Effects of temporal resolution on blood-brain barrier permeability measurement with Dynamic Contrast Enhanced MRI in multiple sclerosis enhancing lesions

I. O. Jelescu[1], I. R. Leppert[1], S. Narayanan[1], D. L. Arnold[1], and G. B. Pike[1]
[1]Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada

Introduction: Contrast enhanced MRI using Gd-DTPA has proven to be a powerful tool in the detection of active multiple sclerosis (MS) lesions. Dynamic acquisitions during uptake of the contrast agent combined with realistic pharmacokinetic models can give quantitative estimates of two biological parameters: the blood-brain barrier (BBB) permeability constant (K_{trans}) and the extravascular extracellular leakage space (v_e). Access to an accurate and reproducible measurement of K_{trans} would benefit both follow-ups of lesion activity and comparison of detection sensitivity between different conventional protocols. Previous Dynamic Contrast Enhanced MRI (DCE-MRI) studies[1][2][3] show that the acquisition of an individual arterial input function (AIF) is always preferable if the latter benefits from sufficient SNR and temporal resolution. In the case of MS, the method is challenging as it requires high spatial resolution (SR) (due to the relatively small size of MS lesions) and high temporal resolution (in order to accurately sample the first pass bolus in the blood) at the same time. However, the high temporal resolution is only required in the first 50-60 seconds after injection, when Gd concentration variations in the blood and plasma are very rapid, but prior to any measurable uptake in the lesions. We took advantage of this timing difference to acquire DCE-MRI data with high temporal resolution and low SR in the first minute after injection, and low temporal resolution and high SR after on. We further investigate the impact of temporal resolution on (K_{trans}, v_e) estimates by down-sampling the acquired data. Results for a wide range of permeability values are assessed through simulations.

Temporal resolution	5 s part + 32 s part	32 s	64 s
K_{trans} (min^{-1})	0.0083	0.0092	0.0110
K_{trans} change with respect to 5 s + 32 s:		11%	33%
v_e	0.15	0.14	0.13
v_e change with respect to 5 s + 32 s:		-5%	-9%
Adjusted R^2 of fit	0.98	0.95	0.91

Table 1: Effect of temporal sampling on parameters estimated in lesion

Methods: Three MS patients with a recent relapse were scanned on a 3T TIM-Trio (Siemens Medical Systems, Erlangen, Germany). Gd-DTPA (Magnevist®, Bayer, Canada) was injected intravenously to a dose of 0.1 mM/kg, followed by 40 cc of saline. The DESPOT1 technique[4] was used to acquire pre-contrast T_{10} and M_0 maps, with a 1x1x3 mm^3 resolution, covering a 256x192x120 mm^3 volume that allowed for brain and sagittal sinus coverage. Time series were 3D-FLASH images ($\alpha = 20°$, TR = 5.6 ms, TE = 2.61 ms). 10 to 13 volumes were acquired during and right after the contrast injection (5 s temporal resolution, 2x2x6 mm^3 SR, GRAPPA factor 2) followed by 36 additional volumes (32 s temporal resolution, 1x1x3 mm^3 SR).
T1-weighted images and the M_0 map were used to generate T_1 maps at each time point and further converted to concentration maps using the T_{10} map and Gd-DTPA relaxivity in plasma. Enhancing voxels in the sagittal sinus and in lesions were manually segmented. The contribution of venous voxels to the AIF was automatically determined based on peak amplitude to limit partial volume effects. K_{trans} and v_e were fit using the two-compartment model[5] and a non-linear least squares algorithm. The analysis was then re-run on the data (AIF and uptake curves) after temporal re-sampling to 32 s and 64 s resolutions.
Experimental data were compared against simulations run over 1000 iterations with identical imaging parameters and noise levels. Simulations were then further used to predict the impact of temporal resolution on accuracy and precision of K_{trans} estimates over a wider range of K_{trans} values going from 0.005 min^{-1} to 0.05 min^{-1}, comparable to values quoted in the MS literature[5].

Temporal resolution	5 s part + 32 s part	32 s	64 s
K_{trans} (min^{-1})	0.0092	0.0105	0.0123
$\sigma(K_{trans})$ (min^{-1})	0.0006	0.0007	0.0009
K_{trans} change with respect to 5 s + 32 s		(15 ± 15) %	(34 ± 18) %
RMSE(K_{trans}) %	10	8.3	25
v_e	0.16	0.15	0.14
$\sigma(v_e)$	0.02	0.02	0.02
v_e change with respect to 5 s + 32 s		(-6 ± 16) %	(-11 ± 4) %
RMSE(v_e) %	13	8.5	8.4
Adjusted R^2 of fit	0.94	0.89	0.94

Table 2: Simulated evolution of parameters with temporal sampling

Results: Of the three patients scanned, enhancement was visible over 33 voxels. Fitted (K_{trans}, v_e) values across this ROI were (0.0085 ± 0.0033 min^{-1}, 0.16 ± 0.07) – with a high mean adjusted-R^2 = 0.94. The average uptake curve was also analyzed in conjunction with the measured AIF for the three different temporal resolutions considered (Table 1). Simulations run with one measured AIF as an input and (K_{trans} = 0.01 min^{-1}, v_e = 0.15) theoretical values (Table 2) confirm that the relative changes in parameter values due to temporal resolution are highly similar in real data and our simulation. This validates the reliability of the simulation. Figure 1 shows one AIF and its sampling at lower rates. Simulation results of K_{trans} estimation using these AIFs are plotted in Figure 2.

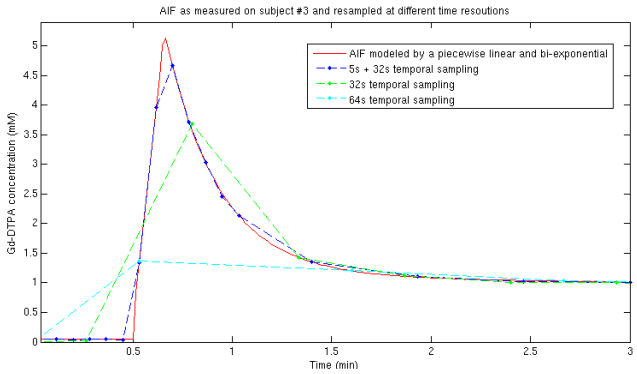

Figure 1: Effect of temporal resolution on acquisition of first pass bolus

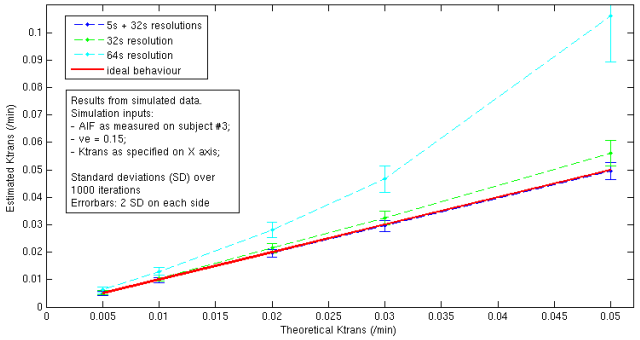

Figure 2: Impact of the temporal resolution on estimated K_{trans} values

Discussion: Experimental data and simulations show that the temporal resolution of the acquisition during the first pass bolus has an important impact on (K_{trans}, v_e) estimates in the lesions, even though the contrast uptake in the lesions occurs at a later time. The associated changes were quantitatively consistent between experimental data and simulation. Simulations show that an acquisition at 5 s resolution for the first 50 s provides accurate estimates of BBB permeability over the range of K_{trans} encountered in MS enhancing lesions. Acquiring at a 32 s resolution throughout results in accurate K_{trans} estimates in slowly enhancing lesions ($K_{trans} \leq 0.02$ min^{-1}), but provides systematic overestimates at higher permeability values, up to 12% in the case illustrated in Figure 2. Acquisitions at a resolution of 64 s or lower, found in literature[5], result in much poorer accuracy and precision, despite the gain in SNR. The "dual-temporal resolution" acquisition method therefore yielded encouraging results: good accuracy in BBB permeability estimates was achieved over a wide range of potential values, with no cost in terms of SNR and spatial resolution. The study is on-going and analysis in a larger pool of enhancing lesions should allow full experimental validation of the method.

References: [1] McGrath D.M. et al, MRM 2009, 61:1173-1184; [2] Parker G.J.M. et al, MRM 2006, 56:993-1000; [3] Yankeelov T.E. et al, MRM 2007, 57:353-361; [4] Deoni S.C.L. et al, MRM 2003, 49:515-526; [5] Tofts P.S., JMRI 1997, 7:91-101;