Comparison of 3D pseudo-CASL and $H_2^{15}O$ PET for quantification of cerebral blood flow

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Introduction MRI using arterial spin labeling (ASL) allows for measurements of cerebral blood flow (CBF) without contrast injection, promising an accessible tool for non-invasive CBF quantification in research and clinical settings. At present, $H_2^{15}O$ positron emission tomography (PET) is considered to be the gold standard for quantification of CBF and, consequently, various implementations of ASL have been compared with $H_2^{15}O$ PET [1,2,3,4]. While Xu et al [4] have compared a similar implementation of pseudo-continuous ASL (PCASL) as the one used in the present study, they did not quantify PET data. The purpose of the present study was to compare absolute CBF estimates obtained using $H_2^{15}O$ PET and PCASL MRI in patients with well-controlled type 1 diabetes (T1DM) and healthy subjects.

Methods Twenty male T1DM patients and 11 age-matched healthy male subjects (mean age 36 years) underwent both MRI and $H_2^{15}O$ PET scanning in the morning after an overnight fast. The time between MRI and PET varied from 1 day to 1 month. The study had been approved by the Medical Ethics Review Committee of the VU University Medical Center and subjects gave written informed consent prior to inclusion.

MRI: PCASL with background suppression (BS) using a 3D fast spin-echo spiral (FSE) readout without vascular crushers [4] was used on a 3T MRI scanner (Signa HDxt, GE Medical Systems, Milwaukee, WI, USA). The following settings were used: label time 1.5 s, delay 1.5 s, TR 4.3 s, TE 9ms, readout 8 arms x 512 samples, RBW 62.5kHz, effective resolution 3.2x3.2 mm; 36 axial slices of 5.0 mm thickness, NEX 2, scan time ~4 min. A PD weighted image was obtained by saturation recovery (SR). In addition, a 3D T1-weighted scan was obtained (IR-FSPGR, TI 450 ms, TR 7.8ms, TE 3ms, voxel size 0.97x0.97x1 mm). All scans were 3D corrected for gradient distortions. CBF maps were estimated using a single tissue compartment model [5]: CBF = λ * (1-exp(-Tsat/T1GM)) * exp(w/T1B) / (2*T1B*(1-exp(-τ/T1B))*ε) * (ΔS/S0), parameters post-label delay w = 1.5 s; labeling time τ = 1.5 s; partition coefficient λ = 0.9; labeling efficiency ε = 0.8 * 0.75 (label PCASL * BS); T1B = 1.4 s; SR time for PD image Tsat = 2.0 s; correction for SR in PD image T1GM = 1.2 s; ASL difference image ΔS; PD reference image S0.

PET: A bolus of 800 MBq $H_2^{15}O$ was administered 10 s after starting a 10 min 3D dynamic emission scan (HRRT, Siemens/CTI, Knoxvillle, TN, USA). In addition, a transmission scan was acquired for attenuation and scatter correction. During scanning, the arterial input function (AIF) was measured continuously using an on-line sampling device. Manual samples were taken for calibration of the AIF. List mode emission data were rebinned into multi-frame sinograms (frames: 6x10, 2x30, 4x60 and 2x120 s) After normalization and correction for randoms, dead time, decay, scatter and attenuation sinograms were reconstructed using 3D ordinary Poisson OSEM. After smoothing with a 6 mm full-width-at-half-maximum (FWHM) Gaussian filter, parametric CBF images were generated from the dynamic image sequence using a basis function method implementation of the standard single tissue compartment model with arterial blood volume component [6].

ASL and PET CBF images were registered to the T1-weighted MRI scan using FSL 4.1 (fsl.fmrib.ox.ac.uk). Whole brain CBF was derived using a FSL-BET brain mask. FSL-SIENAX provided partial volume (PV) estimates from the T1-weighted MRI scan, and these were used for PV correction (PVC) [7] with a 3D gauss kernel (9.5 mm FWHM). In addition, ASL and PET mean CBF (without PVC) values were obtained for regions of interest (ROI) defined in PVElab (nru.dk/pveout). For this comparison, ASL data were smoothed (6 mm FWHM Gaussian filter) to match the spatial resolution of the PET derived parametric CBF images.

Results Figure 1 shows a typical example of PET and MRI derived CBF images. While MRI shows higher spatial resolution than PET in transverse slices, substantial blurring is visible in sagittal images due to the 3D FSE acquisition. Average CBF values for both PET and MRI are presented in Table 1. The difference between whole brain PET and MRI CBF was 4.3 ml/100g/min (p<0.01), i.e. 7% of the average PET and MRI. Differences were 7% (p<0.01) in GM and 3% (not significant) in WM. Neither mean CBF, nor its variance, nor differences between PET and MRI were different for patients and controls, therefore results were pooled. Figure 2 shows a scatter plot of whole brain CBF, and GM and WM CBF after PVC. In the ROI analysis, significant differences between PET and MRI existed for 17 out of 33 ROIs after correction for multiple comparisons. Marked differences were observed in anterior and posterior cingulate, putamen, superior temporal lobe, and hippocampus.

Discussion Although ASL whole brain mean CBF values were 7% higher than corresponding PET values, differences were considered acceptable given the number of assumptions made in quantifying ASL CBF. As no test-retest study was performed, it was not possible to compare intra-subject variability. Nevertheless, the SD of the difference between PET and MRI (4.3 ml/100g/min) was comparable with reported values for between-session SD of ASL [8]. In addition, between-subject COV was similar for PET and MRI, suggesting that, for cross-sectional studies, the present PCASL implementation may be a suitable replacement for PET. Further test-retest studies are needed to assess whether PCASL can replace PET for longitudinal and interventional studies.

References [1] Bokkers, JCBFM 2010; 30: 222-229. [2] Qiu, 2008; Proc ISMRM 190. [3] Ye, MRM 2000; 44:450–456. [4] Xu, NMR Biomed. 2010; 23: 286–293. [5] Buxton, MRM 1998; 40:383-396. [6] Boellaard, Mol Imag Biol 2005; 7:273-285. [7] Asllani, MRM 2008; 60:1362-1371. [8] Petersen, NeuroImage 2010; 49:104-113.

Table 1: Mean ± SD (COV) CBF values.

	whole brain CBF [ml/100g/min]
PET $H_2^{15}O$	29.8 ± 4.5 (15%)
MRI ASL	34.1 ± 5.1 (15%)
Difference	*4.3 ± 5.0 (17%) **

* p<0.01
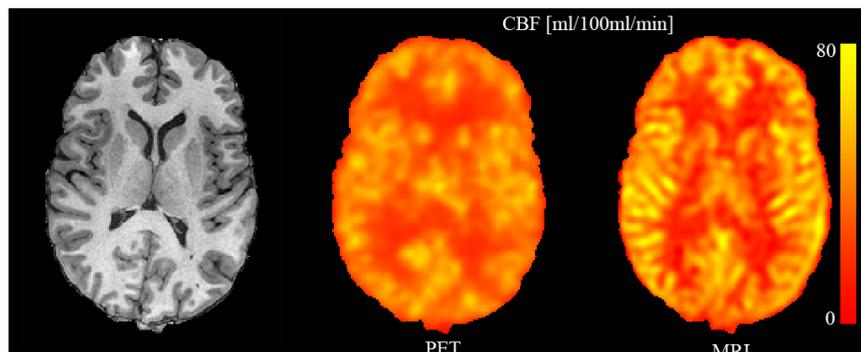
Figure 1: T1-weighted anatomical image with corresponding PET and MRI parametric CBF images.
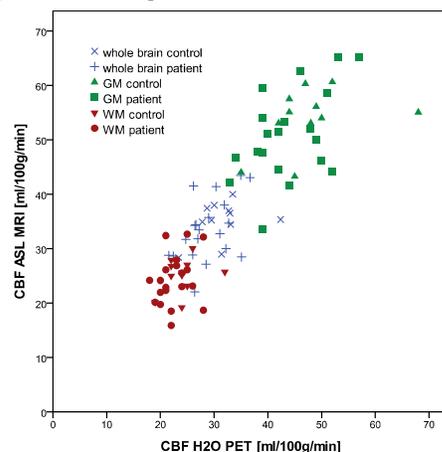
Figure 2: Scatter plot of CBF at subject level for mean whole brain, and mean partial volume corrected GM and WM. Note, that whole brain values include GM and WM voxels and may therefore not be regarded as independent samples.