



Deposited via The University of Leeds.

White Rose Research Online URL for this paper:

<https://eprints.whiterose.ac.uk/id/eprint/145612/>

Version: Accepted Version

---

**Article:**

Khot, MI, Armstrong, G, Andrew, H et al. (2019) The current status of phototherapy in multimodal anti-cancer nanomedicines. *Photodiagnosis and Photodynamic Therapy*, 26. p. 350. ISSN: 1572-1000

<https://doi.org/10.1016/j.pdpdt.2019.04.024>

---

© 2019 Elsevier B.V. All rights reserved. Licensed under the Creative Commons Attribution-Non Commercial No Derivatives 4.0 International License (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).

**Reuse**

This article is distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs (CC BY-NC-ND) licence. This licence only allows you to download this work and share it with others as long as you credit the authors, but you can't change the article in any way or use it commercially. More information and the full terms of the licence here: <https://creativecommons.org/licenses/>

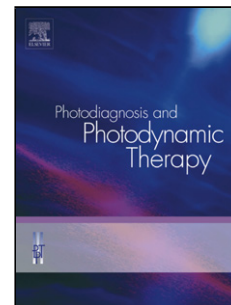
**Takedown**

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing [eprints@whiterose.ac.uk](mailto:eprints@whiterose.ac.uk) including the URL of the record and the reason for the withdrawal request.

## Accepted Manuscript

Title: The current status of phototherapy in multimodal anti-cancer nanomedicines

Authors: M. Ibrahim Khot, Gemma Armstrong, Helen Andrew, Candice L. Downey, David G. Jayne



PII: S1572-1000(19)30202-9  
DOI: <https://doi.org/10.1016/j.pdpdt.2019.04.024>  
Reference: PDPDT 1417

To appear in: *Photodiagnosis and Photodynamic Therapy*

Received date: 25 April 2019

Please cite this article as: Khot MI, Armstrong G, Andrew H, Downey CL, Jayne DG, The current status of phototherapy in multimodal anti-cancer nanomedicines, *Photodiagnosis and Photodynamic Therapy* (2019), <https://doi.org/10.1016/j.pdpdt.2019.04.024>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. 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.

**Title:** The current status of phototherapy in multimodal anti-cancer nanomedicines

**List of Authors:** M. Ibrahim Khot, Gemma Armstrong, Helen Andrew, Candice L. Downey and David G. Jayne

**Authors' affiliation:** School of Medicine, St James's University Hospital, University of Leeds, Leeds, UK

**Corresponding author:**

M. Ibrahim Khot

Section of Translational Anaesthesia and Surgical Sciences,  
Level 9, Wellcome Trust Brenner Building, St James's University Hospital,  
Beckett St, Leeds, LS9 7TF, UK

E-mail: M.I.Khot@leeds.ac.uk

Highlights

- Nanomedicines can improve the precise delivery of therapeutics
- PDT and PTT can be efficiently delivered through nanomedicines
- Further investigation is crucial for clinical translation

Dear Editor,

We have read with great interest, the recently published article by Vivek *et al.* (2018), describing the authors' research on the therapeutic applications of a multifunctional

nanomedicine [1]. This paper discusses the combined efficacy of photodynamic therapy (PDT), photothermal therapy (PTT) and carboplatin (CBP) chemotherapy, using CBP and indocyanine green (ICG) loaded nanoparticles (NPs), functionalised with polyethylene glycol and folic acid. Significant uptake and retention of NPs *in vitro*, was observed in the folate receptor-overexpressing breast cancer cell line, MCF7. The intracellular acidic pH environment of cancer cells induced the release of therapeutic agents into the cytoplasm. Upon near-infrared light irradiation, the increase in intracellular temperature and simultaneous increasing production of reactive oxygen species, was attributed to the photothermal conversion and photodynamic properties of ICG respectively [2]. The dual synergistic effect of PDT and PTT resulted in an apoptotic cell death. Furthermore, significant regression in tumour growth with no noticeable adverse effects, was observed in animal models treated with NPs and near-infrared light irradiation.

This study is a good example of the rapid growing interest in multifunctional anti-cancer nanomedicines, combining PDT, PTT and conventional chemotherapy. We recently reviewed the scope of photothermal therapy-based nanomedicines, in colorectal cancers and highlight the diverse combinations of phototherapeutic, chemotherapeutic, optical imaging and cancer-targeting nanomedicines that have been investigated in the past decade [3]. These nanomedicines have shown to significantly improve the management of solid colorectal cancers, by efficiently packaging different treatment methods into a single entity.

Unlike the study by Vivek *et al.* (2018) which demonstrated both PTT and PDT through ICG [1]. Seo *et al.* (2014) synthesised and evaluated PTT and PDT using NPs comprised of gold nanorods (to induce PTT) and methylene blue (to induce PDT) [4]. The authors successfully show synergy between PDT and PTT, in comparison to PDT

or PTT alone. The aforementioned studies, demonstrate the flexibility in customising PTT and PDT inducing NPs, using different types of photosensitising agents.

Thus far, many novel multimodal PDT and/or PTT nanomedicines have been the subject of 'proof-of-principle' pre-clinical studies, showing potential clinical applications. Currently, PDT and PTT (through thermal ablation) are utilised in clinics to treat cancers and both techniques have independently proven to be successful as stand-alone methods and in combination with more conventional means of treatment [5,6]. However, due to the apparent lack of controlled and randomised clinical trials investigating phototherapy nanomedicines, it is difficult to design appropriate clinical protocols and identify key candidates for further evaluation and clinical translation. Nevertheless, the remarkable progression in this field with a focus on precision medicine means that the clinical application of phototherapy nanomedicines is feasible in the near future.

### **Funding sources**

The National Institute for Health Research (NIHR) infrastructure at Leeds. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

### **Conflicts of interest**

None

## References

- [1] R. Vivek, N. Varukattu, R. Chandrababu, S. Alok, P. Thondhi, V. Alagarsamy, S. Kannan, Multifunctional nanoparticles for trimodal photodynamic therapy-mediated photothermal and chemotherapeutic effects, *Photodiagnosis Photodyn. Ther.* 23 (2018) 244–253. doi:10.1016/j.pdpdt.2018.06.025.
- [2] J.T. Alander, I. Kaartinen, A. Laakso, T. Pätälä, T. Spillmann, V. V. Tuchin, M. Venermo, P. Välisuo, A Review of Indocyanine Green Fluorescent Imaging in Surgery, *Int. J. Biomed. Imaging.* 2012 (2012) 1–26. doi:10.1155/2012/940585.
- [3] M.I. Khot, H. Andrew, H.S. Svavarsdottir, G. Armstrong, A.J. Quyn, D.G. Jayne, A Review on the Scope of Photothermal Therapy–Based Nanomedicines in Preclinical Models of Colorectal Cancer, *Clin. Colorectal Cancer.* (2019). doi:10.1016/j.clcc.2019.02.001.
- [4] S.H. Seo, B.M. Kim, A. Joe, H.W. Han, X. Chen, Z. Cheng, E.S. Jang, NIR-light-induced surface-enhanced Raman scattering for detection and photothermal/photodynamic therapy of cancer cells using methylene blue-embedded gold nanorod@SiO<sub>2</sub> nanocomposites, *Biomaterials.* 35 (2014) 3309–3318. doi:10.1016/j.biomaterials.2013.12.066.
- [5] K.F. Chu, D.E. Dupuy, Thermal ablation of tumours: biological mechanisms and advances in therapy., *Nat. Rev. Cancer.* 14 (2014) 199–208. doi:10.1038/nrc3672.
- [6] K. Moghissi, K. Dixon, S. Gibbins, A Surgical View of Photodynamic Therapy in Oncology: A Review, *Surg. J. (New York, N.Y.).* 1 (2015) e1–e15. doi:10.1055/s-0035-1565246.

ACCEPTED MANUSCRIPT