Intra-scan reproducibility of white matter perfusion in dementia using pseudo-continuous arterial spin labeling

Henri JMM Mutsaerts[1], Dennis FR Heijtel[1], Charles BLM Majoie[1], Edo Richard[2], and Aart J Nederveen[1]

[1]Radiology, Academic Medical Center, Amsterdam, North-Holland, Netherlands, [2]Neurology, Academic Medical Center, Amsterdam, North-Holland, Netherlands

Introduction Because of its proven robustness, investigators currently add arterial spin labeling (ASL) to clinical imaging studies to assess its value in specific patient groups.[1] Due to its low signal-to-noise ratio (SNR), ASL generally requires long scanning times to capture reliable perfusion signal in white matter (WM) voxels.[2] Due to the limited scanning time available in clinical practice, investigators primarily focus on gray matter (GM) perfusion. However, although its perfusion values are relatively small, the total WM volume is relatively large compared to GM. We hypothesize that the total WM perfusion can be reliably measured in acquisition times as short as two minutes. This would be the case if the total WM perfusion does not vary substantially in consecutive time windows of two minutes. Total WM perfusion could be a clinically relevant marker as WM degradation is involved in, and may even be the onset of, many neurological disorders.[3] The current study assesses the intra-scan repeatability of ASL WM in a group of 34 patients with neurodegeneration.

Methods 34 patients (15 men/19 women, 54.5 to 88 years) were drawn from the neurodegenerative disease cohort of the Dutch Parelsnoer Study. This heterogeneous cohort varies from mild cognitive impairment (MCI) to advanced types of dementia. Magnetic resonance imaging (MRI) measurements were conducted on a 3 Tesla Philips Intera scanner, using a SENSE-8-channel head coil. The parameters of the pseudo-continuous ASL (p-CASL) sequence with background suppression were respectively TR/TE: 4000/14 ms; flip angle: 90 degrees; FOV: 240x240 mm^2; matrix size: 80x80; 17 slices; thickness: 7mm; no gap; gradient-echo single-shot EPI; SENSE 2.5; post-labeling delay: 1.525 to 2.1 seconds; 30 dynamics; total scan duration 4 min. Background suppression was achieved by applying a saturation pulse preceding labeling and two inversion pulses respectively 1680 and 2830 ms after the saturation pulse. Matlab (MathWorks, Natick, USA) and SPM (Wellcome Trust Centre for Neuroimaging) software were used for post-processing. A high-resolution 3D T1 sequence was used to obtain GM and WM-masks. The 30 ASL dynamics were divided into 2x15 and pairwise subtracted and averaged to obtain images: ΔM_1 and ΔM_2. The GM-mask was registered and the WM-mask co-registered to the average of these two ΔM –images, with partial volume fraction thresholds set to 0.5 and 0.95 for GM and WM respectively (*figure 1*). As the current study focuses on the intra-scan repeatability no quantification model was used and the average GM and WM ΔM-values were scaled to previously reported values.[4] Negative values were excluded. As measure for the reproducibility the repeatability index (RI) is used. The RI is defined as the 95% confidence interval for repeated measurements and given by $RI = 100\% \frac{1.96 \times SD\Delta_{M1,2}}{mean\ CBF}$, with $SD\Delta_M$ being the standard deviation of the difference between the ΔM –images (*figure 2*).
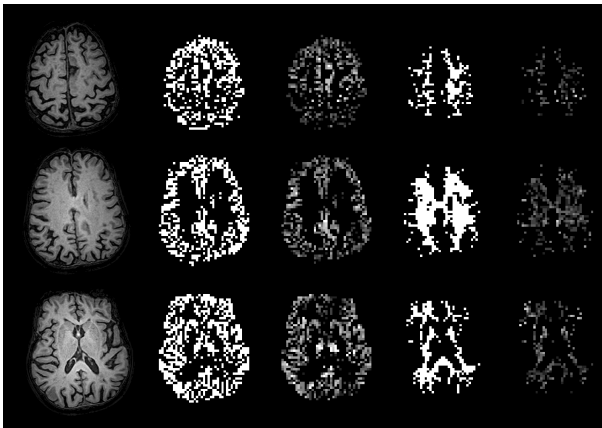

Figure 1 shows 3 slices of a single subject. Columns present respectively 3DT1 anatomical scan (1), GM mask (2), GM perfusion ΔM_1(3), WM mask (4), GM perfusion ΔM_1(5).
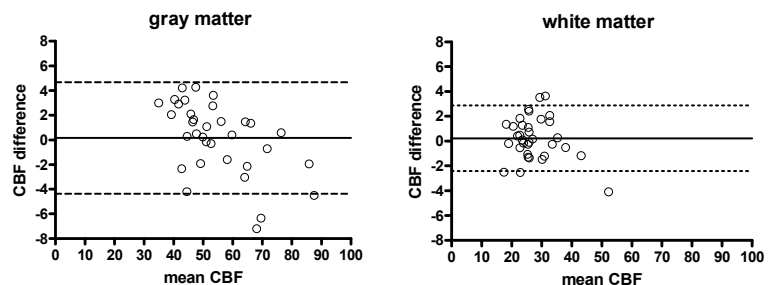

Figure 2 Bland-Altman plots showing the difference between the repeated cerebral blood flow (CBF) measurements and mean CBF (mL/100g/min). Solid lines indicate the mean of the paired differences. Dotted lines indicate the 95% confidence interval for the difference between repeated measurements.

Results and discussion The RI of GM and WM were 8.3% and 9.6% respectively. The RI reported here for GM is small compared to p-CASL numbers available in the literature for between weeks repeatability (20-25%).[5] This could be due to less physiological variation of perfusion, which may occur on larger timescales. Furthermore, previously reported values are often whole brain values, which may include voxels with lower perfusion values and thus lower repeatability. The present data suggest that total WM perfusion can be obtained from relatively short scantimes using p-CASL with background suppression in dementia. Rather than disregarding WM perfusion data because of too low SNR for voxel-wise analyses, this data encourages to analyze the whole WM perfusion as potential extra marker.

References [1]Deibler, AJNR 2008; [2]Van Osch, MRM 2009; [3]Medina, Neurobiology of Aging 2006; [4]Parker, MRM 2002; [5]Gevers, JCBFM 2011