Simultaneous assessment of Perfusion with [^{15}O]water PET and arterial spin labeling MR using a hybrid PET/MR device

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Introduction:

The combination of Positron Emission Tomography (PET) and Magnetic Resonance (MR) is a promising tool in biomedical research and clinical diagnostic imaging. In this study we performed to our knowledge the first simultaneous PET and MR perfusion measurements using [^{15}O]water, as a PET perfusion marker, and arterial spin labeling (ASL), for MR perfusion measurements, in small animals. Due to the isochronous collection of data we were able to minimize confounding parameters such as variations in the physiology and compare quantitatively these two perfusion measurement approaches.

Material and Methods:

The studies were performed using a small animal PET insert designed by our group. The PET ring consists of 10 detector cassettes, each with a 12x12 lutetium oxy-orthosilicate crystal block (LSO, single crystal size 1.6x.6x4.5 mm^3) and an avalanche-photo-diode (APD) array. Inside the PET insert a quadrature transmit/receive coil for MR data acquisition was installed. The combined PET/MR field of view is 19 mm in axial direction and 35 mm in transversal direction using the above-mentioned coil. MR and PET data can be acquired without fundamental mutual interference using this system [1].

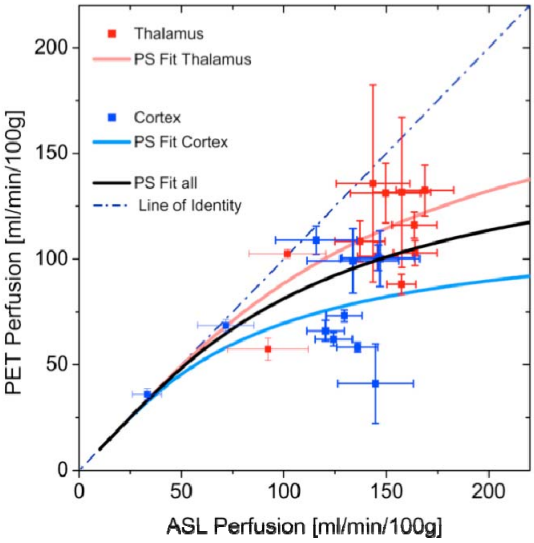

Figure 1: Simultaneous acquired PET and MR perfusion data for different regions of the mouse brain. An increasing mismatch between PET and ASL perfusion is observed for higher perfusion rates. A fit of the BBB PS product in the various brain regions is shown. For the thalamus (red) PS=(216±24)ml/min/100g, for the cortex (blue) PS=(119±20)ml/min/100g and total thal. and cortex (black) PS=(168±20)ml/min/100g was found.

For the simultaneous perfusion studies Balb/c mice (n=5) were used. An *i.v.* catheter for injection of PET tracers was placed in the tail vain of the animals. In a first scan, the brain of the animals was positioned at the center of the combined PET/MR field of view. An MR ASL sequence (FAIR-True-FISP, TR=4.1ms, TE=2.1ms, TI=1800ms, FOV=25x25mm^2, matrix=64x64, slice thickness=2mm, 40 selective and 40 non-selective images and one M_0 image, scan interval=7sec) was started. During the run of the ASL sequence 48 MBq [^{15}O]water ($T_{1/2}$=122s) was simultaneously injected as a PET perfusion marker. PET perfusion data were acquired over 10 minutes. After these simultaneous brain perfusion measurements the heart of the animal was placed in the center of the PET/MR FOV and the [^{15}O]water injection was repeated to generate an image derived arterial input function (AIF) from the left ventricle of the mouse.

ASL perfusion values were analyzed using an extended Bloch equation. For the PET image data, the AIF from the left ventricle of the mouse was corrected for various effects such as spoilage from the ventricle tissue wall, dispersion, and time delay. The corrected AIF was then used in combination with the obtained brain PET perfusion data to model (1 compartment) quantitatively the perfusion in the mouse cortex and thalamus. The same tissue regions were analyzed in the PET as well as in the MR, by exact co-registration of the MR Regions of Interest (ROIs) to the PET image data.

PET and MR perfusion values were compared for cortex and thalamus on a global level (group average) as well as a correlation plot involving individual animals was obtained.

Results:

A difference ($p<0.01$) between PET and MR ASL perfusion values was observed. For the cortex region the PET average was (78±23)ml/min/100g and for ASL (132±11)ml/min/100g. For the thalamus region PET yielded (116±17) ml/min/100g and ASL (156±11)ml/min/100g. A plot of PET vs. ASL perfusion values is shown in Figure 1. For high flow rates a discrepancy between PET and ASL perfusion was observed, with a tendency towards higher ASL perfusion values. At lower flow rates, PET and ASL perfusion values matched. A fit using $CBF_{PET}=CBF_{ASL}(1-\exp(-PS/CBF_{ASL}))$ yielded blood-brain-barrier (BBB) permeability surface area product (PS) values (average of cortex and thalamus) for the mouse brain of (168±20)ml/min/100g, for the thalamus area (216±24)ml/min/100g and cortex area (119±20)ml/min/100g.

Discussion and Conclusions:

The mismatch between PET and MR perfusion might be partially explained by the complexity of the applied methodologies. However, it is also important to take the BBB permeability in the mouse brain into account, which seems to be limited at high flow rates for radioactive water. This is in agreement with studies performed in baboons by Raichle et al. [2]. In addition, recent literature suggests that the effect of BBB permeability limitations seems to have only a small effect on ASL measurements, within a certain modeling regime [3]. The exact quantification of perfusion in vivo is of utmost importance for many imaging studies in the fields of neurology, oncology or cardiology. Thus, an accurate cross validation between measurements of different modalities is mandatory. To support our data we are currently performing further in vivo and in vitro studies. This study shows one possible application of combined PET/MR for simultaneous functional imaging to validate methods between modalities, and opens the scene for a wider range of multifunctional-imaging studies.

References:

[1] Judenhofer MS, Wehrl HF, Newport DF, et al. Simultaneous PET-MRI: a new approach for functional and morphological imaging. Nat Med 14(4):459-465 (2008)

[2] Raichle ME, Martin WR, Herscovitch P, et al. Brain blood flow measured with intravenous H2(15)O. II. Implementation and validation, JNM 24(9):790-798 (1983)

[3] Carr JP, Buckley DL, Tessier J, Parker GJM What Levels of Precision Are Achievable for Quantification of Perfusion and Capillary Permeability Surface Area Product Using ASL? MRM 58:281–289 (2007)