

Accuracy and precision of pseudo-continuous arterial spin labeling perfusion during baseline and hypercapnia: a head-to-head comparison with ¹⁵O H₂O positron emission tomography

Dennis F R Heijtel¹, Henri J M M Mutsaerts¹, Esther Bakker², Patrick Schober³, Markus F Stevens⁴, Esben T Petersen⁵, Bart N M van Berckel², Charles B L M Majoie¹, Jan Booijs⁶, Matthias J P van Osch⁷, Ed T van Bavel⁸, Ronald Boellaard², Adriaan A Lammertsma², and Aart J Nederveen¹

¹Radiology, Academic Medical Center, Amsterdam, Netherlands, ²Radiology and Nuclear Medicine, VU University Medical Center, Amsterdam, Netherlands, ³Anesthesiology, VU University Medical Center, Amsterdam, Netherlands, ⁴Anesthesiology, Academic Medical Center, Amsterdam, Netherlands, ⁵Radiology, University Medical Center Utrecht, Utrecht, Netherlands, ⁶Nuclear Medicine, Academic Medical Center, Amsterdam, Netherlands, ⁷C.J. Gorter Center for High Field MRI, Radiology, Leiden University Medical Center, Leiden, Netherlands, ⁸Biomedical Engineering and Physics, Academic Medical Center, Amsterdam, Netherlands

Introduction: Measurements of cerebral blood flow (CBF) and cerebrovascular reactivity (CVR) provide useful information about cerebrovascular condition and regional metabolism. Pseudo-continuous arterial spin labeling (pCASL) is a non-invasive MRI technique to quantitatively measure the CBF, whereas additional hypercapnic pCASL measurements are showing great promise to quantitatively assess the CVR. ¹⁵O H₂O positron emission tomography (PET) is currently regarded as the most accurate and precise method to measure CBF, though it is a highly invasive method as well. The main aim of the present study was to assess the accuracy of quantitative pCASL CBF and CVR measurements by performing a head-to-head comparison with ¹⁵O H₂O PET, based on quantitative CBF values under baseline (B) and hypercapnic (H) conditions. A second aim was to compare the precision of both ¹⁵O H₂O PET and pCASL by means of the intra- and inter-session reproducibility.

Materials & Methods: Sixteen healthy volunteers (9 male, 7 female, age range 20-24 years) were included in this study. MRI examinations were performed on a Philips 3T Intera system, equipped with an 8-channel receive head-coil. PET examinations were performed on a Philips Gemini TF-64 PET/CT system. For each modality, the volunteer underwent five (3 baseline and 2 hypercapnic) CBF measurements distributed over two sessions as depicted in figure 1. During baseline, normal air was administered through a mask set-up, while for the hypercapnic measurements the air delivery switched to a 5% CO₂ and 95% air gas mixture. A nasal capnograph placed within the mask measured the end-tidal CO₂ (etCO₂) for the CVR calculation. pCASL imaging parameters were: resolution: 3x3x7 mm², 17 slices, labeling duration: 1650 ms, delay: 1525 ms, GE-SSh-EPI read-out, BSup: 1680/2830 ms, NSA: 54, TR/TE: 3850/14 ms, T_{acq}: 7 min. PET imaging consisted of an injection of 800 MBq bolus of ¹⁵O labeled water, followed by acquisition of 25 frames with gradually increasing duration for 10 minutes. After data acquisition, all CBF images were post-processed with SPM8. The accuracy was assessed by means of the equality in CVR and inter-modal agreement. Reproducibility was assessed by means of the reproducibility index (RI), which is defined as 1.96 times the standard deviation of the difference between successive scans, divided by the mean.

Results: Figure 2 shows an example of all 10 acquired CBF scans in a single volunteer. Table 1 shows the average grey matter (GM) CBF values, CVR, and reproducibility for each modality. Since 5 volunteers did not complete the full ¹⁵O H₂O PET acquisition scheme, the number of included volunteers is noted for each parameter. Solely for the combined conditions, a significant CBF difference of 3.6 ml/min/100g was observed between modalities, with no

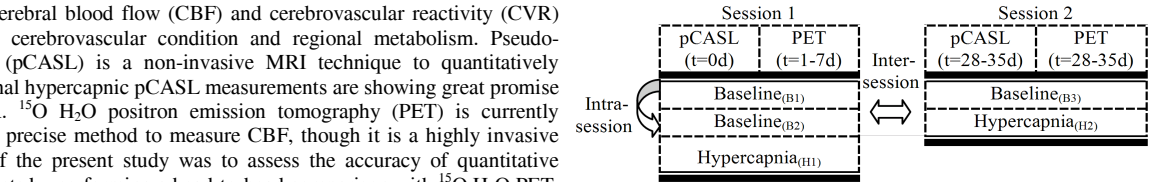


Figure 1: Schematic diagram of the study design and

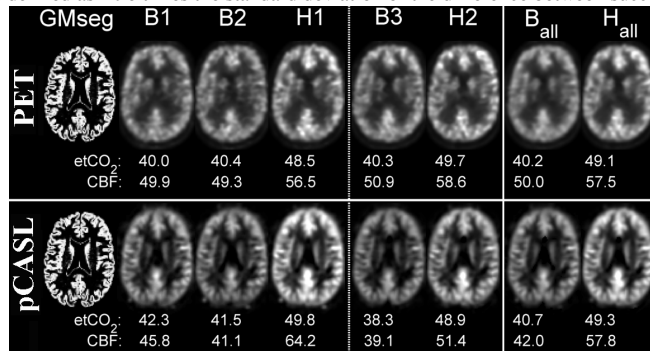


Figure 2: Single slice example of the CBF images in a single subject

		N	PET	pCASL
CBF* (ml/min/100g)	B _{all}	13	48.5±5.6	50.8±6.5
	H _{all}	12	59.3±5.3	64.4±10.0
CVR (%CBF/mm Hg)		11	2.5±0.9	2.8±1.2
RI intra session (%)	B ₁₋₂	15	23.5	18.2
RI inter session (%)	B ₁₋₃	14	27.6	25.1
RI inter-modality	H ₁₋₂	12	43.0	24.8
RI inter-modality 1 week (%)	B _{all}	13	---	22.9%
	H _{all}	12	---	30.3%

Table 1: Measured GM CBF (mean ± standard deviation), CVR and reproducibility's for ¹⁵O H₂O PET and pCASL. * p=0.03 (paired t-test of the combined conditions).

significant difference in reproducibility between PET and pCASL. Figure 3.A illustrates the overall quantitative CBF agreement between both modalities in a scatter plot with accompanying regression and correlations, the corresponding inter-modality Bland-Altman and voxel-wise scatter plot of the GM CBF with corresponding correlations. Additional to the voxel-wise GM correlations, whole brain voxel-wise correlations were: $r^2_B=0.63$, $r^2_H=0.61$ and $r^2_{All}=0.64$. The intra-session and inter-session reproducibility's for both modalities are illustrated in figure 3.B.

Discussion and Conclusion: Quantitative analysis of the CBF and CVR showed a one-to-one agreement between ¹⁵O H₂O PET and pCASL, though a small overestimation of pCASL CBF was observed. The correlation between modalities in the total GM increased due to the hypercapnia from 0.30 to 0.47, which is in line with previous research (no correlation to $r^2=0.30-0.55$)^{1,2,3}. Voxel-wise correlations were also in line with previous research⁴ ($r^2=0.39$ for only the GM of the baseline, group averaged data and $r^2=0.64$ when also the WM was included). The RI of both modalities was not significantly different, illustrating that the reproducibility of pCASL is similar to ¹⁵O H₂O PET. To conclude, this research shows that pCASL is accurate with a precision comparable to ¹⁵O H₂O PET in GM regions.

References: [1] Bokkers et al., JCBFM 2010;30:222-229; [2] Xu et al., NMR Biomed 2010;23:286-293; [3] Henriksen et al., JMIR 2012; 35:1290-9; [4] Ye et al., MRM 2000;44:450-456

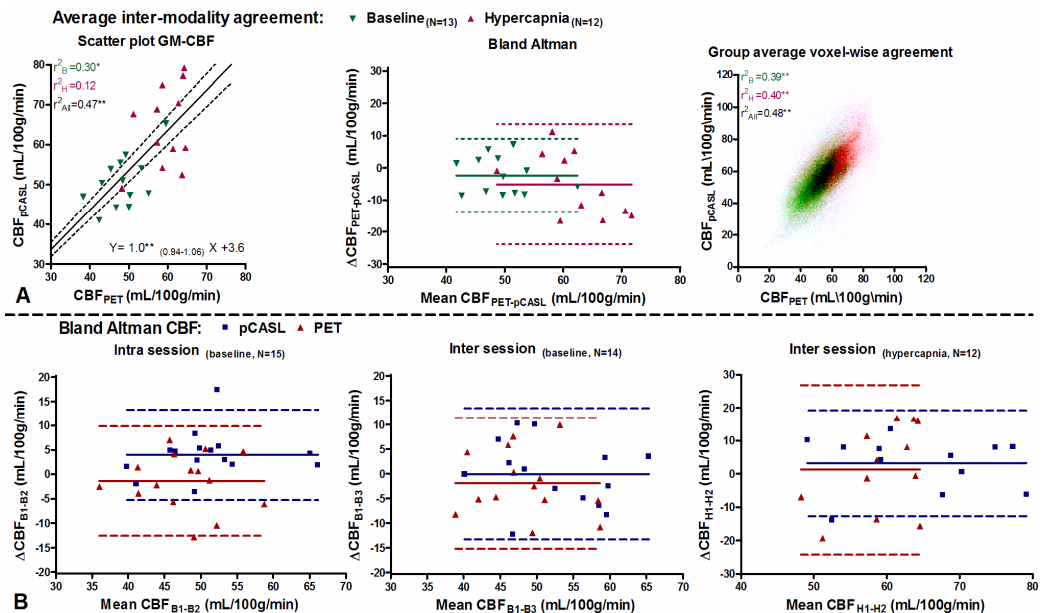


Figure 3.A) The averaged inter-modality agreement between PET and pCASL, for baseline (green, N_{vol}: 13, N_{scan}: 3) and hypercapnia (red, N_{vol}: 12, N_{scan}: 2). 3.B) Bland-Altman plots of the intra- and inter session reproducibility of PET (red) and pCASL (blue) GM-CBF. * p<0.05, ** p<0.001 (paired t-test).