

# Dynamic Susceptibility Contrast Perfusion Weighted Imaging in Multiple Sclerosis: A Follow-up Study

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**Introduction:** Multiple sclerosis (MS) is an autoimmune neurodegenerative disorder characterized by vascular inflammation, demyelination, gliosis, and axonal loss.<sup>1,2</sup> Increasing body of evidence<sup>3</sup> has suggested abnormal alteration in hemodynamics secondary to vascular inflammation and occlusion in MS that may be a primary event in the evolution of the disease. Several perfusion weighted imaging (PWI) studies<sup>4-6</sup> have demonstrated reduced cerebral blood flow (CBF) and cerebral blood volume (CBV) from normal appearing white matter (NAWM), cortical and subcortical gray matter regions in MS patients compared to those of controls. Wuerfel *et al*<sup>7</sup> observed significant elevation in CBF and CBV from NAWM, several weeks before focal leakage of the blood-brain barrier and MS plaque formation. In another study, Ge *et al*<sup>8</sup> also reported increased perfusion from enhancing lesions suggesting inflammation-mediated vasodilatation. In a solitary longitudinal PWI study, However, to our knowledge, a longitudinal study evaluating the changes in perfusion parameters from deep gray matter regions has not been reported in MS patients. In the present study, we sought to determine the pattern of longitudinal changes in hemodynamic parameters from thalami and basal ganglia in MS patients.

**Materials and Methods:** A total of 15 patients with clinical definite relapsing-remitting MS (with sporadic episodes of attacks) were recruited and followed-up in this study. All patients were treated with immunomodulatory drugs. Following pre-contrast conventional T2- and T1-weighted imaging, dynamic susceptibility contrasts (DSC)-PWI was performed on a 3 Tesla MR system. All patients underwent two MRI scans at an interval of approximately 2 years. DSC-PWI T2\* weighted gradient-echo echo planar images were obtained during the first pass of the standard dose (0.1 mmol/kg) of bolus injection using the following parameters: TR/TE = 956/32ms, FOV = 22 × 22 cm<sup>2</sup>, matrix size=128 × 128, in-plane resolution = 1.72 × 1.72 mm<sup>2</sup> with 3mm thickness, and 13 slices covering the thalami, basal ganglia and periventricular white matter regions. Sixty sequential measurements were acquired for each section with a temporal resolution of 1.06 s. To compute the arterial input function (AIF), ROI was defined in a feeding artery from middle cerebral artery branches. Leakage corrected CBV, CBF and mean transit time (MTT) maps were generated using Nordic ICE software (Nordic Imaging Lab). Since the proportionality constant between tissue tracer concentration and  $\Delta R2^*$  were not known, relative quantitation was performed in the current study. At both time points, ROIs were drawn on thalami and basal ganglia through 3-contiguous slices bilaterally, and the averaged CBV, CBF and MTT values were computed and normalized with respect to corresponding values from the NAWM encompassing frontal periventricular regions to obtain relative values. While drawing the ROIs, care was taken to avoid the cerebral blood vessels and T2 lesions. One tailed paired t-tests were performed to evaluate the changes in the hemodynamic parameters between the baseline and follow-up periods.

**Results:** Representative CBV, CBF and MTT maps from the baseline study are shown in Fig.1. The percentage changes in rCBV, rCBF and rMTT values between the baseline and follow-up period from basal ganglia and thalamus are shown as bar diagrams in figure 2. Compared to baseline values, a significant elevation in rCBV at follow-up ( $2.09 \pm 0.47$  vs.  $2.21 \pm 0.48$ ;  $p=0.026$ ) was observed from thalami. Additionally, significant increases in rCBF were observed both from thalami ( $2.77 \pm 0.66$  vs.  $3.02 \pm 0.59$ ;  $p=0.016$ ) and basal ganglia ( $2.95 \pm 0.67$  vs.  $3.23 \pm 0.76$ ;  $p=0.031$ ) between the two time points. Moreover, significant reduction in rMTT ( $0.71 \pm 0.08$  vs.  $0.65 \pm 0.06$ ) was observed from basal ganglia.

**Discussion:** Our findings demonstrate significant alterations in perfusion parameters from thalami and basal ganglia at a follow-up period compared to baseline, which may indicate underlying fluctuating inflammatory activity in patients with MS. As relative measures of blood flow and volume were used to ascertain the changes in perfusion parameters in this longitudinal study, our findings should be treated with caution. One may speculate that high rCBF and rCBV from thalami and high rCBF from basal ganglia may reflect either high perfusion in thalami/basal ganglia or reduced haemodynamics from NAWM<sup>4,5</sup> or combination of both. It is well known that early inflammatory activities may trigger vasodilatory mechanism and increased perfusion.<sup>9</sup> However, the subsequent apoptosis and damage to endothelial cells may activate a clotting cascade leading to vascular occlusion and consequently reduced CBF and CBV in MS patients.<sup>10</sup> We believe that future follow-up studies with absolute measures of perfusion parameters are warranted to understand the true changes in these parameters from deep gray matter regions. **Acknowledgement:** This work was supported by NIH grant numbers: R01 NS029029, NS-029029-20S1 and NS076588.

**References:** 1. Compston A, et al. Lancet. 2002;359: 1221-31. 2. McDonald WI, et al. Ann Neurol. 2001;50: 121-7. 3. Adams CW, et al. J Neurol Sci. 1989;92:291-306. 4. Adhya S, et al. Neuroimage. 2006;33:1029-35. 5. Rashid W, et al. J Neurol Neurosurg Psychiatry. 2004;75:1288-93. 6. Ingrid M, et al. Invest Radiol. 2012 ;47:252-8. 7. Ge Y et al. Am J Neuroradiol. 2005; 26:1539-47. 8. Wuerfel J, et al. J Clin Pathol. 2004;57:129-33. 9. Wakefield AJ, et al. J Clin Pathol. 1990;43:786-90. 10. Putnam TJ. N Engl J Med 1933;209:786-90.

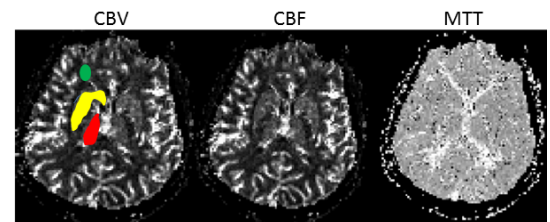


Fig 1. Representative baseline CBF, CBV and MTT maps from a MS patient. Regions of interest from right thalamus (red), basal ganglia (yellow) and NAWM (green) are shown.

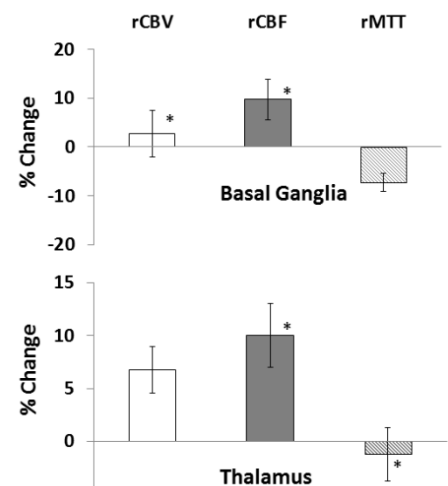


Fig 2. The percentage changes in perfusion parameters from baseline to follow-up period are shown as bar diagrams. \* represents significant change