An empirical DSC-MRI data model including first-pass, recirculation and leakage components fully characterises signal changes in tumours and normal brain

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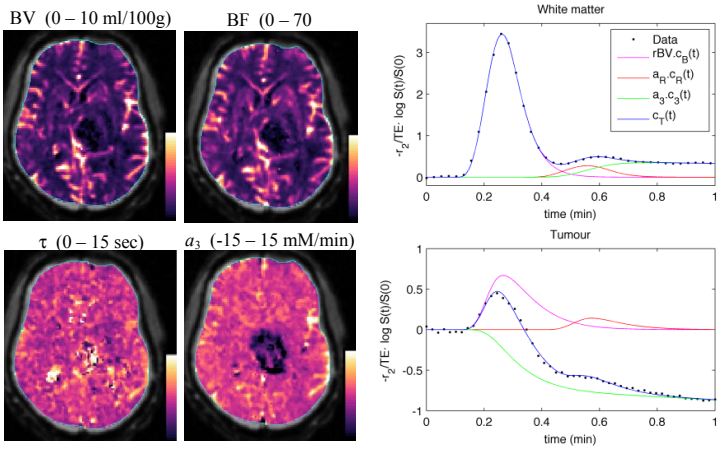
Introduction DSC-MRI methods are designed to probe vascular properties such as blood flow, blood volume and transit time by analyzing the first-pass curves obtained from dynamic T_2^*-weighted imaging. The presence of recirculation and leakage will bias these measures, so this effect is typically minimized by cropping the data to exclude these features. Whilst recirculation causes similar signal changes to those in the first pass, leakage is very difficult to quantify as the signals are affected by changes in T_1, and leakage also directly reduces the susceptibility effect used to observe T_2^* changes. In this abstract we present an empirically motivated model that can be fitted to DSC-MRI data quantified assuming only T_2^* effects that accurately fits the curves without cropping, including first-pass, recirculation and leakage components. The idea is that leakage has very complex effects on signal generation, and while these can in principle be modeled in the forward sense [1], it is much more challenging to apply these models in the inverse sense to fit data acquired using standard methods. Instead, the model described here is designed simply to accurately characterize all the data from all pixels: if the residuals after fitting are only noise then the biological information content of the data must be contained in the estimated model parameters. Accounting for recirculation and leakage in this way avoids the need to define cut-off times, makes use of all the data and may reduce bias. The feasibility of this model is demonstrated on an example taken from a patient with a glioblastoma multiforme.

Model Data are modeled using three curve components, corresponding to the first-pass, second-pass and tertiary features observed in DSC-MRI data. Example curves are shown in the right-hand figures, where the three components of the model are shown along with the overall fit. The first-pass component is modeled with a raised-cosine function convolved with a 2nd-order gamma-variate function, which we show in another abstract (submitted) to give very good fits to first-pass data. The first-pass curve component is given by $C_1(t) = (1-\cos(m_1 t)) \otimes t\,\tau^{-2}.\exp(-(t-t_0)/\tau)$, where m_1 and τ are rate constants related to the arterial input function (AIF) and the mean transit time of the tissue, and t_0 is the contrast arrival time. The recirculation component is modeled similarly but with an additional delay term t_2, and an independent cosine rate constant m_2, $C_2(t) = (1-\cos(m_2(t-t_2))) \otimes t\,\tau^{-2} \exp(-(t-t_0)/\tau)$. Tertiary features of the data curves are dominated by two effects: (1) in tissues with an intact BBB there is continued signal loss (quantified to positive contrast concentration) affected by additional recirculation passes and contrast washout into the body leakage space, (2) in leaky tissues T_1 shine-through causes signal increase that is quantified as a negative contrast concentration, and this process is affected by the tissue leakage rate and volume fraction. An empirical model for both effects is:

Recirculation: if $a_3>0$ then $m_3>0$ and $C_3(t) = a_3 C_2(t) \otimes \exp(-m_3 t)$

Leakage: if $a_3<0$ then $m_3<0$ and $C_3(t) = a_3.C_1(t) \otimes \exp(-m_3 t)$

Note that the recirculation case is related to the recirculation curve $C_2(t)$, so $C_3(t)$ starts at the same time as $C_2(t)$. For the leakage case it is related to the first-pass curve and so starts at the same time as $C_1(t)$, i.e. leakage starts at the same time as the contrast arrives in the tissue, as indeed it must. The overall model curve is $C_T(t) = \mathrm{BV}.C_1(t) + a_2.C_2(t) + C_3(t)$, where BV is the blood volume and a_2 is the recirculation amplitude. The *local* parameters t_0, τ, BV, a_2, a_3 and m_3 are estimated per pixel, and the *global* parameters m_1, m_2 and t_2 are estimated per examination. The global parameters are estimated by fitting all nine parameters to the mean curve from the whole brain (excluding any tissues displaying leakage) and discarding the local parameters. The local parameters are then estimated pixel-wise using the previously derived global parameters. Four of the local parameters are constrained to be positive $\{t_0, \tau, \mathrm{BV}, a_2\} > 0$, which is easily included in standard least-squares fitting functions. The constraints on a_3 and m_3 form two non-overlapping feasible regions, and so to find the overall minima the fitting is done twice over all six local parameters, initializing the optimization in both feasible regions, and the result with the smallest error is reported. The estimated blood volumes are normalized to give BV = 2.0 ml/100g [2] in a region of interest inside white matter.



Data Acquisition Data were acquired from a glioblastoma multiforme patient imaged at DSC-MRI with a Seimens Avanto 1.5T and the following parameters: multi-slice GE-EPI, TR/TE = 1500/30 ms, flip-angle = 90°, 20×5mm axial slices, 128^2 acquisition matrix, 230^2 mm FOV, 40 dynamic points at 1.48 sec/volume. Dotarem contrast agent was hand delivered (0.2ml/kg), and signal changes were converted to concentrations assuming exponential signal changes and a relaxivity of 6.7 mM/ms.

Results and Discussion The table shows BV, τ and BF (= 60×BV/τ) estimates from ROIs placed in white matter, grey matter and in the tumour. These are obtained using the proposed model (Full fit), and by cropping the data at t = 0.35 min and using only the first-pass component of the model (First-pass). Also given are reference values for white and grey matter taken from reference [2]. For white and grey matter, τ and BF agree very well with the reference values for the full fit, and almost as well for the first-pass fitting. However, in the tumour the full fit and first-pass estimates are quite different, in particular τ is around a factor of 10 smaller for the first-pass fitting. Although strong conclusions cannot be made from this feasibility study, the bottom panel showing the curve fit in the tumour shows why these estimates are so different. The first-pass (pink) and leakage (green) components combine to describe the first 0.4 min of data, and the effect of this is that the first-pass curve can be much broader than the data itself over the same period. The parameter maps show that BV and BF are correlated over the whole brain, and the tumour appears as a hypo-intense region in the centre. There is very little contrast in the τ map between white matter and grey matter, and the estimates in the tumour are largely similar except for a small bright region. The map of the tertiary amplitude parameter very clearly delineates the tumour as a region of negative values.

Parameter	White matter			Grey Matter			Tumour	
	Full fit	First-pass	Reference	Full fit	First-pass	Reference	Full fit	First-pass
BV (ml/100g)	(2.0)	(2.0)	2.0	4.6	4.8	3.5	2.0	1.1
τ (sec)	3.7	4.9	4.0	4.4	7.1	3.5	7.2	0.87
BF (ml/100g/min)	33	24	30	63	40	60	17	78

Conclusions A model for describing salient features of DSC-MRI data curves in both leaky and non-leaky tissues has been presented and its feasibility demonstrated with an example. This model enables parameters to be estimated without the need to define a cut-off time. Further work is needed to assess if this approach reduces bias in the estimates of BV and BF, and if the additional parameters (in particular a_3) are reproducible and sensitive to changes.

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