Quantitative assessment of perfusion and permeability in Multiple Sclerosis: Feasibility and initial results

M. Ingrisch[1], S. Sourbron[1], D. Morhard[2], 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, Institute of Clinical Radiology, Ludwig Maximilian University, Munich, Germany, [2]Institute of Clinical Radiology, Ludwig Maximilian University, Munich, Germany, [3]Institute for Clinical Neuroimmunology, Ludwig Maximilian University, Munich, Germany
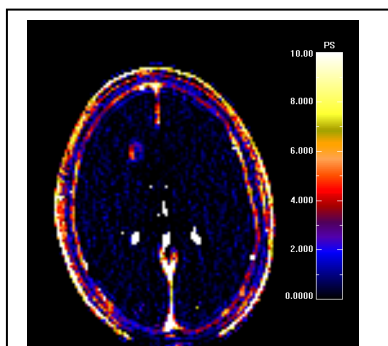
Figure 1: Permeability map in a patient with a ring-enhancing lesion

	CBF	CBV	PS	VEE
2CX	X	X	X	X
2CU	X	X	X	-
2CT	-	X	X	X

Table 1: Overview over the hemo-dynamic parameters defining the 3 models; CBF: cerebral blood flow, CBV: cerebral blood volume, PS: permeability surface product, VEE: extravascular, extracellular volume

	NAWM	NE-lesions	CE-lesions
CBF	15.8(6.7)	19.1(12.4)	22.9*(22.7)
CBV	0.76(0.19)	1.00**(0.35)	1.18*(0.48)
PS	0.04(0.03)	0.05(0.04)	0.98*(0.46)
VEE	n/a	n/a	10.7(3.46)

Table 2: Mean values (standard deviations) of all parameter estimates

Purpose: Recently, it has been shown that T1-weighted DCE-MRI allows for absolute quantification of perfusion and permeability in normal brain tissue and in brain tumors [1]. In this study, we evaluate the feasibility of a rapid 3D-DCE-MRI approach for and the clinical potential of quantitative assessment of perfusion and permeability in normal appearing white matter (NAWM), in non-enhancing (NE) and in contrast-enhancing (CE) white matter lesions in multiple sclerosis (MS).

Materials and Methods: 19 consecutive untreated patients with clinically active MS were included in the study and underwent DCE-MRI at 3T (Magnetom Verio, Siemens) 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 Gadobutrol. The arterial input function (AIF) 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 (2CU) [1, 2]; ROIs were defined in NE- and CE-lesions and in normal appearing WM (NAWM). All ROI curves were analyzed with the 2-compartment exchange (2CX) model [1, 4], the 2CU model and the 2-compartment Tofts (2CT) model, an overview over the parameters defining each model is given in Table 1. For each ROI, the most appropriate model was selected with the Akaike Information Criterion [4, 5].
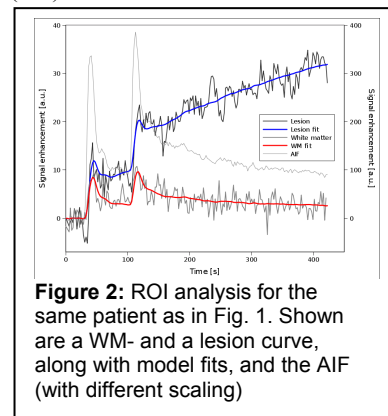

Figure 2: ROI analysis for the same patient as in Fig. 1. Shown are a WM- and a lesion curve, along with model fits, and the AIF (with different scaling)

Results: All CE-lesions that were visible on post-contrast T1-weighted images could be identified on the PS maps (Fig.1). In total, 53 CE-lesions were detected and analyzed in nine patients; typical curves and model fits are shown in Fig 2. Furthermore, 13 NE lesions and 19 NAWM regions were analyzed. The resulting parameter estimates are shown in Table 2; CE lesions exhibited significantly increased CBF, CBV and PS compared to NAWM (p<0.001) with a high standard deviation in all parameters, NE lesions showed a significantly increased CBV (p<0.05), compared to NAWM, and higher variation in CBF and CBV as NAWM. In NAWM, both CBF and CBV were lower than expected.

Conclusion: The rapid 3D sequence allows for characterization of multiple lesions scattered throughout the brain, even without previous knowledge of their location. The sequence has more coverage and similar spatial resolution as T2*-weighted DSC-MRI sequences previously utilized in MS (e.g. [6, 7]), and offers the advantage of absolute quantification of perfusion and blood-brain barrier permeability. The separation of perfusion and permeability is allowed by the use of improved modeling and the measurement with 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.

CBF and CBV values in NAWM are lower than literature values (see e.g. [1]). This is in accordance with other studies that investigated perfusion in NAWM in MS (e.g. [6]), but due to the lack of a control group, we cannot confidently confirm this result. CE lesions are clearly separated from WM by the increased permeability and have more heterogeneous vascular parameters CBF and CBV, thus suggesting a potential for lesion characterization. An investigation of the effects of disease-modifying drugs on perfusion and permeability would be of particular interest.

In conclusion, our approach yields additional and potentially valuable insight into lesion hemodynamics, without the need of additional contrast agent administration

References: [**1**] Sourbron et al *MRM* 62:205-217(2009), [**2**] Bazelaire et al, *Eur. Radiol.* 15:2497(2005) [**3**] Brix et al, *MRM* 52:420(2004) [**4**] Glatting et al, *MedPhys* 34:4285 (2007) [**5**] Brix et al, *MedPhys* 36(7):2923 [**6**] Adhya et al, *NeuroImage* 33:1029(2006 [**7**] Wuerfel et al, *Brain* 127:111 (2004) [**8**] Tofts et al, *JMRI* 10:223 (1999)