

## Cross-Platform (MRI/PET) Neuroimaging

Todd A. Sasser<sup>1</sup>, Jens Waldeck<sup>1</sup>, Andrew Van Praagh<sup>1</sup>, W. Matthew Leevy<sup>2,3</sup>

Positron Emission Tomography (PET) has been successfully applied in neurological studies for a range of disease models including stroke/ischemia (Balsara et al., in Press, Sobrado et al., 2011, Pozo et al., 2008), Alzheimer's disease (Martin-Moreno et al., 2012), Parkinson's disease (Fernández et al., 2011) and temporal brain activity (van der Veen et al., 2012). The Albira PET system has been proven to be an ideal platform for PET brain imaging studies, thanks to its combined high resolution and high sensitivity (Spinks et al., 2014), flexible imaging capacity and the capability to automatically fuse (optional) integrated computed tomography (CT). The brain volume-of-interest (VOI) tools, included as standard, as well as the kinetic modeling tools in PMOD (PMOD Technologies Ltd; Zurich, Switzerland; [pmod.com/technologies/index.html](http://pmod.com/technologies/index.html)) can be extended with dedicated modules such as pBRAIN for Alzheimer's disease modeling.

### Complementary Cross-Platform Brain Imaging

There are several benefits to applying cross-platform (PET/MRI) imaging in neuroimaging. Functional PET can be complemented by the anatomical soft tissue imaging of MRI. In fact, Sabrado et al. (2011) and Pozo et al. (2008)

reported on complementary Albira PET and MR imaging in just this fashion. In this work, PET image ROI placement for analysis of ischemic stroke model rats was based on complementary MR apparent diffusion coefficient maps. Cross-platform imaging can be facilitated through the use of a multimodal animal bed and system mounts (see Figure 1). This solution enables the combination of preclinical imaging modalities, since it is compatible with the full range of Bruker preclinical imaging systems, including the BioSpec<sup>®</sup>, ICON<sup>™</sup>, Albira<sup>™</sup>, micro-CT 1176, In-Vivo Xtreme<sup>™</sup> and In-Vivo MS FX PRO. The multimodal animal bed approach thus enables imaging on dedicated, high-performance, individual modality systems, without sacrificing performance. Furthermore, this approach facilitates fast scan times and an increased number of animal scans compared to combined systems. Beyond neurological applications, the cross-platform approach offers several benefits for other applications where soft tissue anatomy has a certain value over CT information or instances where multi-probe approaches are required.

### Brain Volume of Interest Analysis

Cross-platform brain imaging studies may be accomplished



Figure 1: Multimodal animal bed and mounts for cross-platform imaging in Bruker preclinical imaging systems. Imaging with the cross platform, multimodal animal bed conserves anatomical position.

without a specific transport bed, but involves more animal handling. To achieve brain multimodal co-registrations without a universal transport bed, margins of the brain cavity in a CT image can be aligned with an MR brain margin using PFUS (see Figure 2). The software includes tools for applying a regional brain VOI atlas to obtain regional brain SUV values (see Figure 2).

The Albira PET system and PFUS brain atlas tools were recently used in a temporal brain study by van der Veen et al. (2012). Mice were imaged on the Albira PET platform across daylight cycles. As part of this work, SUV values for regional brain  $^{18}\text{F}$ -FDG activity in mice were determined (see Figure 3). Interestingly, this revealed a high nocturnal  $^{18}\text{F}$ -FDG brain uptake, corresponding to the nocturnal

nature of mice. In addition to providing general insights into the temporal brain activity of animals, these studies demonstrated that for valid, relative comparisons, imaging at consistent temporal phases is critical when studying brain disease models. The workflow for brain imaging and brain VOI analysis using the Albira PET system and PMOD brain VOI tools is detailed in an upcoming report by Balsara et al. (In Press).

### Dynamic and Kinetic Imaging

The Albira PET system also enables re-slicing of dynamic PET datasets post acquisition, which means that critical time points and intervals may be analyzed for receptor occupancy and dynamic imaging studies. Additionally, PKIN software enables advanced kinetic modeling, including multi-tissue compartments, Logan and Patlak plots and input functions, including image-derived cardiac input functions. The Albira system has also been used with catheter and auto-injector systems for safe and automatic administration of radiopharmaceuticals or agents (Sebastian Eigner, personal communication).

### Conclusion

Cross-platform imaging with Bruker's high performance PET and MR imaging technologies, in combination with strong, reliable analysis and validation features, enables researchers to gain new, multimodal data sets in advanced neurology studies.

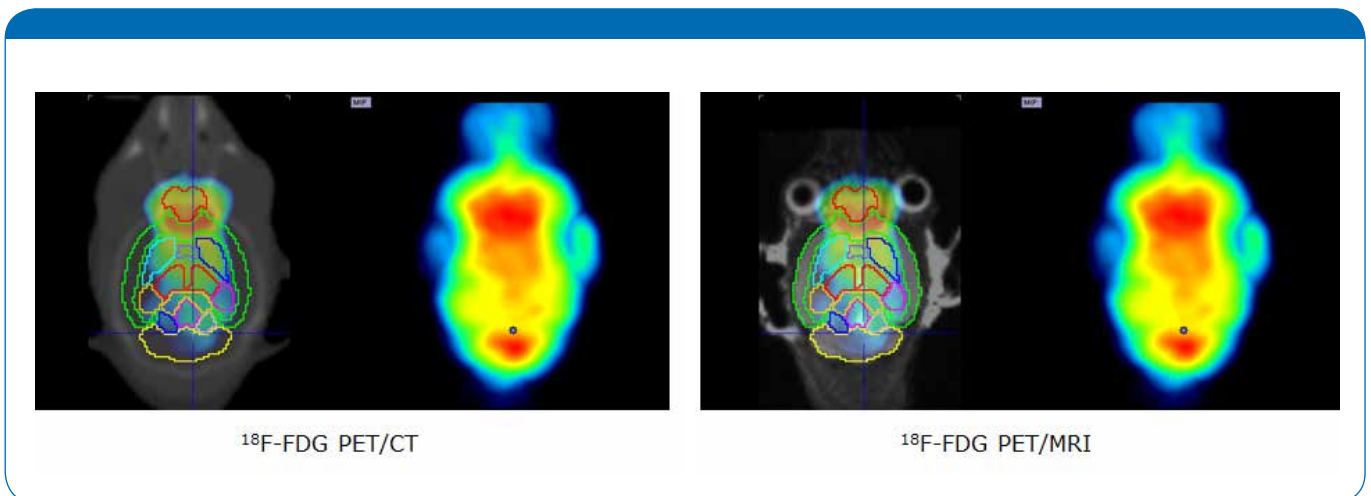


Figure 2: Left: Multimodal Albira PET/CT image of control mouse receiving  $^{18}\text{F}$ -FDG with a PFUS brain VOI atlas applied. The PMOD brain VOI atlas applied for regional  $^{18}\text{F}$ -FDG SUV calculations. Right: BioSpec MR image of the same animal, fused with the Albira PET image. Courtesy Dr. Paul Rosenberg, Boston Children's Hospital, MA, USA.

### Amplitude of Brain Regions

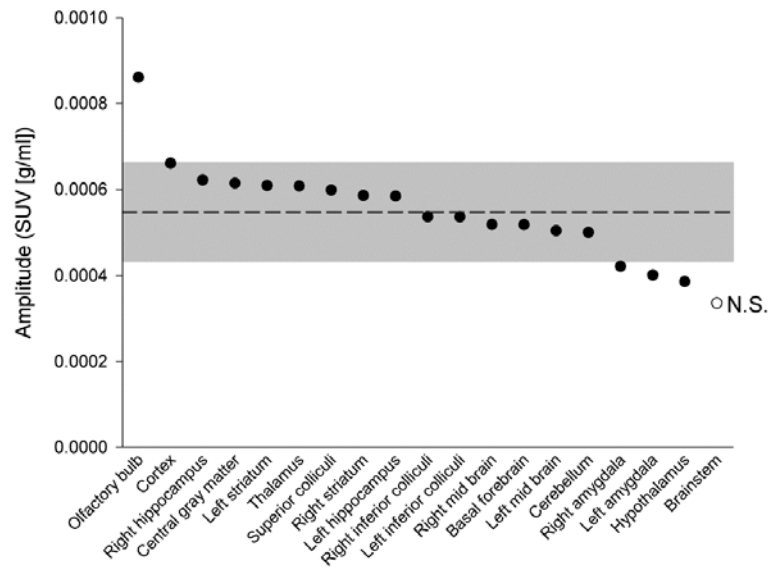


Figure 3:  $^{18}\text{F}$ -FDG SUV amplitude of brain regions in mice at day and night cycles with imaging and analysis performed using the Albira PET system and PMOD PFUS tools. Reprinted (adapted) with permission from PLoS One 7(2): e37192.

## References

Balsara R, Chapman S, Donahue D, Castellino FJ, Leevy WM (In Press) FDG-PET imaging and analysis of cerebral ischemia in living rats. JOVE.

Sobrado M, Delgado M, Femández-Valle E, García- García L, Torres M, Sánchez-Prieto J, Vivancos J, Manzanares R, Moro MA, Pozo MA, Lizasoain I (2011) Longitudinal studies of ischemic penumbra by using 18F-FDG PET and MRI techniques in permanent and transient focal cerebral ischemia in rats. *NeuroImage*, 57, 45-54.

Pozo MA, Delgado M, Sobrado M, García- García L, Balcerzyk M, Kontaxakis G, Moro MÁ, Lizasoain I. (2008) Metabolic PET imaging in experimental animal model of ischemic stroke. WMIC Poster Session.

Van der Veen RD, Shao J, Chapman S, Leevy WM, Duffield GE (2012) A 24-hour temporal profile of in vivo brain and heart PET imaging reveals a nocturnal peak in brain F-fluorodeoxyglucose uptake. *PlosONE*. 7(2), e31792.

Martín-Moreno MA, Brera B, Spuch C, Carro E, García- García L, Delgado M, Pozo MA, Innamorato NG, Cuadrado A, de Ceballos ML (2012) Prolonged oral cannabinoid administration prevents neuroinflammation, lowers  $\beta$ -amyloid levels and improves cognitive performance in Tg APP 2576 mice. *J Neuroinflammation*, 9, 8-15.

Fernández M, Negro S, Slowing K, Fernández-Carballido A, Barcia E (2011) An effective novel delivery strategy of rasagiline for Parkinson's disease. *Int J Pharma*. 419. 271-280.

Spinks TJ, Karla D, Leach MO, Flux G (2014) Quantitative PET and SPECT performance characteristics of the Albira trimodal pre-clinical tomograph. *Phys Med Bio* 59, 715-731.

## Authors

Todd A. Sasser<sup>1</sup>, Jens Waldeck<sup>1</sup>, Andrew Van Praagh<sup>1</sup>, W. Matthew Leevy<sup>2,3</sup>

<sup>1</sup>Bruker Molecular Imaging, 44 Manning Rd, Billerica, MA 01821 USA; <sup>2</sup> Department of Chemistry and Biochemistry, University of Notre Dame, 236 Nieuwland Science Hall, Notre Dame, IN 46556 USA; <sup>3</sup>Notre Dame Integrated Imaging Facility, University of Notre Dame, Notre Dame, IN 46556 USA