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Themed Issue: Molecular imaging - visual themed issue

EDITORIAL

Molecular imaging - The first visual themed issue published in The British Journal of Pharmacology

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LINKED ARTICLES

This article is part of a visual-themed issue on Molecular Imaging. To view the other articles in this section visit.....

Abbreviations

AI, artificial intelligence; CT, X-ray computed tomography; CVD, cardiovascular diseases; FAIPVAT, perivascular Fat Attenuation Index; MRI, magnetic resonance imaging; PET, positron emission tomography; PVAT, perivascular adipose tissue.

With this *British Journal of Pharmacology* ‘Molecular imaging - visual themed issue’, we have provided an up-to-date account of a select group of molecular imaging techniques that we believe have and will enable interrogation of the pharmacology of novel compounds and ultimately to the development of new therapeutics.

Molecular imaging is the visualization and quantification of molecules within living patients. Revealing information on biomarkers and cellular and molecular pathways can improve disease diagnosis and therapeutic intervention. In addition, these advanced techniques also offer opportunities to identify novel pharmacological targets, thus facilitating both drug discovery and treatment stratification. The optimum molecular imaging modality ideally should possess high sensitivity and resolution, an acceptable safety profile, and be capable of non-invasive quantitative multiplexing imaging. However, none of the current clinical imaging modalities is routinely used in clinic for molecular imaging, therefore new approaches are required to meet this goal.

The aim of this *British Journal of Pharmacology* visual-themed issue is to provide an up-to-date overview of a select molecular imaging techniques with substantial potential, focusing particularly upon cardiovascular medicine and cancer. This themed issue is not intended as an exhaustive list of molecular imaging modalities; but is deliberately focused on a few select approaches to test a completely new ‘visual’ layout for the *British Journal of Pharmacology*.

Each of the four invited reviews has been designed and presented in a format with a predominance of visual material over text. Seeing is believing as they say, and so we have attempted to select the most helpful representative images and videos for each topic covered, to guide the readers through the respective merits and limitations of established and emerging imaging modalities, whilst also highlighting their potential theranostics applications. Video podcasts and figures, available in PowerPoint format, complement each published article.

The themed issue starts with an article by MacRitchie et al. (2021). The authors provide an overview of molecular imaging of cardiovascular inflammation. Immuno-inflammatory responses play key roles in the development and clinical manifestation of several cardiovascular diseases (CVD) (Rodriguez-Iturbe et al, 2017; Libby et al., 2018; Schloss et al., 2020). However, routinely used medical imaging modalities are restricted to anatomical or functional imaging and are unable to reveal the cellular and molecular inflammatory pathways at the level of resolution required for a more timely and precise diagnosis and pharmacological treatment (MacRitchie et al., 2021). In this visual review, the authors discuss strengths and

weaknesses of molecular imaging modalities in CVD, spanning from those already being used in the clinic such as magnetic resonance imaging (MRI) and positron emission tomography (PET), to novel technologies emerging at the pre-clinical stage.

In CVD, not only does inflammation cause thrombosis but the vice versa is also true, i.e. that thrombosis can trigger inflammation (Stark & Massberg, 2021). As such, faster and more reliable imaging modalities for the diagnosis of thrombosis are needed. In this visual issue, Wang et al. (2021) discuss the state-of-the-art in molecular imaging of arterial and venous thrombosis, highlighting recent improvements in the identification of biomarkers for thromboembolic diseases; the development of optimised contrast agents with improved signal to noise ratio; and recent developments in scanner technologies with higher sensitivity and resolution. The review covers modalities used for the clinical imaging of thrombosis, including PET, MRI, X-ray computed tomography (CT) and ultrasound imaging, to preclinical fluorescence and bioluminescent imaging modalities.

A clear demonstration of the potential to translate molecular imaging into clinical practice is presented in the review of Kotanidis & Antoniadis (2021), providing a virtual guide to perivascular fat imaging using CT. The authors discuss their recent elegant work (Antonopoulos et al., 2017; Oikonomou et al., 2018; Oikonomou et al., 2019), demonstrating non-invasive phenotyping of perivascular adipose tissue (PVAT) using CT as a promising marker for early detection of vascular inflammation in atherosclerosis. In particular, they highlight the use of the Perivascular Fat Attenuation Index (FAI_{PVAT}) for cardiovascular risk stratification and the diagnostic and prognostic value of macroscopic adipose tissue radiomics.

Along similar lines, the use of artificial intelligence (AI), a set of advanced computational algorithms that can accurately perform predictions for decision support, is thoroughly covered in the fourth visual review article by Klein et al. (2021), where the authors discuss the use of AI for solid tumour diagnosis in digital pathology. With digital pathology, specimen slides are digitized and analysed using AI. AI-assisted analysis improves accuracy, speed, and image analysis workflows. Developments in this field, enabling rapid and uniform analysis of large numbers of slides from any single tissue sample or patient, will inevitably lead to more informed pharmacotherapy decisions and improved prediction of therapy response outcomes and thus a better quality of care coupled with reduced healthcare costs.

In summary, this first visual-themed issue of the *British Journal of Pharmacology* provides readers with a pictorial representation of key emerging molecular imaging techniques and

analysis approaches, mainly focusing on cardiovascular medicine and cancer. We plan to use this novel format to cover future topics of the Journal, allowing readers to ‘see’ results as they are reading them. We hope that the increased use of visual material across a variety of formats will help to convey complex information and highlight key messages.

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Conflict of Interest

The authors wish to acknowledge that PM has co-authored papers with Karlheinz Peter, Charalambos Antoniades and Maria Chiara Maiuri. CA has co-authored papers with Karlheinz Peter and Pasquale Maffia. CA is a founder and shareholder of Caristo Diagnostics Ltd., a CT image analysis company. CA methods for analysis of the perivascular fat attenuation index described in this editorial are subject to patent PCT/GB2015/052359 and patent applications PCT/GB2017/053262, GB2018/1818049.7, GR20180100490, and GR20180100510, licensed through exclusive license to Caristo Diagnostics.

References

- Antonopoulos, A. S., Sanna, F., Sabharwal, N., Thomas, S., Oikonomou, E. K., Herdman, L., Margaritis, M., Shirodaria, C., Kampoli, A. M., Akoumianakis, I., Petrou, M., Sayeed, R., Krasopoulos, G., Psarros, C., Ciccone, P., Brophy, C. M., Digby, J., Kelion, A., Uberoi, R., Anthony, S., ... Antoniadis, C. (2017). Detecting human coronary inflammation by imaging perivascular fat. *Science translational medicine*, 9(398), eaal2658. <https://doi.org/10.1126/scitranslmed.aal2658>
- Klein, C., Zeng, Q., Arbaretaz, F., Devêvre, E., Calderaro, J., Lomenie, N., & Maiuri, M. C. (2021). Artificial Intelligence for solid tumor diagnosis in digital pathology. *British Journal of Pharmacology*,
- Kotanidis, C. P., & Antoniadis, C. (2021). Perivascular Fat Imaging by Computed Tomography: A Virtual Guide. *British Journal of Pharmacology*,
- Libby, P., Loscalzo, J., Ridker, P. M., Farkouh, M. E., Hsue, P. Y., Fuster, V., Hasan, A. A., & Amar, S. (2018). Inflammation, Immunity, and Infection in Atherothrombosis: JACC Review Topic of the Week. *Journal of the American College of Cardiology*, 72(17), 2071–2081. <https://doi.org/10.1016/j.jacc.2018.08.1043>
- MacRitchie, N., Frleta-Gilchrist, M., Sugiyama, A., Lawton, T., McInnes, I. B., & Maffia, P. (2020). Molecular imaging of inflammation - Current and emerging technologies for diagnosis and treatment. *Pharmacology & therapeutics*, 211, 107550. <https://doi.org/10.1016/j.pharmthera.2020.107550>
- MacRitchie, N., Noonan, J., Guzik, T. J., & Maffia, P. (2021). Molecular Imaging of Cardiovascular Inflammation. *British Journal of Pharmacology*,
- Oikonomou, E. K., Marwan, M., Desai, M. Y., Mancio, J., Alashi, A., Hutt Centeno, E., Thomas, S., Herdman, L., Kotanidis, C. P., Thomas, K. E., Griffin, B. P., Flamm, S. D., Antonopoulos, A. S., Shirodaria, C., Sabharwal, N., Deanfield, J., Neubauer, S., Hopewell, J. C., Channon, K. M., Achenbach, S., ... Antoniadis, C. (2018). Non-invasive detection of coronary inflammation using computed tomography and prediction of residual cardiovascular risk (the CRISP CT study): a post-hoc analysis of prospective outcome data. *Lancet (London, England)*, 392(10151), 929–939. [https://doi.org/10.1016/S0140-6736\(18\)31114-0](https://doi.org/10.1016/S0140-6736(18)31114-0)
- Oikonomou, E. K., Williams, M. C., Kotanidis, C. P., Desai, M. Y., Marwan, M., Antonopoulos, A. S., Thomas, K. E., Thomas, S., Akoumianakis, I., Fan, L. M., Kesavan, S.,

- Herdman, L., Alashi, A., Centeno, E. H., Lyasheva, M., Griffin, B. P., Flamm, S. D., Shirodaria, C., Sabharwal, N., Kelion, A., ... Antoniadou, C. (2019). A novel machine learning-derived radiotranscriptomic signature of perivascular fat improves cardiac risk prediction using coronary CT angiography. *European heart journal*, 40(43), 3529–3543. <https://doi.org/10.1093/eurheartj/ehz592>
- Rodriguez-Iturbe, B., Pons, H., & Johnson, R. J. (2017). Role of the Immune System in Hypertension. *Physiological reviews*, 97(3), 1127–1164. <https://doi.org/10.1152/physrev.00031.2016>
- Schloss, M. J., Swirski, F. K., & Nahrendorf, M. (2020). Modifiable Cardiovascular Risk, Hematopoiesis, and Innate Immunity. *Circulation research*, 126(9), 1242–1259. <https://doi.org/10.1161/CIRCRESAHA.120.315936>
- Stark, K., & Massberg, S. (2021). Interplay between inflammation and thrombosis in cardiovascular pathology. *Nature reviews. Cardiology*, 1–17. Advance online publication. <https://doi.org/10.1038/s41569-021-00552-1>
- Wang, X., Ziegler, M., McFadyen, J. D., & Peter, K. (2021). Molecular Imaging of Arterial and Venous Thrombosis. *British Journal of Pharmacology*,