Quantification of subtle blood-brain barrier permeability in white matter using DCE-MRI

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Target audience: Neuroscientists, data analysts, computer scientists, clinicians

Purpose: Recently, there is growing interest in the application of dynamic contrast-enhanced MRI (DCE-MRI) to pathologies associated with subtle blood-brain barrier (BBB) permeability, such as ageing-related white matter disease[1]. The purpose of this study was to quantify BBB permeability in normal-appearing white matter (NAWM) and white matter lesions (WML). Furthermore, we aimed to investigate the relationship between model-based estimation of permeability parameters and model-free measurements.

Methods: 183 mild stroke patients underwent DCE-MRI (1.5T, spoiled gradient echo, TR/TE/FA=8.2ms/3.1ms/12°) with 20 post-contrast (0.1 mmol/kg Gd-DOTA) acquisitions over approximately 23 minutes; an additional acquisition (FA=2°) was acquired for T1 estimation. Following alignment of the dynamic series and tissue segmentation[2], signal enhancement curves over time were generated and converted into contrast agent concentration profiles. We fitted the Patlak model[3] to the curves in order to estimate the pharmacokinetic parameters K^{Trans} (volume transfer constant) and v_p (fractional plasma volume), using a patient-individually measured vascular input function. Moreover, we calculated the area under the contrast agent concentration curve (*AUC*) and the late slope of the curve ($m_{5\text{-}23}$), both of which represent non-model based approaches.

Results: The resulting parameters values are shown in Table 1. All four calculated parameters were significantly higher in WML compared to NAWM (Wilcoxon's signed-rank test P<0.0001). Figure 1 illustrates the relationship between the model-free and pharmacokinetic parameters. We found a strong positive correlation between $m_{5\text{-}23}$ and Patlak's K^{Trans} (Pearson's ρ=0.73, P<0.0001), while showing a moderate negative correlation with v_p (ρ=-0.57, P<0.0001). The *AUC* values were shown to be positively correlated with K^{Trans} (ρ=0.50, P<0.0001) and v_p (ρ=0.56, P<0.0001). There was no correlation between the two model-free estimates *AUC* and $m_{5\text{-}23}$ (ρ<0.1, P=0.27).

Discussion/Conclusion: This study illustrates that model-free measurements show a correlation with vascular permeability and fractional plasma volumes. Hence, in situations with unclear underlying physiology or low temporal resolution of the dynamic imaging series, model-free estimates are a robust alternative to pharmacokinetic modelling. Both pharmacokinetic and model-free parameters suggest that permeability is higher in WML than in NAWM. This gives further insight into subtle brain tissue changes with white matter disease and could be used to investigate whether an underlying pathology of the BBB is present in mild stroke.

Table 1: Permeability parameters in normal-appearing white matter and white matter lesions (population average ± standard deviation).

	K^{Trans} ($\cdot 10^{-6}$ s^{-1})	v_p ($\cdot 10^{-2}$)	*AUC* ($\cdot 10^{-2}$ *mM s*)	$m_{5\text{-}23}$ ($\cdot 10^{-4}$ *mM* s^{-1})
NAWM	4.30 ± 2.52	0.51 ± 0.33	16.38 ± 6.25	0.77 ± 1.79
WML	6.75 ± 2.88	0.82 ± 0.76	25.12 ± 11.61	1.32 ± 2.05

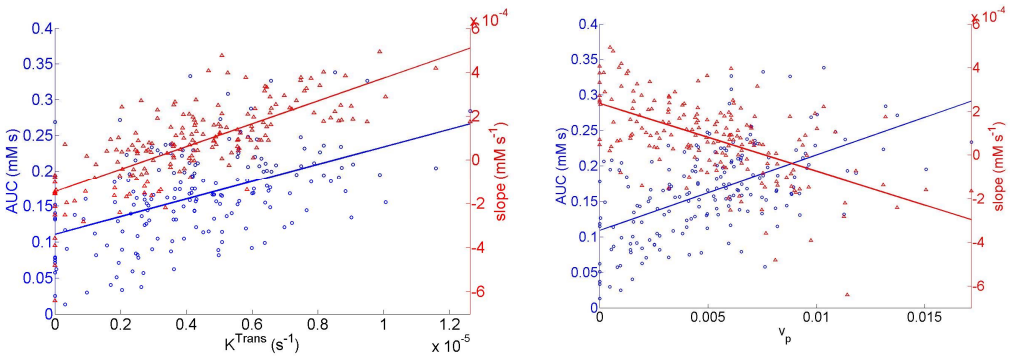

Figure 1: Correlation between model-free measurements *AUC* (blue circles) and $m_{5\text{-}23}$ (red triangles) with the Patlak parameters K^{Trans} (left) and v_p (right) in normal-appearing white matter.

References:

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2. Hernández MdC, et al. Eur Radiol 2010;20(7)1684-91.
3. Patlak CS,et al. J Cereb Blood Flow Metab 1983;3:1-7.