16 March 2021

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2020 Published by Elsevier. This manuscript version is made available under the CC-BY-NC-ND 4.0 license http://creativecommons.org/licenses/by-nc-nd/4.0/

Journal Pre-proof

Title: Global verification of a model for determining daylight photodynamic therapy dose

Author names and affiliations: Paul O'Mahoney[1,2,3] (pzomahoney@:dundee.ac.uk), Marina Khazova[4] (marina.khazova@phe.gov.uk), Ethan LaRochelle[5] (ethan.phillip.m.larochelle.th@dartmouth.edu), Brian Pogue[5] (brian.w.pogue@dartmouth.edu), Sally H Ibbotson[1,2,3] (shibbotson@dundee.ac.uk) and Ewan Eadie[2,3] (ewan.eadie@nhs.scot)

1. School of Medicine, University of Dundee, Dundee, UK
2. Photobiology Unit, NHS Tayside, Dundee, UK
3. The Scottish Photodynamic Therapy Centre, Dundee, UK
4. Public Health England, Didcot, UK
5. Thayer School of Engineering at Dartmouth, Hanover NH, USA

Corresponding author: Dr Paul O'Mahoney, pzomahoney@dundee.ac.uk

Declaration of interest:

Ewan Eadie and Sally Ibbotson has received funding to attend educational conferences from Galderma UK Ltd (EuroPDT 2020) and UCB Pharma Ltd (BAD Annual Meeting 2020).

Highlights:

- DPDT dosimetry model is verified for accuracy globally.
- Accuracy of the model does not depend on location.
- Measurement of illuminance is a low-cost easily accessible method for DPDT dosimetry.

Abstract:

Daylight photodynamic therapy is an effective treatment for actinic keratoses and relies on a minimum PpIX-effective exposure dose being delivered during treatment. As such, daylight dosimetry is an important aspect of this treatment. Relatively simple measurements of illuminance may be converted to PpIX-effective irradiance, and subsequently exposure dose, via a conversion model (the O'Mahoney model). This model has been verified against spectral irradiance data from the UK, however the accuracy of the model has not been determined outside the UK. In this work, we test the O'Mahoney model against spectral irradiance measurements from several global locations to within bounds of a median deviation of ±10%. The median percentage deviations are shown to be independent of location latitude and longitude. The model can be used confidently to determine PpIX-effective irradiance from illuminance measurements irrespective of location and can be widely implemented as an effective and low-cost means of accurately measuring effective light exposure for this important treatment.

Keywords: dpdt; daylight; Photodynamic therapy; irradiance; actinic keratosis

Journal Pre-proof

Journal Pre-proof

Main text:

Background:

Daylight dosimetry in daylight photodynamic therapy (DPDT) has been shown to have an important impact on treatment outcome – patients must receive a minimum threshold protoporphyrin-IX (PpIX)-effective exposure dose of daylight over the exposure duration, typically 1.5 to 2.5 hours [1]. As such, accurate measurement of daylight, and hence conversion to PpIX-effective exposure dose, is critical to better understand, evaluate and predict the success of DPDT.

We previously published a model for converting PpIX-effective exposure dose from relatively simple measurements of illuminance, using an inexpensive luxmeter for example [2]. This model was verified against measurement data from the UK and was independently validated by Manley *et al.* [3]. As the model has dependencies on latitude and longitude, it is anticipated to be globally relevant; however, the robustness of this model outside of the UK has not been demonstrated yet.

Aims:

In this work we aim to investigate the published DPDT dosimetry model against several global locations to determine its use world-wide. We check for significance relating to median percentage deviation and location (latitude and longitude).

Methods:

Measurements of daylight spectral irradiance are obtained from several locations: Lebanon NH, USA (43.7°N, 72.40°W); Paris, France (48.86°N, 2.35°E); Nakhon Pathom, Thailand (13.82°N, 100.05°E); and Ribeirão Preto, Brazil (21.18°S, 47.81°W). These spectral irradiances are converted to illuminance and PpIX-effective irradiance using the appropriate weighting functions [4,5], and the illuminance is then converted to PpIX-effective irradiance by use of the O'Mahoney model. The two sets of corresponding PpIX-effective irradiances (denoted here as 'actual' and 'model') are compared, and the percentage deviation of the model PpIX-effective irradiance from the actual measured values is found. Data is framed in the context of the previous work carried out on verification of UK spectral irradiance [2], from the locations: Dundee, UK (56.46°N, 2.97°W); Nottingham, UK (52.96°N, 1.15°W); Salisbury, UK (51.07°N, 1.79°W).

Data are measured between 09:00 and 18:00 local time in all weather conditions throughout the year. Wavelength ranges of the spectral irradiance measurements are at least 380 – 780 nm. Statistical analyses (simple linear regression) were carried out using GraphPad Prism (Prism 8, GraphPad Software, USA). Location coordinates are sourced from OpenStreetMap (© OpenStreetMap).

Results:

Journal Pre-proof

Journal Pre-proof

A map of all the locations studied is shown in Figure 1, and the results of the analysis are presented in Figure 2. The median percentage deviation of the model from the actual PpIX-effective irradiance is within ±10% (range –4.36% to 8.30%), with the 95% confidence intervals within a clinically acceptable ±20%, and the standard deviation of the mean ranging from 4.52% to 10.5%. Therefore, the O'Mahoney model can be used globally to accurately determine the PpIX-effective exposure doses in daylight PDT.

A simple linear regression of the data (within and outwith the UK) indicated no significance of median percentage deviation of the model from the actual PpIX-effective irradiance against latitude ($p=0.19$) or longitude ($p=0.28$).

Conclusions:

The PpIX-irradiance calculated by the O'Mahoney model indicate good agreement with the actual PpIX-irradiances. Measurements of daylight through a range of locations, weather conditions, seasons and times of the day vary greatly, and this model was designed to mitigate these factors as much as possible, within an acceptable margin of error. In the original work presenting the O'Mahoney model, the model was shown to have a mean percentage deviation of 0.04% and a standard deviation of 6.8%, and Manley *et al*. showed comparable data, with a mean percentage deviation of -0.3% and standard deviation of ±5.5% (up to the 40,000 lux calibration limit of the detector used). The insignificance of latitude and longitude with median percentage deviation lends further weight that the model is suitable for the conversion of illuminance measurements to PpIX-effective irradiance irrespective of location.

The use of illuminance in DPDT dosimetry may assist with verification of other technologies [6]. Spectral irradiance is, in general, a more expensive and technically challenging quantity to measure compared to illuminance. With the ability to accurately carry out DPDT dosimetry with illuminance measurements, verification of dosimetry models becomes much simpler. Whilst newer, more accurate satellite-based technologies exist for the determination of PpIX-effective exposure doses in daylight PDT [6], illuminance remains a low-cost easily accessible method.

References:

[1] S.R. Wiegell, S. Fabricius, M. Gniadecka, I.M. Stender, B. Berne, S. Kroon, B.L. Andersen, C. Mork, C. Sandberg, K.S. Ibler, G.B.E. Jemec, K.M. Brocks, P.A. Philipsen, J. Heydenreich, M. Haedersdal, H.C. Wulf, Daylight-mediated photodynamic therapy of moderate to thick actinic keratoses of the face and scalp: A randomized multicentre study, British Journal of Dermatology. 166 (2012) 1327–1332. https://doi.org/10.1111/j.1365-2133.2012.10833.x.

[2] P. O'Mahoney, M. Khazova, M. Higlett, T. Lister, S. Ibbotson, E. Eadie, The use of illuminance as a guide to effective light delivery during daylight PDT in the UK, British Journal of Dermatology. 176 (2016) 1607–1616. https://doi.org/10.1111/bjd.15146.

[3] M. Manley, P. Collins, L. Gray, S. O'Gorman, J. McCavana, Quantifying the radiant exposure and effective dose in patients treated for actinic keratoses with topical photodynamic therapy using daylight and LED white light, Physics in Medicine and Biology. 63 (2018). https://doi.org/10.1088/1361-6560/aa9ea7.

Journal Pre-proof

[4] M. Taniguchi, J.S. Lindsey, Database of absorption and fluorescence spectra of 300 common compounds for use in PhotochemCAD, Photochemistry and Photobiology. 94 (2018) 290–327. https://doi.org/10.1111/php.12860.

[5] CIE, Commission Internationale de l'Éclairage Proceedings, in: Commission Internationale de l'Éclairage Proceedings, Cambridge University Press, Cambridge, 1924.

[6] L.J. McLellan, M. Morelli, E. Simeone, M. Khazova, S.H. Ibbotson, E. Eadie, SmartPDT®: smartphone enabled real-time dosimetry via satellite observation for daylight photodynamic therapy., Photodiagnosis and Photodynamic Therapy. (2020) 101914. https://doi.org/10.1016/j.pdpdt.2020.101914.

Acknowledgements:

The authors would like to thank the following for their contributions to the provision of data used in this work: Prof Luciano Bachmann and Prof Gilberto Braga (University of São Paulo, Brazil), Dr Sumaman Buntoung (Silpakorn University, Thailand) and Dr Einapak Boontaveeyuwat (Chulalongkorn University, Thailand)

Funding:

Dr Paul O'Mahoney is funded by Medi-lase (registered charity SC 037390) and the Alfred Stewart Trust.

Journal Pre-proof

Journal Pre-proof

Figure captions:

Figure 1: Map showing each location: 1) Lebanon NH, USA, 2) Ribeirão Preto, Brazil, 3) Dundee, Salisbury and Nottingham, UK, 4) Paris, France, and 5) Nakhon Pathom, Thailand. Horizontal and vertical dashed lines indicate the Equator and Prime Meridian respectively. Map data © OpenStreetMap.

Figure 2: Plot of median percentage variation of model PpIX-effective irradiance compared to actual measured values for each location. Dashed box represents previously published UK data for comparison. Number of measurements for each location are displayed above the x-axis. Whiskers in the plot represent 5-95% confidence intervals (outliers are not shown for clarity).

Journal Pre-proof

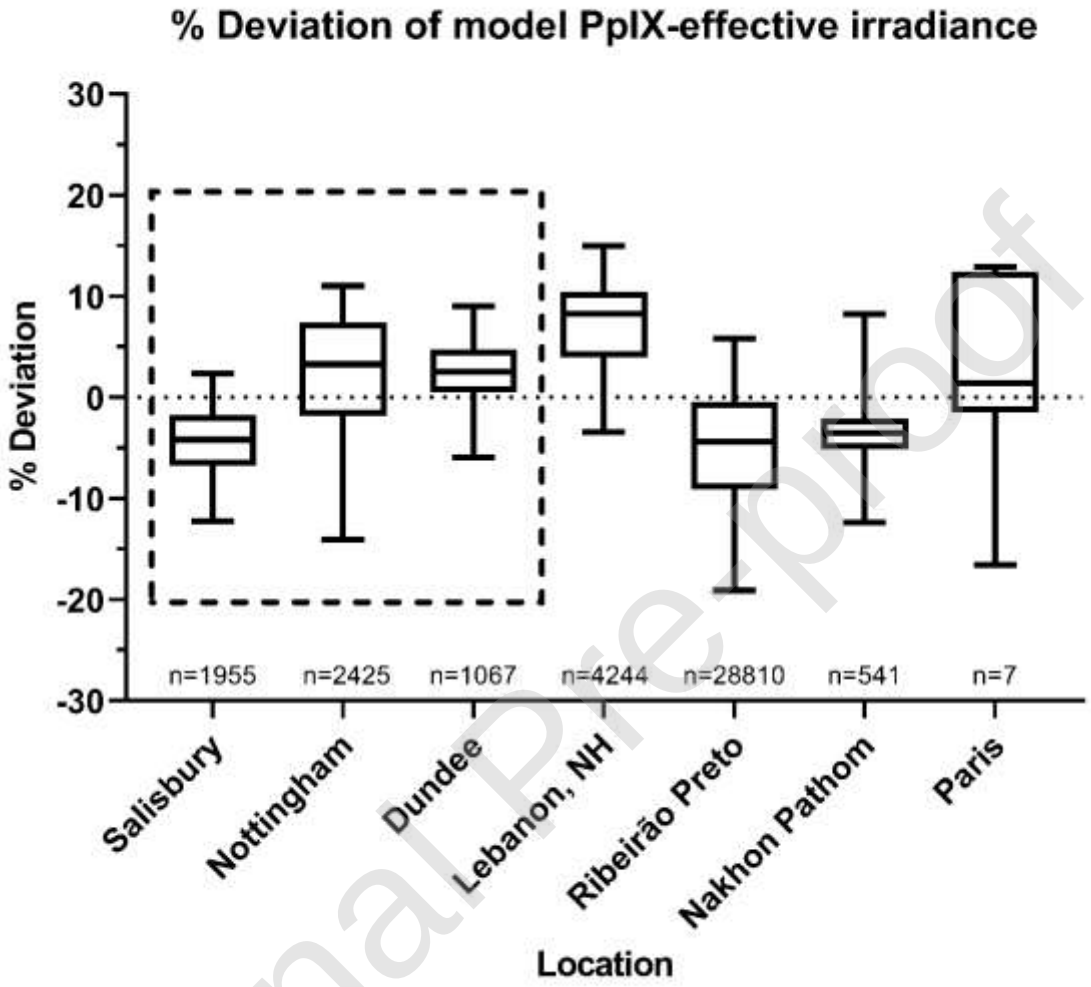
Journal Pre-proof

Figure 1:

Journal Pre-proof

Journal Pre-proof

Figure 2:



Journal Pre-proof