Combining MRI with PET for partial volume correction improves image-derived input functions in mice

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Target Audience Users of preclinical models; multi-modality imagers

Purpose Positron emission tomography (PET) is quantitative with high sensitivity and specificity. Kinetic modelling allows metabolic measures to be obtained, but requires the tracer arterial input function (AIF), defined as the time-activity curve (TAC) in plasma. This measure is obtained by blood sampling in humans, but this is prohibitive in mice due to low blood volumes (~1-2ml). If large areas of blood signal can be seen, the AIF can be measured from reconstructed images. In this study we present a comparison of PET- and MR-based region-of-interest (ROI) analysis to obtain an accurate image-derived AIF from the left ventricle (LV) of a mice model. ROI-based partial volume correction (PVC) was performed in order to overcome the limited resolution of the PET scanner (1.5– 2 mm) and improve quantification.

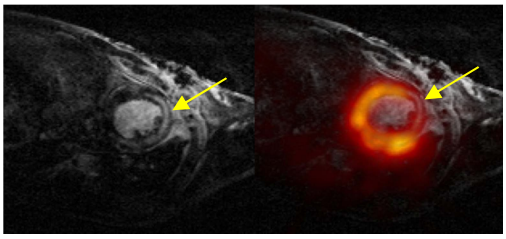

Figure 1: FLASH MR shown axially through control mouse heart (left) and fused with ^{18}F-FDG static PET (right). Infarcted region indicated by arrow.

Methods *Image acquisition* Structural MRI and dynamic PET images were obtained from a recent study investigating treatment effects in 12 mice following myocardial infarction[1], where half the mice received a new treatment and half did not. Prospectively gated MRI (4.7T Bruker BioSpec 47/40, FLASH TR/TE 400/3ms, 36mm FOV, matrix 256, spatial resolution 140µm over 8 slices, 1mm thick) were acquired prior to PET acquisition on a novel split-magnet PET camera[2]. PET acquisition was cardiac gated in order to minimize heart motion and improve image quantification (~25MBq ^{18}F-FDG bolus, 45 minute emission listmode acquisition reconstructed with 3DRP in four cardiac frames, gated by simultaneous ECG recordings). To minimize animal movement, the mouse bed was transferred directly between scanners. Images were then co-registered using SPMMouse[3] (see Figure 1).
AIF extraction ROIs were manually drawn on either the co-registered MR images or directly onto the last dynamic frame PET images, covering LV lumen, myocardium, lungs/body and background. AIFs were obtained by taking mean time courses from the LV Lumen ROIs, with an example shown in Figure 2A. The regional geometric transfer matrix method was applied for PVC[4], using ROIs derived from the PET data (see Figure 2B) or the co-registered MR (see Figure 2C).
Kinetic modeling For each AIF obtained, Patlak analysis[5] (PMOD v2.5) was performed to evaluate glucose metabolism.

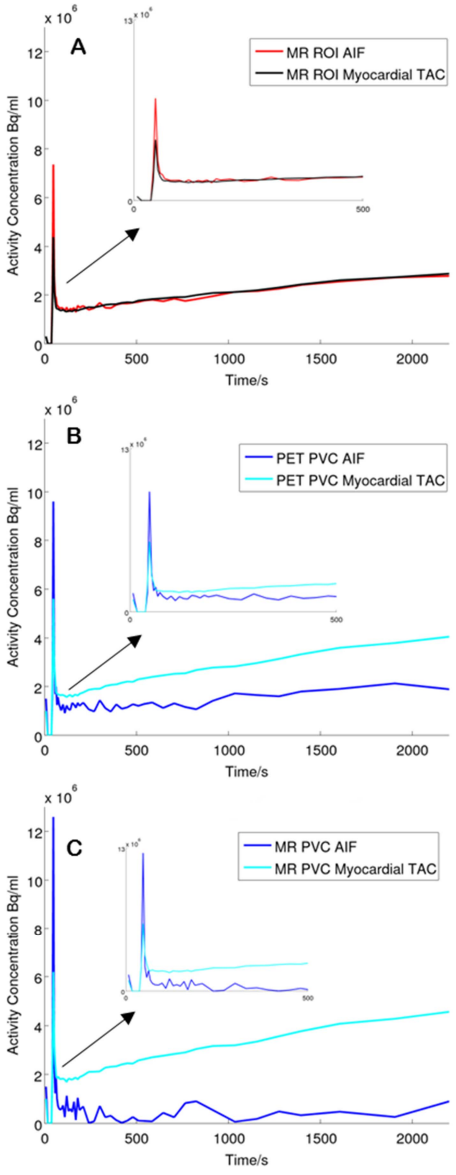

Figure 2 (right): ^{18}F-FDG AIF and Myocardial TACs derived for single subject using (A) MR ROIs, (B) PET ROIs with PVC and (C) MR ROIs with PVC. Zoom insets detail first 500s.

Results and Discussion Uncorrected AIFs and myocardial TACs produced by manual ROI delineation using the PET data or the MRI (Figure 2A) display contamination with myocardial signal. The effect of PVC for each case is shown in Figure 2B and 2C, where the AIFs and myocardial curves become distinguishable. MR PVC AIFs were found to better reflect blood sampled AIFs (i.e. sharper and larger peak, descending tail) and this was seen in the improved K_i results displayed in Table 1. Importantly, only MR-based PVC (but not PET-based PVC) produced significant differences between the treated and untreated groups.

Table 1	Glucose metabolism K_i (ml/min/cm^3), Mean ± SD			
	without PVC		with PVC	
Group	PET ROIs	MR ROIs	PET ROIs	MR ROIs
Untreated	0.03 ± 0.01	0.03 ± 0.01	0.4 ± 0.3	0.6 ± 0.2*
Treated	0.03 ± 0.01	0.03 ± 0.02	0.2 ± 0.3	0.2 ± 0.2*

Conclusion We have shown that PVC is crucial for deriving AIFs and gives best results when ROIs are based on MRI data, due to its high-resolution and excellent soft-tissue contrast that allows better ROI delineation compared to PET.

References [1] Buonincontri et al, *NIMA A*, in press, DOI: 10.1016/j.nima.2013/08.066, [2] Lucas et al., *IEEE Nucl Sci Symp Record*, 2345-8, (2006), [3] Sawiak et al. *Proc. ISMRM.*, 17, (2009), [4] Rousset et al., *J Nucl Med*, 39, 5, 904-911, (1998), [5] Patlak et al., *J Cereb Blood Flow Metab*, 3,1,1-7, (1983)