**Increased Blood-Brain Barrier Leakage in Alzheimer’s Disease Detected with Dual Time-Resolution Dynamic Contrast Enhanced MRI**

Harm J van de Haar, Saartje Burgmans, Matthijs IP van Osch, Jacobus FA Jansen, Frank CG van Bussel, Sau May Wong, Martijn Wolters, Cécile RLPN Jeukens, Mark A van Buchem, Paul AM Hofman, Frans RJ Verhey, and Walter H Backes

University of Maastricht, Maastricht, Netherlands; Leiden University Medical Center, Leiden, Netherlands; Maastricht University Medical Center, Maastricht, Netherlands

**Target audience.** Neuroscientists, neuroradiologists, physicists

**Purpose.** Blood-brain barrier (BBB) disruption is a potential underlying mechanism for dementia. Dynamic Contrast Enhanced (DCE)-MRI in combination with pharmacokinetic modeling can be used to detect BBB defects by measuring the leakage rate of contrast media. To investigate the distribution of contrast medium in the brain, a dual-temporal resolution DCE-MRI protocol was applied. Our aim was to detect differences in terms of and leakage (K) and fractional plasma volume (v) in brains of patients suffering from dementia due to Alzheimer’s Disease (AD) compared to healthy controls.

**Methods.** Acquisition: The dual-temporal resolution protocol consisted of two integrated DCE-MRI sequences (3T Achieva TX, Philips). A saturation recovery gradient recalled sequence (TR/TE 5.2/2.5 ms, 25.6×20×5 cm³ FOV, 128×100×10 voxels, Dynamic Scan Time (DST) 3.2 s) with a 90° nonselective saturation prepulse given at a delay time (TD, 120 ms) was used during bolus injection for 1.5 minutes. This resulted in 29 volumes including 4 precontrast scans. Immediately afterwards a different saturation recovery gradient recalled sequence (TR/TE 5.6/2.5 ms, 25.6×25.6×10 cm³ FOV, 256×256×50 voxels, DST 30.5 s) with the same saturation prepulse was used for 25 minutes, resulting in 45 volumes with 3 precontrast scans. The two scans spatially overlapped at the periventricular region. The contrast agent, gadobutrol, was injected intravenously (dose 0.1 mmol/kg, injection rate 3 ml/s) using a power injector. T2-weighted FLAIR scans were used to detect abnormal appearing white matter (AAWM). T1 weighted structural scans served for segmentation the brain into white matter, Gray Matter (GM) and CSF. For the translation of contrast-enhanced signal changes to concentration curves, a scan series with different TD settings (120–4000 ms) was used to determine pre-contrast T1 maps.

Subjects: 13 patients with mild cognitive impairment (n = 9) and AD (n = 4) were included; mean age 74.9±8.3 Y (mean±sd), Mini Mental Status Examination (MMSE) score 26.7±1.6, Fazekas 2.0±0.9, AAWM volume 14.3±15.1 cm³. 14 healthy controls were included; mean age 75.8±6.6 Y, MMSE 29.7±2.5, Fazekas 1.2±0.9, AAWM volume 4.3±6.0 cm³.

**Analysis:** White matter was segmented into AAWM and NAWM using the FLAIR scans. A vascular input function (VIF) was obtained from the sagittal sinus. The Patlak plot analysis was used to calculate K and v in each voxel. Histogram analysis of K and v at bin level was applied to compare patients with controls. Significance was inferred from Student’s t-tests when p<0.05.

**Results.** Example time curves are given in fig. 1. In the K range 0.8 - 1.3 x 10⁻³ min⁻¹ patients exhibited significantly stronger leakage than controls in NAWM (fig. 2) but not in GM. Similar analysis showed no difference in v distribution throughout the NAWM or GM. The mean K or v did not differ between the groups in NAWM or GM and was not correlated with AAWM volume. This was also evident in the K maps, which revealed rather spatially diffuse patterns of higher leakage which did not systematically colocalize with AAWM.

**Conclusion/Discussion.** The results suggest significantly stronger leakage in NAWM in the patients compared to the healthy controls, which confirms our hypothesis that BBB leakage is increased in patients with (preclinical) Alzheimer’s dementia. Longitudinal research is necessary to reveal the exact relationship with Alzheimer pathology and small vessel disease.

**References.**