SPECIAL SECTION GUEST EDITORIAL

Small-Animal Optical Imaging

There is a prominent biological research shift occurring over recent years, where the gap between the petri dish and clinical practice is decisively bridged by means of using elaborate animal models with human disease phenotypes. While the animal has always served as an important test bed for clinical propagation, advanced genomic technologies have now allowed an increased availability of disease models and endogenous contrast mechanisms that can allow the study of complex disease patterns, cell traffic, or molecular pathways and the response of disease to environmental factors and drugs. Correspondingly, attention has shifted to methods that can measure and analyze anatomical, functional, and molecular parameters noninvasively in entire animals. These new methods go beyond the study of thin tissue sections or cell cultures to technologies that can operate *in vivo* with a high degree of sensitivity and specificity.

All major clinical imaging approaches have been modified for animal use as a response to this trend. X-ray computed tomography, magnetic resonance, and nuclear imaging approaches have been miniaturized to optimally accommodate small animal volumes, correspondingly increasing the resolution and sensitivity achieved. Ultrasound has also been adapted to small animal imaging by operating at higher frequencies than clinical implementations, which similarly improves the resolution and better interfaces with the penetration depths required in small animal imaging. Yet photonic methods carry significant advantages by utilizing largely diverse contrast mechanisms, high detection sensitivity, and high dissemination potential in the biological laboratory. Coupled with advances in the engineering of optical agents with distinct optical contrast characteristics and the ability to target specific biological processes and biomarkers, photonic small animal imaging is seeing a revolution of technologies and applications in recent years.

This field of small animal optical imaging captures important new developments in the development of targeting agents and probes, endogenous generation of optical contrast via transgenic technologies, and the corresponding development of imaging systems and methods that allow for unprecedented visualization of gene function and regulation, protein activity, cellular and subcellular function, physiological responses, and highly detailed anatomical contrast. Small animal imaging can allow for biomedical observations at the system level and can serve as the backbone for monitoring therapeutic interventions at the preclinical level in a manner that can accelerate clinical translation. Noninvasive imaging further facilitates the use of a smaller number of animals compared to current observations based on statistical testing of samples obtained from large animal cohorts *in vitro* and improves the accuracy of the observations by yielding longitudinal observations on the same animal as a function of different external stimuli.

A generic classification of optical methods separates techniques by their enabling imaging feature, i.e., anatomical, physiological, or molecular contrast. However, it is also useful to classify methodologies that operate by (1) utilizing intrinsic tissue contrast, i.e., a native photon-tissue interaction, (2) employing extrinsically administered agents that modify contrast of an optical parameter, for example, absorption, scattering, or fluorescence, or (3) requiring the use of genetically engineered cell lines or transgenically modified animals that endogenously express optical contrast, typically in the form of fluorescence or bioluminescence. Optical imaging instrumentation also includes a wide variety of technologies, ranging from high-resolution microscopy and optical-coherence tomography for examining tissue at the cellular level, to high-sensitivity noninvasive imaging of diffuse light emitted from deep tissue. Noninvasive imaging is particularly effective in small animals, where long-wavelength emission can detected throughout the entire body. Photonic-based methods have been developed to help image or localize optical contrast biodistribution within the body and compensate for effects of photon scattering and absorption. Researchers are also beginning to combine optical imaging with other modalities, such as ultrasound, x-ray, and magnetic resonance imaging, to exploit the best features of each modality and derive more detailed information from each animal experiment.

This special section captures the diversity that exists in small animal imaging methods and showcases the current state of the art in small animal optical imaging visualization. A range of modalities are represented including two-photon microscopy, optical coherence tomography, photoacoustic tomography, and diffuse optical tomography. The papers cover an exciting range of applications including imaging of enzyme activity, animal models of arthritis, extravasation in the brain, expression of CD13/APN in tumors, and tissue morphology in the context of muscular dystrophy. A number of new technological developments are also reported, including strategies for improving the quantitative accuracy and novel data subtraction processing procedures to increase sensitivity. We thank all the authors for their efforts in contributing the manuscripts and look forward to rapid growth in the development and application of light to small animal imaging.

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Special Section Guest Editors