Non-Invasive Quantification of Cerebral Blood Flow by Hybrid MR/PET
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Introduction: Positron emission tomography (PET) using the tracer H\textsubscript{2}\textsuperscript{15}O is considered the gold standard for imaging cerebral blood flow (CBF). However, quantification requires measuring the arterial input function (AIF), which is not only invasive, but an inherently noisy procedure. Arterial spin labeling (ASL) is an attractive MRI-based alternative, but its accuracy is hindered by low signal to noise and arrival time uncertainties (Heijtel et al., 2014), particularly when imaging CBF in patients with cerebrovascular disease. In light of these limitations, we propose a hybrid MR/PET approach that does not require invasive arterial sampling, but still generates quantitative CBF images. With this approach, global CBF is measured by phase-contrast MRI (PC-MRI) (Peng et al., 2015), simultaneously with PET imaging of H\textsubscript{2}\textsuperscript{15}O\textsubscript{2}. Global CBF is then used as a reference to convert H\textsubscript{2}\textsuperscript{15}O–PET activity data into CBF maps, thereby avoiding the need to measure the AIF. In this study, the agreement between simultaneously measured CBF using PC-MRI and PET-only were compared in a large animal model over a range of CBF values.

Methods: Data were acquired in juvenile pigs (n = 7, 21.7 ± 2.7 kg) at baseline, hypercapnia and hypocapnia. Animals were anaesthetized and pCO\textsubscript{2} was manipulated by adjusting the breathing rate and volume. After a rapid intravenous bolus injection of H\textsubscript{2}\textsuperscript{15}O (475±153 MBq), 5 min of PET list-mode data were acquired with a 3T PET/MR system (Biograph mMR Siemens). Arterial blood was sampled at 5mL/min using an MR-compatible blood sampling system (Swisstrace, Switzerland). For PC MRI, an imaging plane orthogonal to the internal carotid and basilar arteries was identified by time-of-flight angiography. Gated PC images (TR/TE: 34.4/2.87ms, voxel size: 0.625 x 0.625 x 5 mm\textsuperscript{3}, VENC: 80 cm/s in the through-plane direction, 8 averages) were acquired simultaneously with PET scanning. For structural reference, sagittal MPRAGE T1-weighted images were acquired (TR/TE: 1780/2.45ms, voxel size: 1mm isotropic).

Average whole brain flow was measured with PC-MRI data by contouring the feeding arteries in MATLAB and scaling by the brain tissue weight. Raw PET data were reconstructed into 37 dynamic frames (3s x 20; 5s x 6; 15s x 6; 30s x 5) using a CT-based attenuation correction map and an ordered subset expectation maximization algorithm (matrix size: 344 x 344 x 127, voxel-size: 0.84 x 0.84 x 2 mm\textsuperscript{3}). The images were smoothed with a 6-mm Gaussian filter, and a non-linear optimization routine was used to fit the Kety model (Kety et al., 1951) including a blood volume term to determine CBF using a blood-brain partition coefficient of water = 90 ml/100g.

Results: Mean pCO\textsubscript{2} at hypocapnic, normocapnic and hypercapnic conditions were 25.0 ± 2.2, 37.6 ± 1.7 and 54.3 ± 4.9 mmHg. Average whole-brain CBF at hypocapnic, normocapnic and hypercapnic conditions measured by PC-MRI were: 24.6 ± 1.8, 46.3 ± 15.4 and 86.9 ± 33.0 ml/100g/min while H\textsubscript{2}\textsuperscript{15}O–PET CBF values were: 25.3 ± 2.1, 42.8 ± 4.5, 77.0 ± 28.3 mL/100g/min. A Line regression showed significant positive correlation (R\textsuperscript{2}=0.92, p<0.05). The Bland-Altman plot demonstrated good agreement between PET and MRI measurements (NS, p=0.22). Interestingly, in the hypercapnic state, our preliminary data shows greater deviation between CBF measurements from PC-MRI and PET (13%). This may be attributed to limited water extraction at higher flow rates (St Lawrence et al., 1998). Future studies will involve comparing this reference method to ASL in CVD patients to assess its ability to quantify perfusion abnormalities.

Discussion and Conclusion: This work presents a non-invasive and quantitative method of imaging CBF by hybrid MR/PET. We believe this method could be useful for patient populations for whom it has proven challenging to obtain accurate perfusion measurements with other methods, most notably ASL, due to significant vascular disease. Linear regression showed significant positive correlation (R\textsuperscript{2}=0.92, p<0.05). The Bland-Altman plot demonstrated good agreement between PET and MRI measurements (NS, p=0.22). Interestingly, in the hypercapnic state, our preliminary data shows greater deviation between CBF measurements from PC-MRI and PET (13%). This may be attributed to limited water extraction at higher flow rates (St Lawrence et al., 1998). Future studies will involve comparing this reference method to ASL in CVD patients to assess its ability to quantify perfusion abnormalities.