Portal delay estimation from DCE-MRI liver tissue data : feasibility and effect on vascular parameter estimates

M. R. Orton[1], J. A. d'Arcy[1], D. J. Collins[1], D. Atkinson[2], D. J. Hawkes[2], and M. O. Leach[1]

[1]Clinical Magentic Resonance Research Group, Institute of Cancer Research, Sutton, Surrey, United Kingdom, [2]Centre for Medical Image Computing, Univeristy College London, London, United Kingdom

Introduction Quantitative modelling of hepatic DCE-MRI data is complicated by the need to model the dual blood supply to the organ, but this property enables other features of its physiology to be probed. In particular, the proportion of arterial to portal blood is known to change in certain disease states, and tumours also tend to have increased perfusion from the hepatic artery[1]. Concentration time curves (CTCs) for the arterial and portal feeding vessels are needed as input functions to a leakage model that allows vascular parameters to be estimated using CTCs from the liver tissue. The portal supply arrives at the liver via the GI tract, and so the initial arrival of contrast in the portal supply is delayed and dispersed relative to the arterial component.

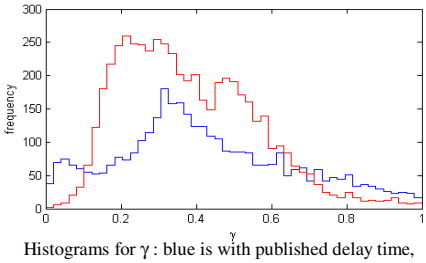
For standard quantitative DCE-MRI modelling it has been shown that using a population-averaged input function improves the repeatability of the estimates when compared to using a measured input function[2]. This work investigates the possibility of using the same approach for modelling liver data, which would simplify the data acquisition and analysis, bringing the technique closer to routine clinical use. However, other workers have reported that the portal delay times vary greatly between individuals, and our own preliminary work has indicated that the vascular parameter estimates using the dual supply model are very sensitive to this delay time. Together these factors mean that using a completely fixed population-averaged dual input function will give unreliable estimates. However, on the assumption that the largest source of variability in the input functions between individuals is in the portal delay, we propose using fixed curve shapes for the arterial and portal input functions, then estimating the portal delay time for each data set. This abstract aims to demonstrate the feasibility of this approach, and to assess its impact on estimates of the arterial-portal partitioning term which is estimated for each voxel.

Methods *Kinetic Model* The dual supply input model is given by $c_P(t) = \gamma c_A(t) + (1-\gamma)c_V(t-t_P)$, where $c_A(t)$ is the arterial CTC, $c_V(t)$ is the portal (venous) CTC, 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. The signal measured in each voxel is described using the standard Kety model[3], $c_T(t) = v_e k_{ep} c_P(t) \otimes \exp(-k_{ep}[t-\tau_0])$, which neglects any contribution from contrast agent in the blood plasma. The vascular parameters v_e, k_{ep}, τ_0 and γ are estimated by least-squares fitting of the CTC in each voxel, and γ is of particular interest as this will be close to unity in tumours. During the optimisation v_e and γ are constrained to the interval [0,1] and k_{ep} is constrained to be positive. The portal delay time, t_P, is not fitted for each voxel as this leads to over-fitting, but instead it is considered as a single global parameter that is estimated from the CTCs from all voxels together. Each voxel gives a residual sum of squares (RSS) from the fitting of the vascular parameters, and this is conditional on a given portal delay. A cost function for the portal delay is constructed by summing the RSS over all voxels for the given t_P, and this can be minimised to give an estimate of t_P. In this preliminary work we have made use of a model-based fit to a dual-supply input function published by other workers[4] to give curve shapes for the arterial and portal components.

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 liver[5]. Each breath-hold image was acquired in 5.6 sec, followed by a 6.4 sec breathing gap, and 20 images were acquired giving a total time of 4 minutes. The imaging parameters were TR/TE = 4.36/1.32 ms, NSA = 1, FA = 24°, IPAT = 2, 20 slices @ 5mm thick, FOV = 400mm, 128x128 matrix. The dynamic scan was preceded by a calibration scan at FA = 2° to enable the dynamic sequence to be converted to contrast agent concentration.

Results The proposed approach was evaluated using 7 data sets acquired from 4 individuals. A single slice was selected and an ROI drawn to include all liver tissue in that slice. In order to assess the uncertainty in the estimation of t_P, each data set was partitioned into five subsets and the delay time estimated for each subset. The partitioning was done by taking every fifth voxel from a list of voxel co-ordinates which gives approximately uniform spatial coverage in each subset – each subset contained more than 1000 voxels. Estimates of the delay time are presented in the table. Estimates from the five subsets are remarkably consistent, with the largest range of the estimates (defined as (max-min)/mean×100%) being 4.38%. With this consistency it is possible to compare estimates between individuals, and within the same individual on different visits. These results corroborate those from other groups who have reported similar variability in this delay time[1]. The most interesting feature of this approach is the effect it has on the other vascular parameter estimates, in particular the arterial-venous partition term γ. For normal liver tissue γ is known to be around 0.1-0.3, while for tumour tissue it is expected to be larger, approaching unity[1]. Due to the constraints placed on this parameter, some estimates of γ are exactly 0 or exactly 1, and while large γ estimates are associated with tumour tissue, very small γ estimates are not expected for either normal or tumour tissue. The table shows the number of pixels estimated with extreme values of γ using the dual supply input function with a portal delay as published (Pub.), and using the optimised delay time (Opt.). This shows a substantial reduction in the number of pixels estimated with $\gamma = 0$ when the optimised delay time is used. The figure shows histograms of γ from the data set highlighted in the table using the published (blue) and optimised (red) delay time. Voxels with $\gamma = \{0,1\}$ have been excluded from the histogram, and the numbers of these are given in the table. In this example the number of pixels with extreme γ estimates has reduced, particularly at 0, and the main peak in the histogram is around 0.1-0.3, as expected for normal liver tissue. The table also shows the total χ^2 for each data set using the published and optimised delay times, and this also shows an improvement with the optimised parameter.

Individual		1	1	1	2	2	3	4
t_P raw estimates (sec)		10.59 10.60 10.66 10.64 10.74	14.76 14.98 15.14 15.23 15.42	14.31 14.38 14.41 14.52 14.64	16.63 16.87 16.93 16.99 17.11	16.57 16.58 16.61 16.67 16.68	8.074 8.071 8.165 8.278 8.341	12.56 12.57 12.83 12.83 12.94
t_P mean (sec)		10.65	15.11	14.45	16.91	16.62	8.185	12.72
t_P range (%)		1.39	4.38	2.32	2.84	0.672	3.31	2.93
# pixels		7382	8145	5781	5526	5063	9532	4744
#γ=0	Pub.	1835	2920	961	1649	794	2991	93
	Opt.	557	38	11	40	28	234	66
#γ=1	Pub.	1833	1672	2131	315	239	2074	1925
	Opt.	1673	1262	1636	97	153	1436	1259
Total χ^2	Pub.	418.0	868.9	203.1	352.7	308.0	1197	235.9
	Opt	343.4	783.1	159.6	291.1	244.6	782.5	204.3



Histograms for γ : blue is with published delay time, red is with optimised delay time for highlighted column in table.

Conclusions This work demonstrates the feasibility of estimating portal delay times using DCE-MRI data from liver tissue when the arterial and portal input function shapes are known. The effect of estimating the delay time on estimates of γ has also been shown, especially the reduction in the number of estimates at γ=0. The ability to estimate the portal delay time is necessary for the use of a population-based input function when modelling dynamic data from liver since this parameter will not be measured directly and due to the large degree of inter-individual variability reported for the portal delay time. The next phase of development is to assess the repeatability of the vascular parameter estimates obtained from DCE-MRI liver tissue data using input function shapes measured from a larger population, combined with portal delay estimation.

Acknowledgements This work was supported by Cancer Research UK (C1060/A5117) and EPSRC grants GR/T20434/01 and GR/T20427/01(P).

[1] KA Miles et al, Radiology, 1993, 188:405-411.
[2] GJ Parker et al, Magn Res Med, 2006, 56(5):993-1000.
[3] PS Tofts, J. Magn Res Imag, 1997, 7(1):91-101.
[4] RT Black et al, Proc. Intl. Soc. Mag. Reson. Med. 15 (2007), 3562.
[5] A Melbourne et al, Proc. Intl. Soc. Mag. Reson. Med. 15 (2007), 3709.