

Brain Dynamic Susceptibility Contrast Perfusion Imaging Histograms in Primary Progressive Multiple Sclerosis

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Introduction: Multiple Sclerosis (MS) is a multi-focal, inflammatory, demyelinating disease. In approximately 10–15% of cases, MS follows a primary progressive (PP) course characterized by a progressive clinical decline without superimposed exacerbations. Compared to patients with the more common relapsing remitting course of the disease, PP-MS patients are older and have fewer lesions on MRI scans. In PP-MS, conventional MRI is less useful in monitoring disease activity and response to treatments due to the lower lesion formation rate and level of gadolinium enhancement (1). Prior studies have found decreased perfusion in normal-appearing white matter (NAWM) using analysis of selected regions of interest (2). The current study uses an automated segmentation routine to allow analysis of normal-appearing gray matter (NAGM) and NAWM.

Material and methods: Eight patients (4 female) with PP-MS meeting the revised McDonald Criteria were prospectively enrolled in the study. The patients had a mean age of 57.25 years (range: 50-74), mean disease duration of 9.25 years (range: 4-21 years), and mean EDSS score of 4.5 (range: 3-7). For MRI comparison, eight age- and gender-matched healthy controls (4 female) were recruited. Their mean age was 57.6 years (range: 47-73). Approval for this study was obtained from the Institutional Board of Research Associates of New York University Medical Center and informed consent was obtained. MRI was performed using a 3.0-T scanner (Trio, Siemens Medical Systems, Erlangen, Germany) with an eight-channel phased-array head coil. The following sequences were collected in all subjects during a single MR session: (a) DE turbo SE (b) GRE EPI (TR=1,000 ms, TE=32 ms; 10 contiguous, 3-mm-thick axial slices with a 128x128 matrix; 220x220 mm FOV; flip angle, 30°; signal bandwidth, 1,396 Hz/pixel; in-plane voxel size, 1.7x1.7 mm). Dynamic susceptibility contrast enhanced MR images were acquired during the first pass of a standard-dose bolus (0.1 mmol/kg) of gadopentetate dimeglumine (Magnevist; Berlex Laboratories, Wayne, NJ, USA). Contrast was injected at a rate of 5 mL/sec, followed by a 20-mL bolus of saline also at a rate of 5 mL/sec. A total of 60 images were acquired at 1-sec intervals, with the injection occurring at the fifth image, so that the bolus would typically arrive at the 15th to 20th image. (c) Post-Gd T1-weighted SE.

Proton density images were automatically segmented into gray and white matter (GM and WM) using SPM5 (Wellcome Trust Centre for Neuroimaging, London, UK). Classification of lesions was performed in each patient by a single observer using proton density and T2-W images employing manual lesion identification and user-supervised local thresholding (Jim 3.0, Xinapse System, Leicester, UK). Lesions were then subtracted from the segmented GM, WM, and whole-brain (WB) images. GM, WM, and WB image masks were obtained using a threshold of 0.75. The original T2 images were co-registered to perfusion data and the resulting transformation matrix was applied to the GM, WM, and WB image masks to co-register them to the perfusion images. Absolute cerebral blood flow (CBF), blood volume (CBV), and mean transit time (MTT) were calculated using the method of Rempf et al (3). Vessels were derived from perfusion data and subtracted from the GM, WM, and WB masks, which were then applied to the CBF, CBV, and MTT color maps. Histogram analysis was performed on the CBF, CBV, and MTT color maps. The interval between the minimum and maximum voxel values was divided into 40 equally spaced bins. Normalization was used to allow comparison of histograms from subjects with different brain volumes. Histograms for each segment (GM and WM) were normalized by dividing the number of counts in each bin by the total number of voxels in that segment.

Results and Discussion: There was a trend toward decreased CBF in NAWM and NAGM of patients with PP-MS compared to controls (Fig. 1). However, no statistically significant difference was found in CBF, CBV, or MTT ($p>0.05$) between patients with PP-MS and controls, although this observation may be at least partly due to the small sample size in the current phase of the study. The mean CBF, CBV and MTT in lesions 40.35 ± 14.09 ml/100mg/min.; 2.51 ± 0.65 ml/100mg; 3.95 ± 0.90 sec. were significantly higher than in NAWM ($p<0.05$). No correlation was observed between any of the histogram-derived perfusion metrics and the EDSS score.

Conclusion: Although not statistically significant, global GM and WM perfusion histogram derived metrics show a trend toward decreased tissue perfusion. The study is ongoing and data from a larger sample size will be presented.

References:

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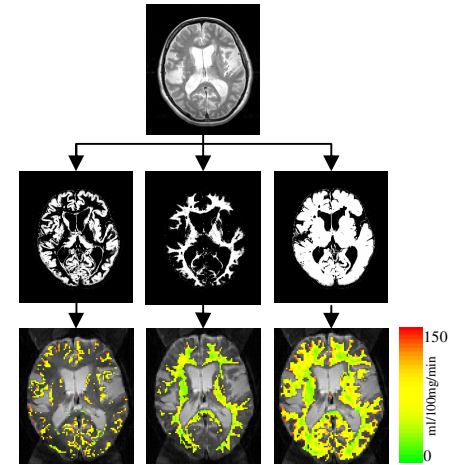


Figure 1. Selected images from a patient with PP-MS show a proton density image (top row) used to generate automated segmentation images (middle row), and vessel- and lesion-masked segmentation masks applied to cerebral blood flow (CBF) color maps from perfusion images (bottom row). Color scale shows CBF values from 0-150 ml/100mg/min.

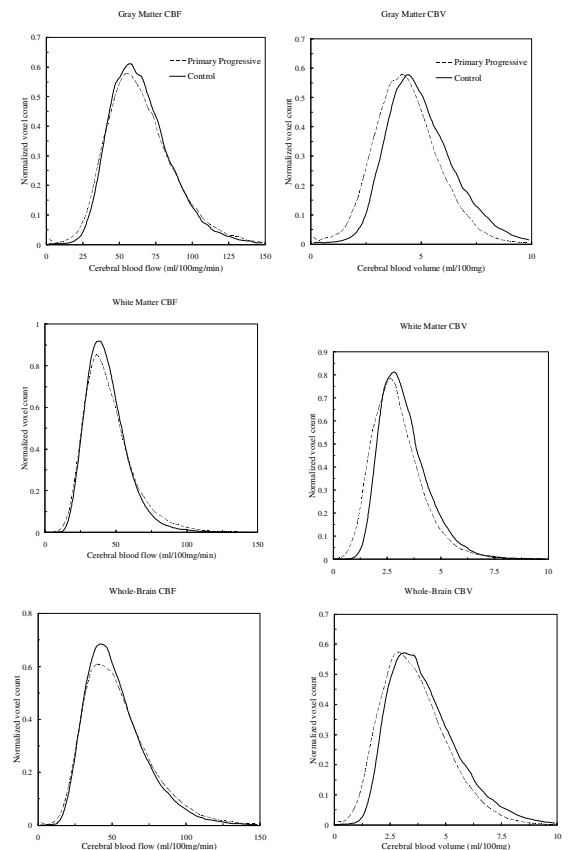


Figure 2. Histogram analysis of cerebral blood flow (CBF) and cerebral blood volume (CBV) in normal-appearing gray and white matter, as well as whole-brain.