

Novel method of portal delay and dispersion estimation for dual-input kinetic modelling of DCE-MRI liver data

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Introduction

Accurate kinetic modelling of DCE-MRI data from liver requires both arterial and portal-venous input functions. Measuring the contrast agent concentration in blood with MR imaging is difficult due to flow artefacts and partial volume effects, and this typically leads to large variability in measured input functions. For liver imaging, where two input functions are required, the impact of this issue is multiplied. For single input DCE-MRI modelling, use of a population input function has been advocated as in practice the variability between patients is typically smaller than the errors involved in measuring the input function¹. Extending this approach to liver modelling would require a population averaged portal-venous input function. The hepatic portal vein receives blood that has travelled from the aorta via the GI tract, stomach and spleen, and can therefore be modelled as a delayed, dispersed and attenuated version of the arterial input function. The variability of these effects between patients is potentially quite large, and so the use of a population averaged portal-venous input function is liable to introduce large errors. Therefore a patient specific portal-venous input function is necessary. In a previous abstract² we introduced a methodology whereby the portal delay was estimated directly from liver tissue DCE-MRI data, and here we extend this approach to include portal dispersion estimation. The advantage of this approach is that the portal-venous input function is patient-specific, and its estimation does not require any additional imaging. The arterial input function can be either a population averaged input function, which we expect to cause similar errors to single-input kinetic modelling, or a measured input function. In either case, avoiding the need to image the portal vein simplifies the image acquisition protocols and planning.

Methods

Kinetic Model For liver data, the dual-input is modelled using $c_p(t) = \gamma c_A(t) + (1 - \gamma)c_V(t - t_p)$, where $c_A(t)$ and $c_V(t)$ are the arterial and portal-venous curves, γ is a partitioning term with $0 < \gamma < 1$, t_p is the portal delay time and $c_p(t)$ is the overall input function curve. Each of the input function components are described using a raised-cosine model³, which is parameterised by a_b , μ_b – first-pass amplitude and duration parameters, and a_e , μ_e – washout amplitude and decay rate parameters. The arterial input function parameters used here were derived from a population averaged input function¹. The portal-venous input function is derived from the arterial curve by means of two key assumptions. Firstly, the washout parameters a_e and μ_e are matched to those for the arterial curve, which is justified since the blood concentration tends towards a uniform equilibrium value. Secondly we assume that the fraction of contrast extracted by the GI tract etc. is negligible, so by mass conservation the area under the first-pass of the arterial and portal-venous curves are the same. This assumption and its implications need further examination, but the results presented in this abstract suggest that this assumption may be a reasonable simplification. The dispersion and zero extraction of the GI tract etc. are simply modelled by scaling the arterial first-pass parameters, i.e. a_b/Δ and $\Delta\mu_b$ for $0 < \Delta < 1$, which ensures that the portal-venous first-pass curve is broader, but has the same area. Ideally this dispersion should be modelled by convolving the arterial first-pass curve with a suitable residue function, but we have found this approach unnecessarily complicated. The tissue uptake is described using a single compartment model, $c_t(t) = v_e k_{ep} c_p(t) \otimes \exp(-k_{ep}(t - \tau_0))$, which neglects any contribution from contrast agent in the blood plasma since the extraction fraction for liver tissue is typically very high.

Data Fitting The parameters requiring estimation are v_e , k_{ep} and γ for each pixel, and the global parameters τ_0 , t_p and Δ , being the global onset time, portal delay time and portal dispersion factor respectively. These parameters are estimated in a stratified optimisation routine whereby the sum of residuals for all voxels is first calculated for a given set of the global parameters. This residual sum is used as a cost function for the global parameters which are optimized using a standard function minimisation routine.

Data Acquisition Protocol DCE-MRI data were acquired coronally on a 1.5T Siemens Avanto using a 3D FFE sequence under sequential breath-hold at expiration, which gives highly reproducible registration of the liver⁴. The imaging parameters were TR/TE = 3.28/1.10 ms, FA = 18°, 12×5mm slices NSA = 1, IPAT = 2, FOV = 350mm, 128×128 interpolated to 256×256 matrix. Two image volumes were acquired during 6 second breath-holds, followed by a 6 second breathing gap, and 40 volumes were acquired over a 4 minute period. The dynamic scan was preceded by a calibration scan with the same parameters except FA = 2° to enable the dynamic sequence to be converted to contrast agent concentration.

Results and Discussion

Figure 1 shows 10 cases of portal-venous input function estimates, along with the arterial input function (AIF) from which they are derived. There is a wide range of delay and dispersion estimates, but all curves are within the range reported in the literature. Example 5 has a negative delay estimate, but also a very small dispersion factor so that although the delay is unphysiological, the curve is still reasonable. This problem may be resolved by using an asymmetric function (e.g. a gamma-variate function) for modelling the portal-venous input, and this is the subject of ongoing work. Figure 2 shows that there is a linear relationship between the portal delay estimates and the dispersion factor estimates, with an R^2 value of 0.86, thus longer delay times are associated with lower portal-venous dispersion (i.e. larger dispersion factors). This kind of relationship is to be expected since low dispersion factors implicitly delay the portal peak time, so less explicit delay is needed for low dispersion factors. A related submission to this conference⁵ compares tissue parameter estimates (γ , arterial perfusion and portal perfusion) obtained with this approach using kinetic models with and without portal dispersion estimation, and using a dual-slope graphical approach. This comparison demonstrates good agreement between the model with dispersion and the dual-slope approach, but a less convincing agreement when the dispersion is not estimated.

Conclusions

A methodology has been described for estimating portal-venous input function parameters directly from liver tissue data. An arterial input function is required in this approach, which can be a measured input function, or as in this case, a population-based input function. Theoretical considerations correctly predict the observed relationship between the delay and dispersion estimates. Further work is needed to assess the impact of neglecting contrast extraction of the GI tract.

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References

- ¹Parker GJ, et al., *Magn Reson Med*. 2006; **56**(5):993-1000.
- ²Orton MR, et al., *Proc. Intl. Soc. Mag. Reson. Med*. 16 (2008), 1709.
- ³Orton MR, et al., *Phys Med Biol*. 2008; **53**(5):1225-39.
- ⁴Melbourne A, et al. *Proc. Intl. Soc. Mag. Reson. Med*. 15 (2007), 3709.
- ⁵Miyazaki K, et al. "Hepatic perfusion quantification using a dual-input kinetic model with a novel portal venous estimation method: Evaluation against other model- and slope-based perfusion quantification approaches." *Proc. Intl. Soc. Mag. Reson. Med*. 17 (2009), submitted.

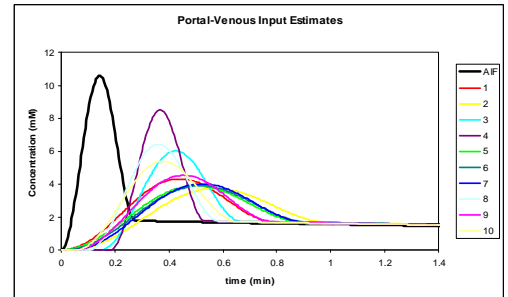


Figure 1: Portal-venous input function estimates, with corresponding arterial input function.

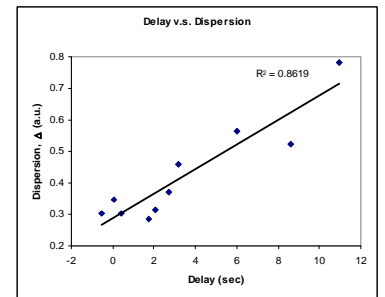


Figure 2: Delay and dispersion estimates with linear regression line.