Pharmacokinetic modelling of DCE-MRI at moderate temporal resolution: dealing with tumours which wash out extremely fast

D. J. Manton[1], M. D. Pickles[1], M. Lowry[1], and L. W. Turnbull[1]
[1]YCR Centre for MR Investigations, Hull-York Medical School, Hull, East Yorkshire, United Kingdom

Introduction: Dynamic, contrast-enhanced MRI (DCE-MRI) often involves a compromise between the spatial resolution (the pixel size) of the images, and the temporal resolution (the time between successive dynamic time-points, DeltaT) of the enhancement-time courses. In order to permit reasonable textural analysis [1] of our dynamic images, we have chosen to carry out DCE-MRI with moderate temporal resolution; i.e. with a delay time of approximately 30 s. With such a relatively low temporal resolution, it was initially assumed that only a very simple pharmacokinetic (PK) model could be applied to the data, and the well-established, two-compartment (blood plasma and tissue extra-vascular, extracellular tissue space, EES, only) Brix model was chosen which assumes that the signal contribution from blood plasma is negligible [2]. It was found that a small number of breast and meningioma tumours demonstrate extremely rapid contrast wash-out (very steep negative tails), presumably due to the presence of a significant signal contribution from blood plasma (SSCP), and that the Brix model was not able to model this behaviour faithfully. In order to improve the quality of our PK modelling, a number of more sophisticated models which include an SSCP have been investigated.

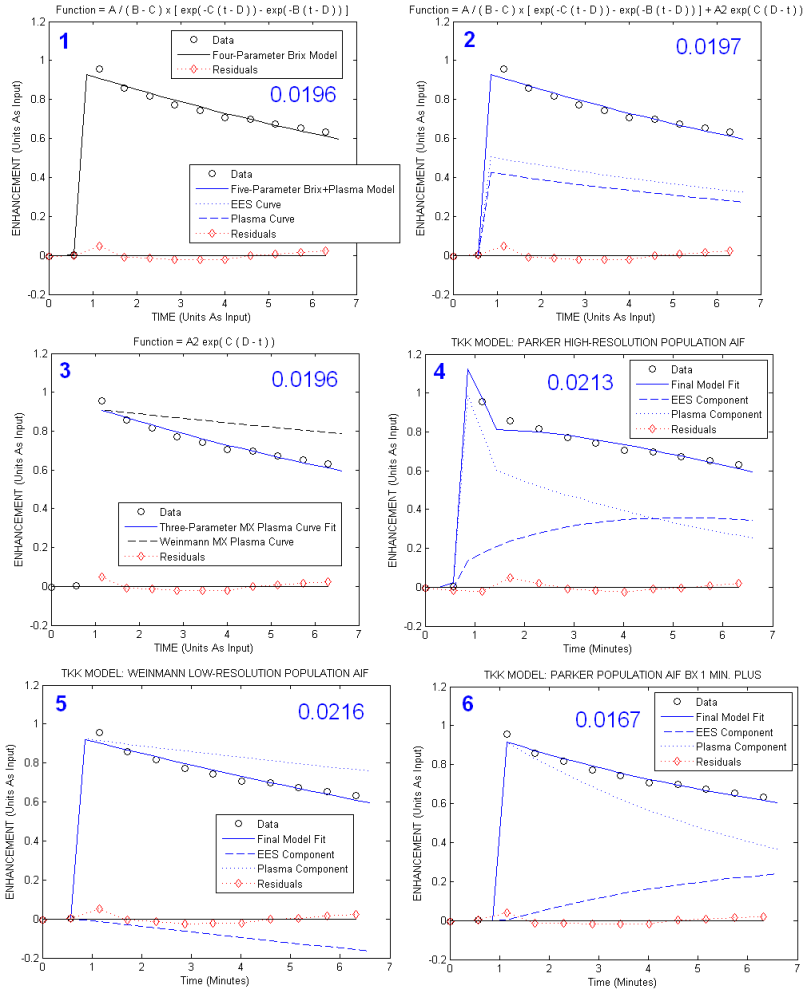
Methods: Enhancement-time courses were obtained from whole-tumour (all slices) regions of interest, as drawn using image analysis software developed using IDL (ittvis.com), and PK modelling was performed using functions implemented in the MATLAB programming environment (mathworks.co.uk). The models investigated were: 1. a two-compartment Brix model without an SSCP (fitted parameters = bolus arrival time / BAT, initial gradient/amplitude, plasma-tumour exchange rate & plasma concentration decay rate); 2. a Brix model with an SSCP added (extra fitted parameter = plasma curve height); 3. a mono-exponential (MX) decay curve (BAT, initial height/amplitude & decay constant); 4. a three-compartment (whole-body EES added) Tofts-Kermode-Kety (TKK) model [2, 3] with an SSCP as modelled by the high-resolution Parker population-averaged arterial-input function (PAIF) [4] (fitted parameters = BAT, K^{trans}, EES volume fraction & plasma volume fraction); 5. a TKK model with an SSCP as modelled by a bi-exponential (BX) fit to the low-resolution Weinmann PAIF which assumes instantaneous bolus mixing [5]; and finally 6. a TKK model with an SSCP as modelled by a BX fit to the latter part of the Parker PAIF (after 1 minute) which ignores the early bolus peaks and assumes instantaneous mixing.

Results: A representative breast tumour case where extremely rapid contrast wash-out was demonstrated is presented. DCE-MRI was carried at 3.0 T using a GE Signa HDx scanner, a dedicated phased-array breast coil and the 3D VIBRANT chemical shift imaging sequence to obtain fat-suppression (TR = 4.1 ms; TE = 1.6 ms fractional; flip angle = 10 degrees; bandwidth = 41.7 kHz; Field-of-view = 22 x 22 cm; matrix = 220 x 160; slice thickness = 4 / -2 mm). DeltaT was 34.0 s in this case, with twelve time-points acquired in a little over six minutes. Imaging was carried out in the sagittal plane which did not permit the acquisition of an appropriate/reliable patient-specific arterial-input function.

The BX fit to the Weinmann PAIF (excluding the final point where percentage error was greater than 100%) yielded the following fixed model parameters: amplitude(1) = 4.783, rate(1) = 0.054, amplitude(2) = 3.009 and rate(2) = 0.007. The BX fit to the latter part of the Parker PAIF yielded the following parameters: amplitude(1) = 0.3847, rate(1) = 0.17038, amplitude(2) = 0.6653 and rate(2) = 0.16742.

Fits to the data in this case, plus residuals, are shown using the model numbers as indicated. The root-mean-square residuals for the fits (RMSR) are also shown.

Model 1 shows a typically poor fit with Model 2 being no better. Model 3 shows that the wash out is not MX suggesting the need for a third model compartment. Models 1 and 2 also appear to be simulating model 3. Model 4 shows the need for an SSCP, but the very poor fit may be due to insufficient temporal resolution to describe the Parker PAIF adequately. Model 5 appears to fail because the Weinmann PAIF does not provide an adequately fast plasma decay. Finally Model 6, with the low-resolution BX plasma decay now being derived from the Parker PAIF, provides a substantial improvement in quality of fit over Model 1 as the RMSR ratio is 85%. Even more importantly, the low K^{trans} value that model 6 yields will be more realistic that the extremely high amplitude value from Model 1, and a realistic estimate for the plasma volume ratio is also available whereas Model 1 wrongly assumes this to be zero.



Conclusion: A more appropriate PK model has been developed which improves the quality of fit in cases where contrast wash-out is marked and also yields parameters which are more physiologically realistic. A Monte Carlo simulation will be necessary in order to determine if new-model parameter precision will be adequate at moderate temporal resolution, however, and better initial guesses for the iterative fitting algorithm may improve robustness.

References: [1] P. Gibbs, *et al. Magn. Reson. Med.* 50:92-98 (2003). [2] P.S. Tofts. *JMRI* 7:91-101 (1997). [3] J.U. Harrer, *et al. JMRI* 20:748-757 (2004). [4] G.J.M. Parker, *et al. Magn. Reson. Med.* 56:993-1000 (2006). [5] H.J. Weinmann, *et al. Phys. Chem. Phys. Med. NMR* 16:167-172 (1984).