Title: A non-invasive hybrid PET/MRI method for imaging the cerebral metabolic rate of oxygen

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Structured Abstract:

Introduction: The gold standard for imaging the cerebral metabolic rate of oxygen (CMRO2) in humans is a complex PET technique that requires three [15O]-tracers and invasive arterial blood sampling. It also suffers from two common sources of error: blood-borne activity and [15O]-water created by metabolism (recirculating water). Hybrid PET/MR offers an alternative to image CMRO2, in which MR is used to image local CBF and whole-brain CMRO2. By using whole brain as a reference region, this hybrid PET/MR approach avoids arterial sampling and reduces PET imaging to only inhaling [15O]-oxygen. The aim of this work was to conduct an initial assessment of this non-invasive, reference-based method.

Methods: To assess the sensitivity to the two common sources of error with PET-only methods, simulated time activity curves including recirculating water and blood-borne activity were generated over a range of CBF values and analyzed with the model solution for the reference-based method. For validation, PET and MR images from an animal model (juvenile pig) were acquired using a 3T Siemens Biograph mMR system. Arterial spin labelling (ASL), oxygenation and flow (OxFlow), anatomical, and angiography MR sequences were acquired. 5min list-mode PET acquisition was performed after injecting 500MBq of [15O]-water and inhaling 2200MBq of [15O]-oxygen. For validation, arterial sampling was obtained using a Swisstrace with a 5mL/min withdrawal rate. Dynamic PET images were reconstructed into 48 time-frames (30×3s, 6×5s, 6×10s and 6×20s). Local CBF was obtained with ASL and [15O]-water, while whole-brain CBF and CMRO2 were obtained with OxFlow. CMRO2 was calculated using the method described previously (Narciso et al., 2019, JCBFM).

Results: Simulations indicated that neglecting recirculating water and blood-borne activity resulted in negligible error in CMRO2 estimates (0.03±0.16% and 0.3±0.6%, respectively). Applying the hybrid PET/MR methods to preliminary data from the animal experiment resulted in mean whole-brain CMRO2 of 1.21±0.48 mL/100g/min, when using [15O]-water PET CBF values, and whole-brain CMRO2 of 1.33±0.36 mL/100g/min, when using ASL-MR CBF values.

Discussion: The insensitivity to recirculating water and blood-borne activity predicted from the simulations indicates the potential of hybrid PET/MR for imaging CMRO2 without the need to correct for these common sources of error. This was reflected in the results of the first experiments since the CBF and CMRO2 estimates were within the expected range. This also reinforces our previous results, in which the reference-based approach applied to [15O]-PET human data generated CMRO2 images that were in good agreement with images derived using the standard PET-only method. These results suggest that quantitative measurements of CMRO2 can be obtained without the need for arterial blood sampling, although further experiments are needed to fully validate the approach.