Estimating DCE-MRI vascular parameters of tumours using a tractable input function formulation : model calculations and results.

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Introduction For quantitative DCE-MRI to become routine in clinical applications the development of efficient software tools are vital. A component of such software will be a methodology for incorporating the arterial input function (AIF) into the analysis, and various approaches have been proposed in the literature. Many groups have used the work of Weinmann [1] to justify the use of a simple bi-exponential form for the AIF, which when combined with standard leakage models leads to equations that can be fitted to the acquired data using least-squares estimation methods. The simplicity of the resulting equations means that parameter estimation is typically very rapid. However, for *in vivo* data the lack of a bolus term in Weinmann's AIF means that DCE-MRI data obtained following a bolus injection cannot be accurately modelled, especially if a significant plasma fraction is present. In this work we give expressions for an alternative to the bi-exponential AIF which incorporates a realistic bolus model. Crucially, this model produces a relatively simple expression for the tissue uptake curves so that the fitting process is well-behaved and efficient. This model has been implemented in our in-house software tool, MRIW, and results are presented showing its application to a data set from a patient with advanced metastatic liver disease.

Theory The AIF is modelled using equation (1), where $c_b(t) = \alpha_b t e^{-\mu_b t}$ is a gamma-variate function describing the initial bolus, and $B(t) = \alpha_e e^{-\mu_e t}$ is an exponential term describing equilibration of the bolus by leakage into the whole-body EES, as described by Weinmann [1]. Equation (2a) shows the explicit expansion of the convolution in equation (1), giving a direct formula for the AIF in terms of the component parameters. Equation (2b) is essentially the same, but common terms have been collected together, and their amplitudes simplified into A_b and A_e. The tissue curve is given by $c_t(t) = c_p(t) \otimes h(t)$, where $h(t)$ is the tissue residue function. For the Tofts model this is $h(t) = K^{trans} e^{-k_{ep}t}$, in which case the tissue curve can be calculated explicitly, and is given in equation (3). If a plasma fraction is also present then an additional term given by v_p times equation (2b) must be added to equation (3). Typically the bolus arrives at the region of interest at some unknown time t_0, so the unknown parameters can be estimated by fitting the acquired data to the curve $c_t(t-t_0)\,u(t-t_0)$, where $u(t)$ is a unit step function at $t = 0$, and $c_t(t)$ is given by equation (3), with the addition of a plasma fraction if appropriate. Equation (3) is not defined when $k_{ep} = \mu_b$ or $k_{ep} = \mu_e$ so special cases must be calculated. If $k_{ep} = \mu_e$ then the first term in the second parentheses of (3) must be replaced with $t\,e^{-\mu_e t}$. Similarly if $k_{ep} = \mu_b$ then the second term in the second parentheses must be replaced with $te^{-\mu_b t}$, and the whole of the first term must be replaced with $K^{trans} A_b t^2 e^{-\mu_b t}/2$.

$$c_p(t) = c_b(t) + c_b(t) \otimes B(t) \quad (1)$$

$$c_p(t) = \alpha_b t e^{-\mu_b t} + \frac{\alpha_b \alpha_e}{\mu_e - \mu_b}\left(t e^{-\mu_b t} + \frac{e^{-\mu_e t} - e^{-\mu_b t}}{\mu_e - \mu_b} \right) \quad (2a)$$

$$= A_b t e^{-\mu_b t} + A_e\left(e^{-\mu_e t} - e^{-\mu_b t} \right) \quad (2b)$$

where $A_b = \alpha_b + \frac{\alpha_b \alpha_e}{\mu_e - \mu_b}$ and $A_e = \frac{\alpha_b \alpha_e}{(\mu_e - \mu_b)^2}$

$$c_t(t) = \frac{K^{trans} A_b}{k_{ep} - \mu_b}\left(t e^{-\mu_b t} - \frac{e^{-\mu_b t} - e^{-k_{ep} t}}{k_{ep} - \mu_b} \right) + K^{trans} A_e \left(\frac{e^{-\mu_e t} - e^{-k_{ep} t}}{k_{ep} - \mu_e} - \frac{e^{-\mu_b t} - e^{-k_{ep} t}}{k_{ep} - \mu_b} \right) \quad (3)$$

Methods The acquired data is first transformed to give absolute estimates of the tracer concentration using established methods [2]. Then equation (3) is applied pixel-by-pixel to give least-squares estimates of the tissue parameters K^{trans}, k_{ep}, t_0 and v_p. The AIF is defined by the four parameters, A_b, A_e, μ_b and μ_e, and these must be supplied as an input to the software. We are currently working on a more complete approach where these are estimated from the tissue data along with the tissue parameters, but for the results presented here they were fixed to A_b = 310 mmol min^{-1}, A_e = 1.05 mmol, μ_b = 20 min^{-1} and μ_e = 0.17 min^{-1}. These were chosen to give a good match to a recently published generalised population AIF [3]. The dynamic part of the study consisted of 40 dynamic measurements acquired every 5.6s (with a 5s gap in between each measurement) using a 3D VIBE sequence with navigator breath-hold and follow (iv. Magnevist® 0.1mmol/kg body weight, TR/TE=4.36/1.34ms, α=24°, interpolated matrix size=256×256, number of slices=12, slice thickness=5mm, NSA=1).

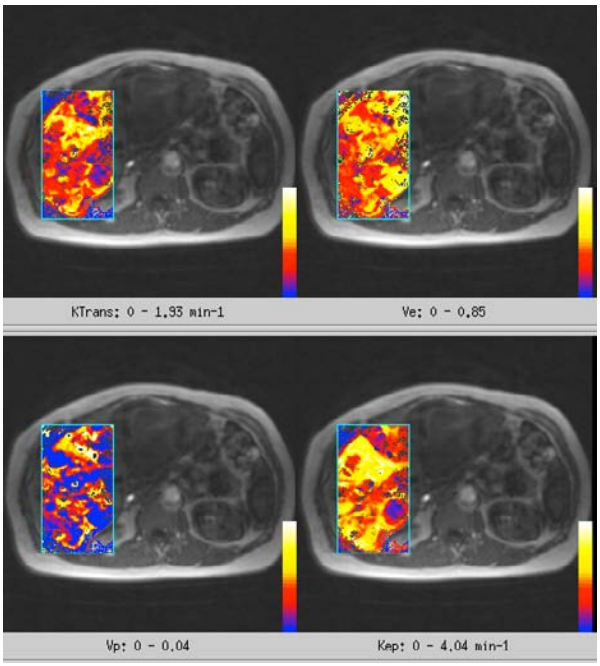

Figure 1 : Parameter maps estimated using the AIF described in the text, overlaid on morphological images.

Results Figures 1 and 2 show parameter maps using this fitting process with data from a patient with advanced metastatic liver disease, overlaid onto an image displaying the general morphology. These values are consistent with literature values, and in particular v_p is in a plausible range.

Conclusions The proposed input function is sufficiently realistic to accurately model data with a non-negligible v_p fraction, whilst remaining simple enough for the fitting to be computationally efficient. This efficiency comes from the use of a model that allows all the necessary convolutions to be carried out analytically before fitting to the data, removing the need for numerical convolutions.

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