



Editorial: Status Go for Preclinical Imaging

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Editorial on the Research Topic

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This special Research Topic includes a collection of reviews and original articles on preclinical imaging. Preclinical imaging encompasses the use of imaging methods to study animal models, tissue samples, and other unique specimens, such as eggs (*in ovo*). Preclinical imaging is driven by advances in medical physics and instrumentation as well as by active research in biology and medicine. Given the multi-disciplinary nature of preclinical imaging, some articles from this collection appear in the journal *Frontiers in Physics* whereas others appear in the journal *Frontiers in Physiology*.

Over time, preclinical imaging has evolved from a technique perceived to be niche and of limited value to an established workhorse in medical research, supporting drug discovery programs, mechanistic studies focused on understanding (patho-)physiology and disease development as well as progression, and aiding the development of paradigms for clinical imaging. Preclinical imaging also encompasses scales of different orders of magnitude, from molecular/microscopic to structural/macrosopic as well as organismic scale, thus providing not only superb anatomical detail but also excellent quantitative functional information. Despite the tremendous and ever-expanding role of preclinical imaging in medical research, its full potential can only be delivered if preclinical researchers apply the same amount of effort and rigor to their preclinical protocols as is used in clinical settings. This means that thoughtful study planning and use of established standardized protocols, accompanied by careful handling of the subjects (e.g., animals, eggs, or tissue samples) is of paramount importance to generate preclinical imaging datasets with translational value. Furthermore, there is a need to implement robust image analysis approaches, including reliable and reproducible methods to obtain quantitative data. Finally, state-of-the-art statistical testing and controlling must be applied.

In the present Research Topic, 13 articles are divided into 6 reviews, 1 mini-review, 4 original research articles, 1 perspective, and 1 brief research report, covering some of the latest research activities on diverse topics including microscopy, positron emission tomography (PET) quantification, single photon emission computed tomography (SPECT) for neuroimaging, small animal magnetic resonance imaging (MRI), ultrasound, *in ovo* imaging, *in vivo* cell tracking using multiple imaging methods and correlated multimodal imaging (CMI).

The review article by Walter et al. provides a comprehensive overview of the challenges of CMI, where information from the same specimen with two or more modalities is combined to create a composite view of the sample. In this review paper, the different imaging techniques available for CMI, including correlated light microscopy, electron microscopy, and biological hybrid imaging, are described alongside the advantages and disadvantages of each modality.

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In this Frontiers special issue, five papers discuss the latest research in nuclear imaging techniques. The paper by He et al. describes strategies for the extraction of an arterial or image-derived input function for quantification of the adenosine type 1 receptors (A1) with PET. The impact of attenuation correction on [^{18}F]FDG PET imaging is described by Wanek et al. using data from phantom and rat studies. Oelschlegel and Goldschmidt's paper focuses on describing the use of cerebral blood flow SPECT imaging to study brain-wide activation patterns in awake rodents. Dual tracer PET/SPECT studies are reported by Blower et al. using phantoms to investigate the cross-contamination of PET signal on SPECT measurements and vice-versa. Finally, a perspective article by Jones et al. provides an outlook at the possibilities of how preclinical imaging might be instrumental to deliver the full potential of the clinical total-body PET technology.

Traditionally, hybrid radionuclide imaging has been used to study the physiology and pathophysiology in humans and rodents. However, it can also be used to examine tumoral uptake of radiotracers together with anatomical information in the Hen's Egg Test Chorioallantoic-Membrane (HET-CAM) model by so-called *in ovo* imaging (Winter et al.). This is an emerging new application for preclinical imaging. Another more routine application of preclinical imaging involves the use of imaging technology to track cells *in vivo* and consequently help with the development of novel cancer immunotherapies. Imaging methods used to track cells are applied as summarized in the review by Iafrate and Fruhwirth.

This special issue on preclinical imaging also covers the utility of preclinical MRI as a promising diagnostic tool to monitor disease progression and response to therapy in preclinical models. Technical aspects of *in vivo* small animal cardiovascular

MRI are summarized in the review by Li et al. whereas Anderson et al. describe the development of MR diffusion imaging protocols for structural connectomics analysis in mouse models of human disease.

Finally, the Research Topic is further complemented by a review on preclinical ultrasound imaging techniques and applications (Moran and Thomson) and a mini-review on recent technological and methodological advances in the field of multiphoton microscopy (Pozzi et al.).

The Research Topic editors greatly appreciate the amount of work from contributors, reviewers, and Frontiers staff. We believe that the articles published in this Research Topic provide further evidence that preclinical imaging is an invaluable tool in medical and biological research and will continue to supply the field with new critical knowledge on the causes, consequences, and treatment options of multiple diseases. This is a moment when the preclinical imaging community needs to go further, continuing to push the limits of this tool.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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