Measuring perfusion and permeability in multiple sclerosis: dynamic contrast-enhanced MRI in 3D at 3T

M. Ingrisch[1], D. Morhard[2], S. Sourbron[1], L-A. Gerdes[3], T. Kümpfel[3], R. Hohlfeld[3], M. F. Reiser[2], and C. Glaser[2]

[1]Josef Lissner Laboratory for Biomedical Imaging, Department of Clinical Radiology, University of Munich - Grosshadern Campus, Munich, Bavaria, Germany, [2]Department of Clinical Radiology, University of Munich - Grosshadern Campus, Munich, Bavaria, Germany, [3]Institute for Clinical Neuroimmunology, University of Munich - Grosshadern Campus, Munich, Bavaria, Germany

Purpose: Recently, it has been shown that T1-weighted dynamic contrast-enhanced MRI (DCE-MRI) allows for absolute quantification of perfusion and permeability in normal brain tissue and in brain tumors ([1], [2]). In this study we propose a rapid 3D approach for DCE-MRI in the brain and evaluate the potential of the method for the characterization of contrast-enhancing white matter (WM) lesions in multiple sclerosis (MS).

Materials and Methods: Ten untreated patients with clinically active MS were included in the study and underwent DCE-MRI at 3T (Magnetom Verio, Siemens, Erlangen, Germany) using a view-sharing 3D FLASH sequence (TE/TR=0.86/2.29ms, pA=.24, pB=.22, PAT 2, 24 reference lines). 200 volumes were acquired every 2.1s with a matrix size of 128*104*44 and a spatial resolution of 2*2*3mm³ after double bolus injection of 0.1mmol/kg Gadovist (Bayer Schering Pharma, Berlin, Germany). The arterial input function was measured in the middle cerebral artery and corrected for partial volume effects with a reference measurement in the sinus. Maps of CBF, CBV and permeability-surface product (PS) were calculated using a 2-compartment uptake model (2CUM) ([1], [3]); regions of interest (ROIs) were defined on the PS map (Fig 1) in lesions and in normal appearing WM. ROI curves were analyzed with the 2CUM and with the 2-compartment exchange model (2CXM) ([1], [4]), yielding an additional parameter EEV (extracellular, extravascular volume). The Akaike information criterion ([5], [6]) was used to choose the best of both models.
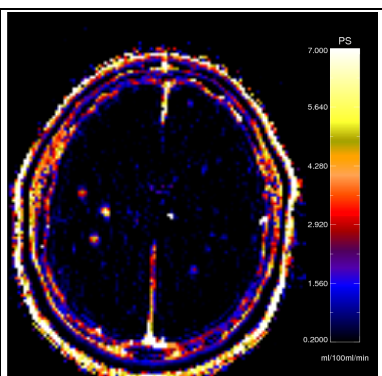

Figure 1: One slice of a PS-map, calculated with the uptake model. Note the three distinct lesions on the right side and one on the left side.

Results: All contrast-enhancing (CE) lesions that were visible on post-contrast T1-weighted images could be identified on the PS map (Fig.1). In four patients, no CE-lesions were detected. In total, 45 CE-lesions were detected and analyzed in six patients (Figures 2, 3). The 2CXM was the best model for all lesions. Median(SD) values of lesion parameters were: CBF: 32(44) ml/100ml/min, CBV: 1.6(0.6) ml/100ml, PS: 1.4(0.7) ml/100ml/min and EEV: 16(6.1) ml/100ml. WM parameters were CBF: 18(4.9) ml/100ml/min, CBV: 1.2(0.5) ml/100ml, MTT 3.8(1.1)s and PS: 0.07(0.04) ml/100ml/min. CBV and PS were significantly higher in lesions than in normal appearing WM ($p<0.01$ and $p<0.001$, respectively).

Conclusion: The rapid 3D sequence allows for characterization of multiple lesions scattered throughout the brain. CBF and CBV values in WM are in good agreement with literature values, which indicates that the technique used here has equal accuracy as the 2D method used in previous studies ([1], [2]). The lesions are clearly separated from WM by the increased PS value, and have more heterogeneous vascular parameters CBF and CBV, suggesting potential for lesion characterization. The sequence has more coverage and similar spatial resolution as T2*-weighted DSC-MRI sequences previously proposed in MS [7], but offers the advantage of absolute quantification and a quantitative measure of blood-brain barrier permeability. The separation of perfusion and permeability metrics is achieved by the used of improved modeling and high temporal resolution. This provides an important advantage compared to previous DCE-MRI methods [8], which only provide mixed parameters like K^{trans} with a sometimes ambiguous interpretation. Further studies will address possible correlations with clinical disease activity and effects of immunomodulatory therapies.

References: [1] Sourbron et al ISMRM:1883(2008) , [2] Larsson et al, *JMRI* 27:754 (2008, [3] Bazelaire et al, *Eur. Radiol.* 15:2497 (2005) [4] Brix et al, *MRM* 52:420(2004) [5] Glatting et al, *MedPhys* 34:4285 (2007) [6] Ingrisch et al, ESMRMB (2008) [7] Wuerfel et al, *Brain* 127:111 (2004) [8] Tofts et al, *JMRI* 10:223 (1999)
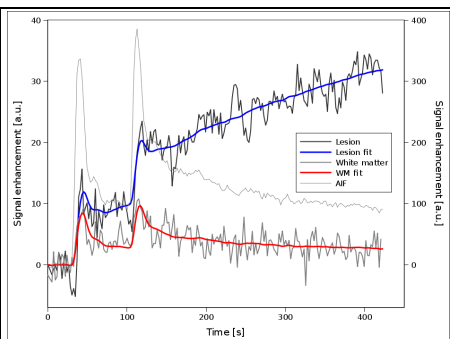
Figure 2: ROI analysis for the same patient as in Fig. 1. Shown are a WM- and a lesion curve, along with model fits, ant the AIF (note the different scaling)
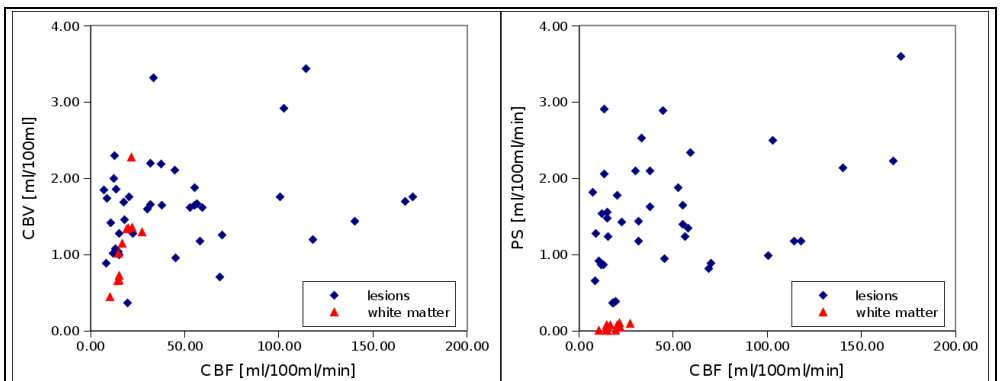

Figure 3: Summary of all calculations. On the left, CBV is plotted vs CBF, on the right, PS vs CBF. Red triangles: WM regions, blue squares: contrast-enhancing lesions