A Functional Form for Arterial Input Function Modelling including an Explicit Arterial Recirculation Phase

M. Orton[1], D. Collins[1], S. Walker-Samuel[1], J. d'Arcy[1], D. Hawkes[2], and M. Leach[1]

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

Introduction Quantification of DCE-MRI data relies on determining an appropriate arterial input function (AIF) for the tissues of interest (TOI). Several approaches for providing an AIF have been proposed in the literature, but the most appropriate method for routine clinical use is still an open question. The work presented here describes progress on a method initially described in [1] where the AIF is modelled with a functional form that is both realistic and mathematically convenient. The parameters of the AIF are estimated directly from the tissue uptake data, and the tissue kinetic parameters are also estimated in the same procedure. This approach gives an AIF that is individualised not only to the patient, but also to the TOI, and specifically it is an estimate of the time-course of tracer concentration in the capillaries of the TOI. This avoids the need to assume that the time-course of tracer concentration in the capillaries is the same as in their feeding vessel(s), which is implicit in methods that make direct measurements of the arterial tracer concentration. Avoiding the need to measure the arterial tracer concentration is beneficial since it gives greater flexibility when planning the scans. There is no need to include feeding vessels for the TOI, or compensate for consequent flow artefacts, and the MR sequence need only be sensitive to tracer concentrations found in tissues, which are typically several times smaller than in feeding vessels. An important application of quantitative DCE-MRI methods is in assessing response to treatment, and a potential benefit of the method described here is that it can account for the variability of the AIF in a subject during scans on different occasions. This is important since it implies that any change in the tissue parameter estimates reflects ground-truth, rather than being due to a change in the AIF.

In order to begin validating this approach it is necessary to determine the limits of what can be inferred about the AIF from the tissue data. In previous work [2] we showed that it is possible to detect the equilibration phase of the AIF, but that renal excretion is undetectable as it occurs over timescales much longer than the examination. The work presented here focuses on modelling the recirculation phase of the AIF, and in particular the model generates a distinct recirculation peak.

Theory The AIF is decomposed into a term for the initial bolus, and a term describing how the bolus is modified by subsequent transport processes – the body transfer function. Mathematically this is described by $c_p(t) = c_b(t) + c_b(t) \otimes B(t)$, where $c_b(t)$ is the initial bolus, $B(t)$ is the body transfer function and $c_p(t)$ is the resulting AIF. The bolus is modelled using a gamma-variate function of the form $c_b(t) = a_b\, \mu_b^2\, t\, \exp(-\mu_b t)$, where the additional μ_b^2 term means that a_b is the area of the bolus. This function has been used in DSC-MRI for some time for first-pass modelling, so its use here is a natural extension of this. The key component is the body transfer function, which is modelled with

$$B(t) = a_e \exp(-\mu_e t) + a_r (t - \tau_r) \exp(-\mu_r (t - \tau_r)).$$

Weinmann showed that equilibration with the whole-body extracellular-extravascular space (EES) follows an exponential decay [3], and this is described by the first term. The second term models recirculation and has the property that it is zero at $t = \tau_r$, and has a duration of order $4/\mu_r$. This recirculation model implements a delay and dispersion when convolved with the bolus term, which mirrors the physiological relationship between the bolus and recirculation.

The tissue concentration is related to the AIF via $c_t(t) = c_p(t) \otimes h(t\text{-}t_0)$, where $h(.)$ is the tissue residue function, assumed to vary over the TOI, and t_0 is the onset time of uptake. The residue function can be chosen to model effects such as spatial leakage and vascular components, but the model used here is the standard Tofts model [4] with the form $h(t) = K^{trans} \exp(-k_{ep} t)$, from which the EES fraction is given by $v_e = K^{trans}/k_{ep}$.

Methods The data analysis problem then comes down to finding estimates of the AIF parameters (μ_b, a_e, μ_e, a_r, τ_r, μ_r) and the tissue parameters (K^{trans}, k_{ep}, t_0, for each pixel) that best fit the acquired data from the TOI. This is a complex fitting task, and the use of gradient-based optimisation methods is problematic because of the large number of parameters. Instead we take a Bayesian estimation approach which means that Markov Chain Monte Carlo methods can be used to find the parameter estimates. Such methods tend to be more stable than gradient-based methods for large scale optimisations. It is not possible to independently estimate a_b and the K^{trans} parameters because they both directly scale the tissue concentration curves. To resolve this ambiguity it is necessary to fix a_b, and in this case we use $a_b = 0.8$, which produces a bolus with an area that agrees with in vivo values in the literature [5].

The model described above was applied to two example data sets from primary breast carcinomas consisting of 442 and 337 pixels. Each pixel has a time-series of 41 measurements, the sample interval was 7.5 seconds, and the acquired signal intensities were converted to tracer (Gd-DTPA) concentration using standard methods.

Results Figure 1 shows the estimated AIFs, including separate curves for the bolus, recirculation and equilibration components. The recirculation delay, τ_r, was estimated at 15.5 and 13.8 seconds for both data sets, which is in good agreement with literature values. Figure 2 shows histograms of the estimated tissue parameters for the two data sets. The first data set (blue) has a bimodal histogram suggesting two classes within the TOI, whereas the second data set (red) has a single class.

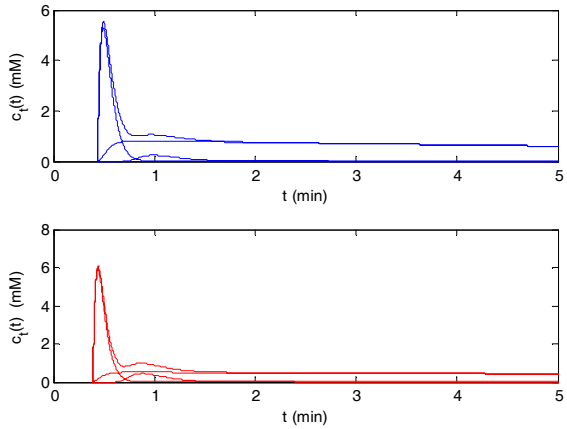

Figure 1 : Estimated AIFs for the two data sets with bolus, recirculation and equilibration components shown separately

Conclusions These preliminary results show that this approach has the ability to detect and estimate all three key phases of the AIF directly from the tissue data. Using this approach the shape of the AIF is entirely determined from the tissue data, though at present it is necessary to fix the AIF scaling a priori. Methods of removing this restriction are being investigated. Further work is needed to assess the impact of issues such as the number of pixels, measurement SNR, measurement time resolution and alternative tissue residue function models.

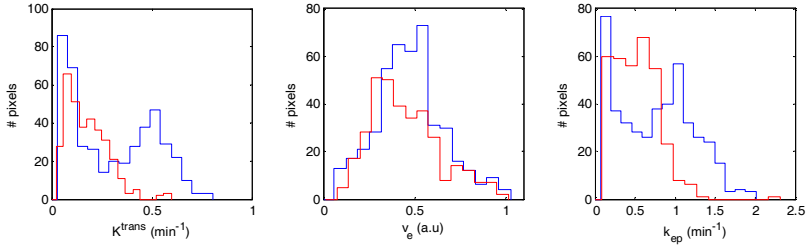

Figure 2: Tissue parameter histograms for the two data sets.

References [1] Orton M, *et al.* Proc. Intl. Soc. Mag. Res. Med. 14, 3490 (2006), [2] Orton M, *et al.* Proc. Brit. Chap. ISMRM. 12, O23, (2006), [3] Weinmann HJ, *et al.* Physiol. Chem. Phys. Med. NMR. 16, 167-172 (1984), [4] Tofts PS, *et al.* J. Magn. Reson. Imag. 10, 223-32 (1999) [5] Parker GJ, *et al.* Proc. Intl. Soc. Mag. Res. Med. 13, 2100 (2005).

Acknowledgements This project was funded by EPSRC grants GR/T20434/01 and GR/T20427/01(P), and CRUK grant C1060/A5117.