Blood Water Volume Fraction of White Matter Hyperintensities

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Introduction: White matter (WM) hyperintensities are commonly observed in the elderly brain on T_2-weighted MRI and may contribute to the cognitive decline of Alzheimer's disease. Two types of hyperintensities are generally recognized: small, focal lesions in the deep WM (dWMHs) and lesions that lie along the ventricles (pWMHs). Although their etiology remains poorly understood, it is likely that ischemic-vascular injury plays an important role in pWMHs, while demyelinating, gliotic processes may contribute more to dWMH pathology.[1] Longitudinal water proton (^1H_2O) relaxation rate constants (R_1) are strongly associated with macromolecular volume fraction[2] and, combined with an intravascular contrast agent, can be a powerful probe of vascular integrity. The purpose of this study is to quantify the intravascular water volume fraction (p_b) in periventricular and deep WMHs in the elderly human brain using a low molecular weight gadolinium contrast reagent.

Methods: 15 elderly subjects (10 male, 5 female; 70 ± 6 yrs) with no history of vascular disease provided informed consent and were enrolled. MR data were obtained on a 7T Siemens MAGNETOM instrument. 3D inversion recovery (IR) T_1-weighted (MPRAGE; TR/TE/TI/FA 2300 ms/ 2.8 ms/ 1050 ms/ 6°; 0.8 mm^3) and T_2-weighted fluid-attenuated IR (FLAIR; TR/TE 8200 ms/ 386 ms/ 120°; 0.8 mm^3) images were acquired. Five full-volume ^1H_2O R_1 maps centered on the lateral ventricles were prepared using variable TI (300, 1800, 3200 ms; and no inversion pulse) MPRAGE acquisitions (TR/TE/FA 3500 ms/ 2.4 ms/ 6°; 1 mm^2; 2 mm slice thickness). IR datasets were collected prior to and ca. 12, 31, 45 and 57 min post contrast (gadoteridol) injection (0.11 mmol/kg; 2 mL/s). ^1H_2O R_1 maps were prepared after registration of all images[3] and voxelwise evaluation of the Bloch equations for each variable TI dataset accounting for all RF pulses and delays and assuming monoexponential IR recovery.[4]

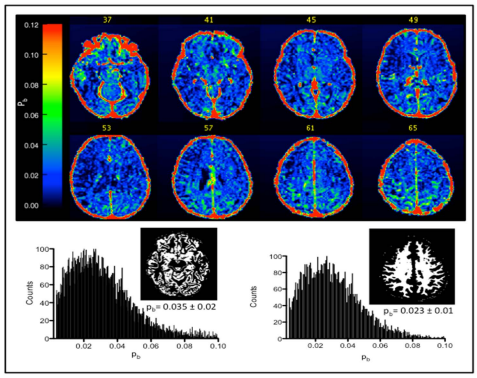

Figure 2. (Top) p_b map of a 66 year old female. (Bottom) Histograms of gray and white matter reveal the expected increase in gray matter p_b.

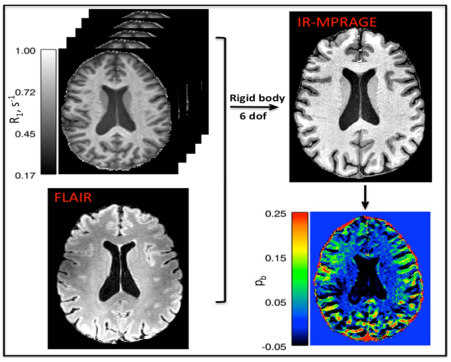

Figure 1. R_1 maps and FLAIR images are co-registered to the anatomic MPRAGE images.

^1H_2O R_1 maps and FLAIR images were co-registered to the anatomic MPRAGE images (Fig. 1).[3] Intravascular water volume maps were obtained by voxelwise fitting of tissue and blood ^1H_2O R_1 values to an equation for two-site (transendothelial) water exchange.[5] A fixed intravascular ^1H_2O lifetime (τ_b= 300 ms)[6] and $K^{trans} \approx 0$ were assumed. Blood ^1H_2O R_1 values were determined from an ROI placed entirely within the sagittal sinus.

WM hyperintensity p_b was determined by semi-automatic segmentation of FLAIR images (Seg3D)[7] and application of masks to p_b maps (thresholded to values > 0). The p_b of normal appearing white matter (NAWM) was obtained similarly, after 3-class segmentation[8] of anatomic MPRAGE images. Statistical analyses were performed in Stata (College Station, TX).

Results and Discussion: Figure 2 shows several slices from the p_b map of a healthy 66 year old female. Histograms of global white and gray matter are also shown. Mean p_b in NAWM was 2.1 ± 0.2%, in reasonable agreement with the 1.5 ± 0.3% measured recently using DSC-MRI[9]. Hyperintensities were present in periventricular and deep WM in 14/15 and 12/15 subjects, respectively (Fig. 3). The mean p_b in all WMHs was 1.9 ± 0.3% and was not significantly different from the p_b of NAWM (P= 0.13; repeated measures ANOVA). Comparison of WMH p_b values (Table 1) reveals significant increases in pWMHs compared to dWMHs (repeated measures ANOVA; P= 0.04). These results are consistent with increased disturbances in microvascular water permeability in periventricular compared to deep WMHs, and suggest that the etiology of lesions in periventricular and deep WM may be different. DCE-MRI studies with increased dynamic range of R_1 values and decreased pharmacokinetic sampling time will be necessary to validate the assumptions of the pharmacokinetic model and substantiate these results.

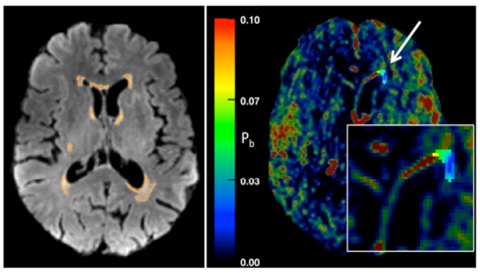

Figure 3. (Left) FLAIR image from a 74 year old male shows good suppression of the cerebrospinal fluid. Both periventricular and more focal, deep lesions are identified (orange). In-plane area of WMHs ranged from 17-147 mm^2. (Right) p_b map with magnification of the periventricular WMH indicated by arrow (inset).

Table 1. WMH blood water volume fraction

White Matter Hyperintensity	P_b (%)	WMH - NAWM (%)
Deep	2.1 ± 0.5	+ 4
Periventricular	2.6 ± 0.6	+ 28

Grant Support: NIH (AG 033638, AG 08017, EB 007258, NS 040801). **References:** **1**. Fernando, et al., *Stroke* 37, 1391-98 (2006). **2.** Rooney, et al., *Magn Reson Med* 57, 308-18 (2007). **3.** Smith, et al., *Neuroimage* 17, 479-89 (2002). **4.** Deichmann and Haase, *J Magn Reson* 96, 608-12 (1992). **5.** Li, et al., *Magn Reson Med* 54, 1351-1359 (2005). **6**. Rooney, et al *PISMRM* 11, 2188 (2003). **7.** www.sci.utah.edu/cibc/software/42-seg3d.html. **8.** Zhang, et al., *IEEE Trans Med Imaging* 20, 45-57 (2001). **9.** Srour, et al., *J Cerebr Blood Flow* 31, 1272 (2011).