Effect of image acquisition protocol on vascular parameter estimates from DCE-MRI liver data

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Introduction The liver is a highly vascular organ, and so a proportion of the change in signal intensity observed in DCE-MRI measurements is caused by intra-vascular contrast agent – the plasma fraction. A convenient simplification when applying pharmaco-kinetic models to such data is to neglect this contribution[1], in which case the physical interpretation of the remaining vascular model parameters is less clear. To avoid this problem the temporal resolution of the imaging sequence must be sufficiently fast to adequately observe the first-pass enhancement. In this case, a model that includes a plasma fraction can be used, and the interpretation of the other vascular parameters is more direct. The dual blood supply to the liver makes this a particularly challenging organ to model, as the concentration time course (CTC) of contrast agent in both the arterial and portal feeding vessels must be specified to derive quantitative vascular parameter estimates by model fitting to dynamic data[2]. Our current dynamic liver imaging protocol acquires a sequence of 3D image volumes, each acquired in 5.6 seconds under breath-hold at expiration with a variable breathing gap, giving an average temporal resolution of 13 seconds. We are developing an extension of this protocol that acquires two volumes per 6 second breath-hold, and so the purpose of this work is to assess the effect of this modification on the vascular parameter estimates obtained with and without the inclusion of a plasma fraction in the pharmaco-kinetic model.

Methods *Kinetic Model* The liver receives blood from the hepatic artery and the portal vein, so the input function to an imaged voxel is modelled as a weighted sum of input functions. That is $c_p(t) = \gamma c_A(t) + (1-\gamma)c_V(t)$, where $c_A(t)$ and $c_V(t)$ are the arterial and venous inputs, and the weighting term $0<\gamma<1$ (hepatic perfusion index – HPI) is taken to be different for each voxel. Each of the input functions is further decomposed using $c_A(t) = c_{bA}(t) + c_{bA}(t)\otimes B(t)$ and $c_V(t) = c_{bV}(t) + c_{bV}(t)\otimes B(t)$, where $c_{bA}(t)$ and $c_{bV}(t)$ describe the first-pass of the bolus for the arterial and venous components, and B(t) is the body transfer function[3] which models leakage into the whole-body EES. The body transfer function is modelled with a single exponential, and the bolus models are described using raised cosine terms, so the convolutions are analytically tractable. The signal measured in each voxel is described using the extended Kety model[1], $c_T(t) = v_p c_p(t) + v_e c_p(t)\otimes\{k_{ep}\exp(-k_{ep}[t-\tau_0])\}$, and the parameters v_p, v_e, k_{ep}, τ_0 and γ are estimated for each voxel. The overall plasma fraction is v_p and the arterial and venous fractions are γv_p and $(1-\gamma)v_p$ respectively.

Data Simulation Data were simulated from the above model with added Gaussian noise with physiologically realistic variance (see figure 1), and the same model used in a least-squares fitting routine to give estimates of the vascular parameters. These estimates can be compared to the values used to generate the data to assess the impact of various changes in the modelling and the image acquisition protocol. The single acquisition imaging protocol was simulated by using a fixed temporal resolution of 13 seconds, while the double acquisition imaging protocol was simulated with measurements at {0, 3}, {13, 16}, {26, 29}, … seconds. The arterial and venous input functions were derived by fitting the above models to a dual-supply input function previously published[4]. The HPI weighting term γ is of particular interest in oncology as it is known to increase in liver tumours[5]. The first simulation experiment (Experiment 1) considers six scenarios which are combinations of the two imaging protocols (single and double acquisition per breath-hold), and three γ values; 0.25, 0.50, 0.75. For each scenario 2000 curves were generated with the other vascular parameters independently sampled at random from the following intervals: $0.2<v_e<0.8$, $0.25<k_{ep}<3.0$, $0.0<v_p<0.2$ and $24<\tau_0<36$. Example curves are shown in figure 1. Estimates of the vascular parameters were obtained by least-squares fitting using the same model form. The second simulation experiment (Experiment 2) was essentially identical, except that the model form used in the estimation routine neglected v_p, while the data-generation model included it as before.

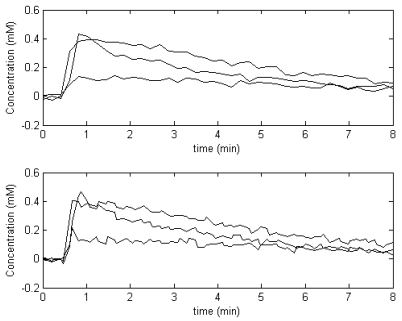

Figure 1 : Example simulated curves for single (top) and double (bottom) acquisition protocols

Results The two tables detail the mean and standard deviation of the estimates of γ from the 2000 simulated curves for the six cases. The first experiment indicates that the double acquisition protocol reduces the estimation bias by a small amount, but more importantly it approximately halves the standard deviation. For the double acquisition protocol an alternative approach might be to combine the pairs of measurements by averaging them to reduce the observation noise. However, this would only reduce the observation standard deviation to 70% of its original value, and by the propagation of errors, the estimation standard deviation would be reduced by the same amount. Preserving the 3 second gap between measurement pairs in the data fitting is therefore important as it improves the accuracy by a greater amount. Experiment 2 demonstrates the need to include the plasma fraction in the model if it is present in the data as all the estimates are substantially biased. The results are worse in this case for the double acquisition protocol: for $\gamma = 0.5$ and 0.75 the estimates have larger bias, and smaller standard deviations giving an inappropriate level of confidence in inaccurate estimates.

Experiment 1 (with v_p)	True γ	0.25	0.50	0.75
Mean γ Estimate	Single acq.	0.271	0.505	0.755
	Double acq.	0.254	0.499	0.752
S.D. γ Estimate	Single acq.	0.190	0.190	0.172
	Double acq.	0.0803	0.0885	0.0869

Experiment 2 (without v_p)	True γ	0.25	0.50	0.75
Mean γ Estimate	Single acq.	0.468	0.646	0.794
	Double acq.	0.430	0.675	0.835
S.D. γ Estimate	Single acq.	0.297	0.263	0.178
	Double acq.	0.314	0.238	0.151

Figure 2 shows the result of applying the above model with a plasma fraction to some in-vivo DCE-MRI liver data. This example is of a neuroendochrine patient with extensive disease in the top right lobe of the liver, and the elevated HPI (γ) estimates in this region confirm this. The HPI of normal liver is in the range 0.1-0.3[5], and the estimates for the lower region of the liver agree well with this.

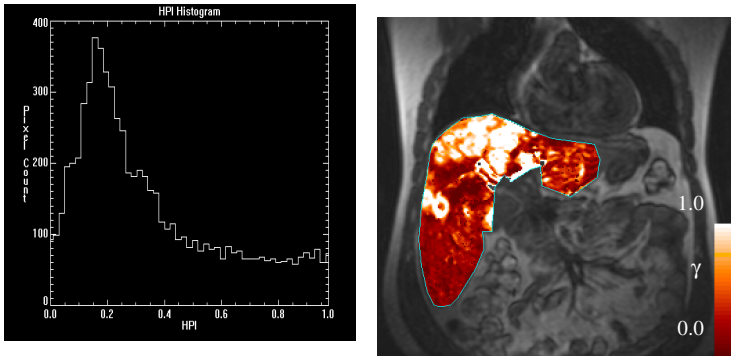

Figure 2 : Left panel is histogram of HPI (γ), right panel is functional image of the same parameter for an example case of a neuroendochrine patient with extensive disease.

Conclusions These simulations demonstrate that a double-acquisition per breath-hold imaging protocol would improve the estimation uncertainty of the HPI parameter by around 50% compared with a single-acquisition protocol. When a plasma fraction is present in the data the simulations also show that the estimates are biased and overly-confident if the fitting model does not include a plasma fraction. An example has been presented of the application of the proposed model to some in-vivo data, and the HPI estimates concur with literature values.

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