Measuring cerebral blood flow and blood-brain-barrier leakage with DCE-MRI at 3T

S. Sourbron[1], M. Ingrisch[1], A. Siefert[2], M. F. Reiser[1], and K. Herrmann[1]

[1]Institute of Clinical Radiology, Ludwig-Maximilian-University Munich, Munich, Germany, [2]Institute of Radiotherapy, Ludwig-Maximilian-University Munich, Munich, Germany

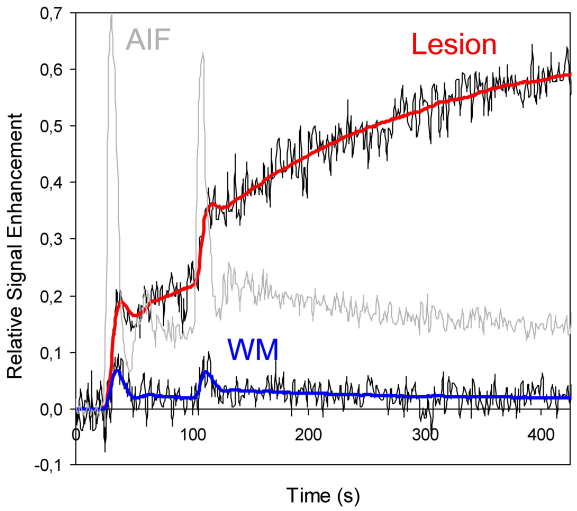

Figure 2. Results of a ROI analysis for the same patient as in figure 1. Shown are the data (thin, black) and a model fit for the lesion (thick, red) and a White Matter ROI (thick, blue). Superposed is a plot of the AIF (thin, grey, not to scale).

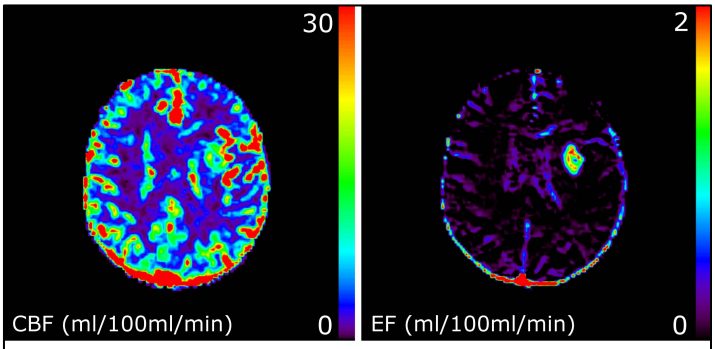

Figure 1. Results of a pixel-by-pixel calculation of both flow parameters: Cerebral Blood Flow (left) and Extraction Flow (right)

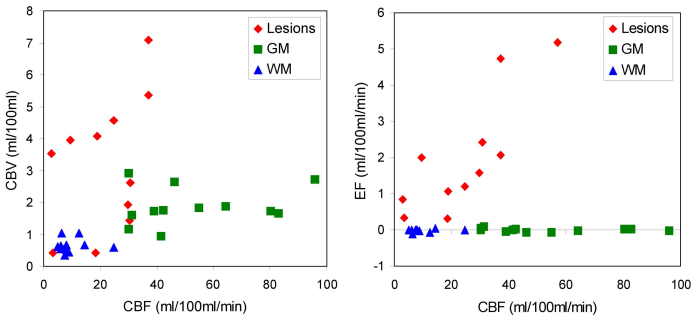

Figure 3. Summary of the ROI-based calculations for all patients. On the left, a plot of the parameters characterizing the vascular space (CBF and CBV), on the right a plot of the extraction flow EF vs. CBF.

INTRODUCTION Cerebral Blood Flow (CBF) measurements with bolus-tracking MRI are typically performed using Dynamic Susceptibility Contrast (DSC-MRI) [1]. The method has the advantage of strong signal changes when the blood volume is small., but Arterial Input Function (AIF) selection is problematic and the difference in T2* relaxivity between blood and tissue causes serious overestimations in CBF [2]. Moreover, when the Blood-Brain-Barrier (BBB) is broken the extravasation of the tracer causes a loss in T2* effects and an increase in T1 effects, leading to ambiguous signal behaviour [3]. An alternative is the use of a T1-weighted acquisition (DCE-MRI), but due to the short-range nature of the T1-effects the signal changes are weak in normal brain tissue [4]. In a previous study, a method was proposed to quantify CBF and BBB-leakage using DCE-MRI at 1.5T [5]. Here we propose an optimization of the protocol at 3T, and evaluate the result using measurements in normal tissue and in brain tumors.

METHODS 15 patients were included in the study, including metastases and primary tumors of the brain, before or after stereotactic radiotherapy. DCE-MRI was performed at 3T (Tim Trio, Siemens) with a 2D Saturation-Recovery Turbo-Flash sequence, acquiring 6 axial slices with a temporal resolution of 1.3s for 7min (128x128 matrix, slice thickness 3.5mm, pixel size 1.875mm, TR 223ms, TI 120ms, TE 1.34ms, FA 15°). The inversion time was increased to improve SNR and T1-weighting. Since this causes a risk of signal saturation in the AIF, the peak arterial concentration was reduced by separating a normal dose (0.1mmol/kg) of Gd-DTPA (Magnevist, Schering) into two equal parts, which were injected 1min apart at a rate of 3ml/s. Data were post-processed off-line using the software PMI 0.3 written in-house in IDL 6.4 (ITT Visual Information Solutions, Boulder, CO). An AIF was selected manually in the ICA on the lowest slice, and the relative signal changes $(S-S_0)/S_0$ were deconvolved pixel-by-pixel [6] to produce maps of CBF, CBV and the Mean Transit Time (MTT). A map of Extraction Flow (EF) was calculated by fitting the pixel data to a two-compartment uptake model [5,7]. Lesion-ROIs were defined manually, and circular ROIs were defined in WM and GM excluding larger vessels (hyperintense CBV regions). CBF, CBV, MTT of the blood (MTT-B) and EF were quantified by fitting the ROI data to a 2-compartment model [5,7,8]. Partial volume effects in the AIF were corrected using a reference measurement in a single pixel inside a large vein.

RESULTS Maps of CBF showed good White-to-Grey Matter contrast (fig 1, left). Not all lesions were differentiated on CBF, but all could be identified on maps of MTT and EF (fig 1, right). The AIFs obtained with this split-bolus protocol showed two clear peaks with no obvious signs of signal saturation (fig 2). All ROI curves showed a clear enhancement and the fits to the models accurately described the data (fig 2). Mean (stddev) of the ROI measurements in GM were: CBF = 58 (28) ml/100ml/min, CBV = 1.9 (0.6) ml/100ml, MTT-B = 2.3 (1.3) s, EF = -0.01 (0.05) ml/100ml/min; in WM we found CBF = 9.4 (5.3) ml/100ml/min, CBV = 0.6 (0.3) ml/100ml, MTT-B = 4.7 (2.2) s, EF = -0.01(0.04) ml/100ml/min. The lesions were more heterogeneous: CBF = 67 (136) ml/100ml/min, CBV = 8.7(12) ml/100ml, MTT-B = 11(12) s, EF = 1.8 (1.7) ml/100ml/min. A graphical overview of all data is given in figure 3 (two highly vascularized lesions are excluded for reasons of clarity). The results show that WM and GM are fully separated on the basis of CBV and CBF (fig 3, left)., but CBF and CBV of the lesions covers the entire range of normality. The values of EF provide full separation between tumors and normal tissue, which has an EF value close to zero (fig 3, right).

CONCLUSION With the optimized protocol at 3T, and despite the use of a minimal slice thickness, maps of CBF, CBV and MTT in normal tissue approach the quality of typical quantitative DSC-MRI images [1]. AIF selection is straightforward, suggesting that (semi)automated strategies are feasible. CBF values in GM agree with gold-standard values, but CBV is at the lower end of typical reference values. This effect may reflect a bias in ROI selection, since pixels with high CBV were excluded from the ROIs. Quantitative ROI values of EF identify exactly which regions are affected by a broken BBB, and to what extent. Compared to conventional approaches of DCE-MRI in tumors at lower temporal resolution [4], the measurement of CBF in addition to EF may improve tumor characterization and assessment of therapy response. In view of the feasibility of the approach in normal tissue, the method may also be useful to measure CBF and BBB leakage in acute stroke [9]. We conclude that, with the optimized protocol at 3T, DCE-MRI provides a viable alternative to DSC-MRI for the quantification of cerebral perfusion and permeability in a wide range of applications.

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