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Unlocking the predictive power of imaging biomarkers: predicting immune checkpoint therapy response in non-small cell lung cancer through baseline tumour vessel perfusions

Suraiya Dubash [1,2] Yat Tsang [3]

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[1]Oncology, Mount Vernon Cancer Centre, Northwood, UK
[2]Surgery and Cancer, Imperial College London, London, UK
[3]Radiation Medicine Program, Princess Margaret Hospital Cancer Centre, Toronto, Ontario, Canada

Correspondence to
Dr Suraiya Dubash;
suraiya.dubash@nhs.net

The search for reliable biomarkers to predict responses to immune checkpoint inhibitor (ICI) therapy in non-small cell lung cancer (NSCLC) has been a significant focus in oncology.[1] Liu *et al*'s recent study introduces an innovative approach by proposing baseline tumour vessel perfusion, quantified as 'onion-mode perfusion' (OMP) from contrast-enhanced CT (CECT) images, as a non-invasive predictive biomarker.[2]

Current biomarkers for predicting ICI response, such as PD-L1 expression and tumour mutation burden, require invasive biopsy procedures and often fail to capture the heterogeneity of the tumour microenvironment (TME), limiting their predictive accuracy.[3] Liu *et al*'s study addresses this limitation by leveraging routine CECT imaging to extract OMP, a global measure of tumour vessel perfusion.[2] Their retrospective multicohort study included a discovery cohort from the ORIENT-11 trial and an external validation cohort, demonstrating that high baseline OMP correlates with longer survival and better responses to ICI therapy.[2] The study shows that OMP, either alone or combined with PD-L1 tumour proportion score (TPS), significantly improves the prediction of therapeutic outcomes. Notably, OMP exhibited a higher predictive value than PD-L1 TPS in patients with low PD-L1 expression, a subgroup traditionally challenging to stratify for ICI therapy.[2] The validation in an external real-world cohort supports OMP as a potential imaging biomarker.

This research aligns with the broader trend of using non-invasive imaging techniques to obtain functional information about tumours, offering a cost-effective, and widely accessible method to potentially guide treatment decisions.[4] While the study presents a promising new tool, several steps are necessary before OMP can be fully integrated into clinical practice. The number of patients eligible for OMP was small, and prospective clinical trials are needed to confirm these findings and determine the practical aspects of implementing OMP measurement in diverse healthcare settings. The study also could not analyse the relationship between OMP and intratumoral T-cell function. Understanding this connection is crucial for elucidating the mechanisms by which OMP may predict the response to ICI therapy.[5] Moreover, understanding the biological underpinnings of OMP and its relationship with the TME and ICI mechanisms could offer deeper insights into cancer biology and treatment resistance. Additionally, there is no established criteria for defining the threshold of tumour size. The relationship between tumour size and perfusion is not linear, complicating the use of baseline tumour size as a predictive imaging biomarker.[6]

The significance of this study lies not only in its immediate findings but also in its contribution to the evolving landscape of precision oncology. By integrating OMP into routine clinical workflows, oncologists could provide more personalised therapy, enhancing treatment efficacy and patient outcomes. As the authors suggest, incorporating OMP into clinical practice could transform how oncologists approach treatment planning for NSCLC.[2] This biomarker provides a dynamic and comprehensive view of the tumour's vascular characteristics, which are critical in determining the delivery and effectiveness of immunotherapy.[2] The methodology described—onion-mode segmentation to

quantify OMP, represents an innovative application of imaging technology.[2] It demonstrates how advanced image analysis can extract valuable clinical information, bridging the gap between diagnostic imaging and therapeutic decision-making.

Despite the extensive use and potential of some imaging biomarkers, many are not adopted because they fail to measure relevant features or predict outcomes, leading to their devalidation.[4] Additionally, many promising imaging biomarkers remain confined to academic literature without real-world application due to inefficient translation strategies. To realise their full potential, imaging biomarkers must undergo thorough validation and qualification.[4]

The study by Liu *et al* marks a significant advancement in the quest for non-invasive imaging biomarkers in oncology. By introducing OMP as a predictive imaging biomarker for ICI therapy in NSCLC, the authors provide a novel tool that could revolutionise precision immunotherapy. The integration of such innovative approaches into clinical practice promises to improve patient stratification, optimise treatment regimens and ultimately enhance patient outcomes. The ability to use routine CECT imaging to predict ICI therapy response in NSCLC patients represents a substantial leap forward. Further research could explore the application of this imaging biomarker in other cancer types and its potential to predict responses to various therapeutic modalities. Such knowledge underscores the importance of developing non-invasive, accessible and reliable imaging biomarkers that can be seamlessly integrated into existing clinical workflows, ultimately paving the way for more personalised and effective cancer treatment strategies.

X Suraiya Dubash @SRDubash and Yat Tsang @YatTsang

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ORCID iDs
Suraiya Dubash http://orcid.org/0000-0003-3407-5214
Yat Tsang http://orcid.org/0000-0002-5369-3299

REFERENCES

1 Bhalla S, Doroshow DB, Hirsch FR. Predictive Biomarkers for Immune Checkpoint Inhibitors in Advanced Non-Small Cell Lung Cancer: current Status and Future Directions. *Cancer J* 2020;26:507–16.
2 Liu Z, Ma K, Jia Q, *et al*. Baseline tumor vessel perfusion as a non-invasive predictive biomarker for immune checkpoint therapy in non-small-cell lung cancer. *BMJ Oncol* 2024.
3 Doroshow DB, Bhalla S, Beasley MB, *et al*. PD-L1 as a biomarker of response to immune-checkpoint inhibitors. *Nat Rev Clin Oncol* 2021;18:345–62.
4 Lambin P, Leijenaar RTH, Deist TM, *et al*. Radiomics: the bridge between medical imaging and personalized medicine. *Nat Rev Clin Oncol* 2017;14:749–62.
5 Zebley CC, Zehn D, Gottschalk S, *et al*. T cell dysfunction and therapeutic intervention in cancer. *Nat Immunol* 2024;25:1344–54.
6 Trinidad López C, Souto Bayarri M, Oca Pernas R, *et al*. Characteristics of computed tomography perfusion parameters in non-small-cell-lung-cancer and its relationship to histology, size, stage an treatment response. *Clin Imaging* 2018;50:5–12.