Temporal resolution and SNR requirements for accurate DCE-MRI measurement of microvascular blood flow and permeability using the AATH model

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Introduction: Dynamic contrast-enhanced MRI has been used in conjunction with tracer kinetics modelling in a wide range of tissues for treatment monitoring, oncology drug development and investigation of disease processes. Accurate measurement of model parameters relies on high quality data, and as model complexity increases to allow measurement of more physiological parameters, the data quality requirements are likely to be even more stringent. In this study, the accuracy of the adiabatic approximation to the tissue homogeneity (AATH) model [1] was investigated through simulation. This model allows separation of blood flow from permeability, rather than combining these parameters in a transfer constant (K^{trans}) as in the more commonly-used Kety model. The effects of temporal resolution and noise levels were examined, and also the impact of an incorrect measurement of the arterial input function (AIF) first pass peak was assessed.

Methods: Tissue uptake curves were simulated using the Johnson and Wilson model [2] and the mean AIF from a previous study [3] fitted with a smooth function similar to that used in [4]. Simulated parameters were extraction fraction, E, (0.5–0.9), plasma flow, F_p, (0.03–0.27 ml (ml tissue)$^{-1}$ min^{-1}), mean transit time T_c (0.05 - 1.25 min) and extravascular extracellular volume, v_e, (0.1-0.6 ml (ml tissue)$^{-1}$), giving a total of 1050 parameter sets. Curves and AIFs were downsampled from the original 1.5 s time resolution (t_{res}) to 3 s, 4.5 s and 6 s, and Gaussian-distributed noise was added with standard deviations of 0.02, 0.05 and 0.1. The curves were fitted using the AATH model as described in [3]. For data simulating a well-designed DCE-MRI experiment (t_{res} = 1.5 s, noise σ = 0.05), curves were fitted using an AIF with the first pass peak height varied between ± 25 % to simulate an incorrectly measured AIF.

Results: The influence of temporal resolution and SNR on the fitted AATH parameters is shown in Fig. 1. For each temporal sampling regime and noise level the median percentage errors and interquartile ranges are shown for each parameter, averaged over all parameter values. All parameters were relatively robust to temporal undersampling and noise. Median errors remained below 10 % at 1.5 s temporal sampling across all noise levels, and below 20 % up to 6 s sampling. For T_c, both the median error and the interquartile range increased with noise level and with sampling over 1.5 s. The trend in error with T_c magnitude is plotted in Fig. 2 for high and low quality data, showing very large errors for short T_c. The impact of AIF peak height error on AATH parameters is shown in Fig. 3. Under the conditions of a well-designed DCE-MRI experiment, an underestimate of the AIF peak results in an overestimate of blood flow, and *vice-versa*. For all other parameters this trend is reversed.

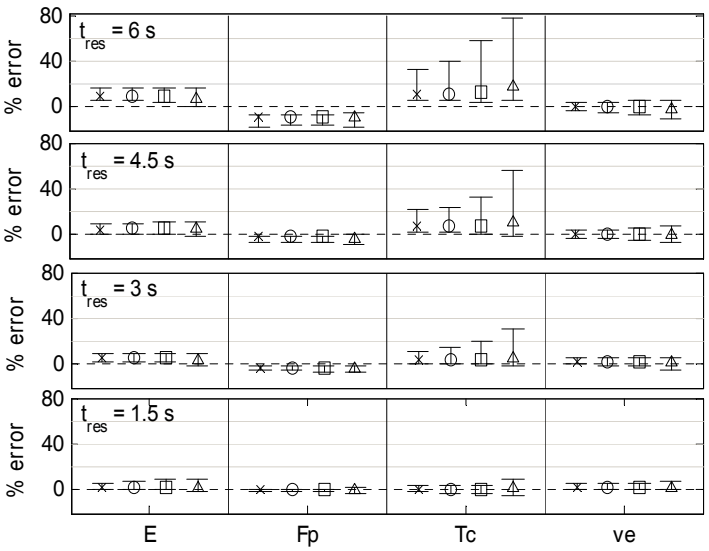

Figure 1 - Errors in fitted AATH parameters under different temporal resolutions and noise levels. Noise levels are: noiseless (x), noise σ = 0.02 (o), noise σ = 0.05 (□), noise σ = 0.1 (Δ)

Discussion: This simulation study investigated the influence of three key factors on parameter accuracy for the AATH model. The advantage of using this model is that it allows separate estimates of blood flow and permeability, which is not possible with simpler models. Although the AATH model has been used in several previous studies, the expected accuracy of the parameters has remained unclear. The results of this study showed that signal to noise ratio did not have a large influence on parameter accuracy, with errors remaining within ± 10 % for all noise levels at 1.5 s temporal sampling. A temporal resolution of 1.5 s is required if all parameters are to be measured with minimal bias, but this can be relaxed to 6 s if T_c need not be measured and small amounts of bias in E and F_p can be tolerated. T_c showed the largest bias and range of errors and the greatest sensitivity to temporal sampling and noise. This result is consistent with previous studies showing large uncertainties associated with T_c for an individual fit [5] and emphasizes that the sampling interval must be smaller or comparable with T_c [1] to capture information about the initial transit through the vasculature. F_p showed a slight bias when the temporal sampling was inadequate to characterise the initial part of the curve which is most sensitive to this parameter [5]. For v_e, slower sampling reduced bias, possibly as a result of parameter covariance with E and F_p. Errors in the measurement of the AIF peak height propagated into errors in parameter estimates, with a 10% error in peak height resulting in an error of at most 10 % in each parameter. The inverse relationship between peak height and blood flow is expected since F_p is the scaling factor for the AIF in the convolution describing the AATH model.

Conclusion: Obtaining data with a high temporal resolution is the most critical factor in ensuring accurate parameter estimates using the AATH model, but this requirement can be relaxed if larger biases can be permitted and T_c need not be accurately measured. The trends observed and the data requirements recommended in this study are applicable to implementations of the AATH model in both MRI and CT data.

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References: [1] St Lawrence *et al,* JCBFM 1998;18:1365 [2] Johnson *et al,* Am J Physiol 1933;210:1299 [3] Kershaw *et al*, JMRI 2009;29:641 [4] Parker *et al,* MRM 2006;56:993 [5] Koh *et al*, MRM 2006;56:986

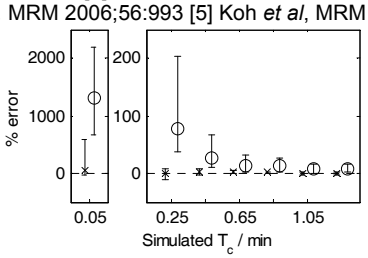

Figure 2 – Trend in error as a function of T_c for good quality data (x) [t_{res} = 1.5 s, noise σ = 0.05] and poor quality data (o) [t_{res}= 6 s, noise σ = 0.1]

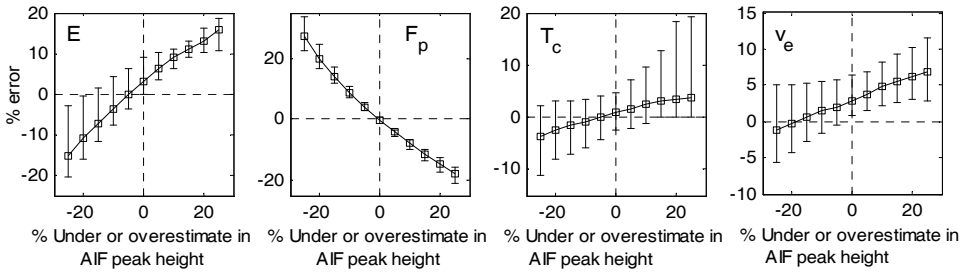

Figure 3 – Effect of AIF peak height measurement error