Quantitative analysis of moderate temporal resolution DCE-MRI data from rapidly enhancing breast tumours: a robust pharmacokinetic-empirical hybrid approach

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Introduction: Dynamic contrast-enhanced MRI (DCE-MRI) of breast tumours is now an established clinical tool, but the relative merits of high spatial and high temporal resolution, and the benefits of pharmacokinetic (PK) analysis over empirical (model-free) analysis are still debated [1]. Some breast tumours achieve maximum enhancement almost instantaneously, suggesting a very high vascular signal contribution, and if moderate temporal resolution DCE-MRI is carried out (~30 s when imaging both breasts), then PK models can become ill-conditioned, i.e. demonstrating very large parameter variability for only small changes in the noise and the best fit curves [2]. Empirical, or model-free, methods for quantifying the shapes of the separate blood plasma and tissue curves produced by a modified Tofts-Kermode-Kety PK model were investigated for use in cases where ill-conditioning is demonstrated.

Methods: DCE-MRI was carried out at 3.0 T using a GE Signa HDx scanner, a dedicated phased-array breast coil and a 3D chemical shift imaging sequence to obtain fat-suppression (VIBRANT; typical TR / TE = 4.1 / 1.6 ms fractional; flip = 10˚; bandwidth = 41.7 kHz; FOV / matrix = 22 × 22 cm / 220 × 160; slice thickness = 4 / –2 mm). Three representative cases from each of four different curve types (Type 1a shallow continuous enhancement, Type 2 plateau, Type 3 pronounced wash out, and Type 3b extremely rapid enhancement with marked wash out) were imaged with temporal resolutions ranging from 29.5 to 37.8 s, and with twelve time-points giving a scan-time range of 5.41 to 6.93 minutes. The sagittal plane was imaged so a reliable, patient-specific arterial-input function could not be obtained, therefore a low temporal resolution population AIF (PAIF) was obtained from a bi-exponential fit to the post-one minute section of the high-resolution Parker PAIF [3]; i.e. ignoring the early bolus peaks and assuming instantaneous mixing. Enhancement-time courses were obtained from whole-tumour, multi-slice regions of interest using in-house IDL software (ittvis.com), and PK modelling was performed using MATLAB (mathworks.co.uk). A traditional three-compartment (tissue interstitial space; blood plasma and whole-body interstitial space) Tofts-Kermode-Kety (TKK) model [4, 5] was modified to include a significant signal contribution from blood plasma giving the following parameters: bolus arrival time (BAT), K^{trans}, interstitial space volume fraction (v_e) and plasma volume fraction (v_p). Parameter uncertainties were estimated using a boot-strap technique whereby fit residuals were randomly selected with replacement and combined with the best-fit curve to give a set of simulated data curves which were themselves fitted to yield parameter standard deviations [6]. Empirical analysis was then performed on both the raw signal-time data and the best-fit plasma and tissue curves to yield amplitudes (maximum slopes) and areas under the curves (AUCs) up to a five minute cut-off. The TKK plasma:tissue AUC ratio was also calculated.

Results: An example model fit for a Type 3b curve is shown in Fig. 1 where the instantaneous enhancement and the dominant plasma volume fraction can be seen. In all three Type 3b cases, boot-strapping indicated that the model was ill-conditioned, with the relative standard deviation of the v_e parameter exceeding 100%, and in the absence of a way to estimate the BAT prior to fitting [6] with Type 3b curves it was decided only to use the empirical data. The medians and ranges of the empirical data are shown in Fig. 2 (LoI = line of identity), and it can be seen that the empirical parameters obtained from the TKK fits (on the vertical axes) are better able to discriminate between the Type 3 and Type 3b curves than the empirical parameters obtained from the raw data.

Figure 1:

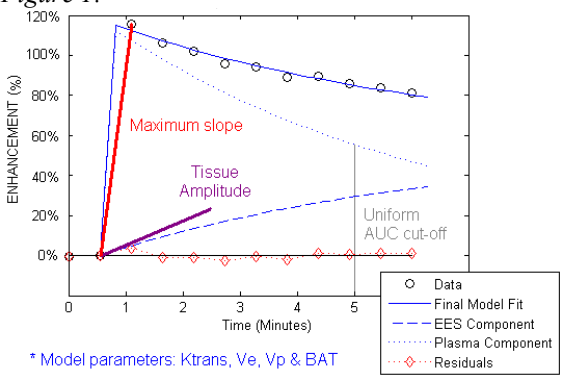
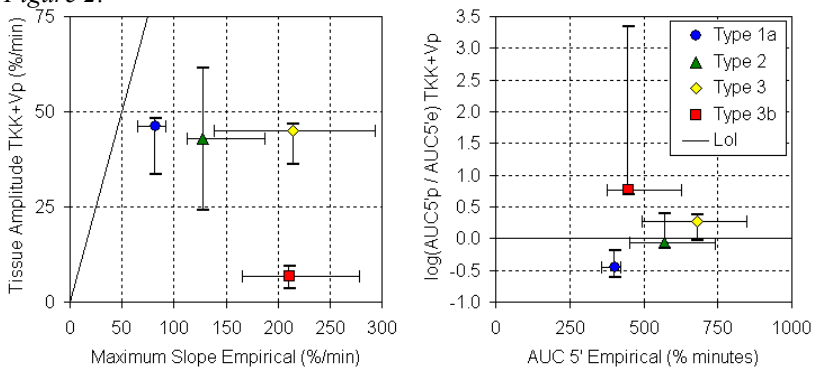


Figure 2:



Conclusions: It has been shown that even a relatively simple TKK model can become ill-conditioned, and therefore unreliable and non-robust, in a moderate temporal resolution regime when contrast enhancement is extremely rapid. In such cases a hybrid pharmacokinetic-empirical approach may be adopted which has the potential to offer greater diagnostic/prognostic discrimination.

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