Dual-relaxation, temporally-constrained, dynamic contrast-enhanced MRI using inversion recovery TrueFISP

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Introduction: Inversion recovery (IR) TrueFISP imaging sequences have recently been used to acquire dynamic contrast enhanced (DCE) MRI data due to their short acquisition time, sensitivity to changes in tissue longitudinal relaxation times and superior signal-to-noise characteristics [1]. Use of an inversion recovery preparation offers the ability to quantify relaxation time changes at each dynamic time point, thereby improving the accuracy of the subsequent pharmacokinetic analysis, albeit at the expense of temporal resolution. However, the signal intensity of such sequences is also sensitive to transverse relaxation (T_2=1/R_2). In the novel analysis approach outlined in this study, T_2 relaxation changes induced by Gd-DTPA are estimated in addition to T_1 changes, using data acquired with an IR-TrueFISP sequence. Furthermore, data analysis is undertaken using a maximum likelihood approach that 1) undertakes pharmacokinetic modelling on an entire dynamic, multiple-inversion time dataset (8 inversion times and 75 time points), thereby providing temporal constraint within the T_1 and T_2 estimation, 2) incorporates a high signal-to-noise, 20 inversion time reference IR-TrueFISP acquisition for accurate native T_1 and T_2 estimation and 3) takes into account the Rician noise distribution associated with magnitude MR data [2]. A pilot study to evaluate the approach is described here, using orthotopic PC3 prostate tumours.

Background Theory:

Data Model: The signal intensity, *S*, given by an IR-TrueFISP sequence is given by $S(TI\,|\,T_1,T_2) = S_{stst}(1-INVe^{-TI/T_1^*})$ [3] where TI is the inversion time. A complex dependence exists between the parameters *INV*, T_1* and flip angle and the parameters of greater interest, T_1 and T_2, which is described in [1]. Upon delivery of Gd-DTPA, we assume that $r_{12}C_t(t) = 1/T_{12}(t) - 1/T_{12,native}$ where $C_t(t)$ is the tissue concentration of Gd-DTPA, r_{12} is the T_1 or T_2 relaxivity and $T_{12,native}$ is the native (pre-contrast) T_1 or T_2. Pharmacokinetic modelling of $C_t(t)$ is provided by the Tofts and Kermode model [4].

Maximum Likelihood: The likelihood that a set of data accords with a data model, for a particular set of parameter values, is given by the product of the probability of each data point for a given noise distribution. Maximum likelihood aims to locate the set of parameter values at which this probability is greatest. Magnitude MR data are Rice-distributed [2], so, to avoid biasing parameter estimates, a likelihood function was utilised that took this distribution into account [5].

Methods and Materials:

Tumour models: PC3 prostate tumours were propagated in the ventral prostate gland of 6 NCr nude mice and allowed to grow until palpable.

Data Acquisition: Each mouse was positioned supine in a 7T Bruker horizontal-bore MR scanner and a multi-slice, T_2-weighted spin-echo sequence was used to localise the tumour. Reference IR-TrueFISP data were acquired in a single slice through the centre of the tumour (TI=130-2592ms, 20 inversion times, TR=4ms, TE=2ms, flip angle=60°, 20 averages, slice thickness=1mm, FOV=3x3cm, matrix size=128x96). This was followed by a dynamic IR-TrueFISP acquisition (TI=130-1036ms, 8 inversion times, TR=4ms, TE=2ms, flip angle=60°, 2 averages, temporal resolution 9.4s, 75 acquisitions), with identical image geometry to the reference acquisition. The dynamic acquisition had fewer TIs than the reference acquisition in order to increase temporal resolution. At one minute following initiation of the dynamic acquisition, Gd-DTPA (Magnevist, Schering) was injected using a power injector (0.1mmol/kg).

Data Analysis: Parameter values were estimated on a pixel-by-pixel basis. Rician noise variance of the reference and dynamic data were estimated from regions of background noise. These were used in the calculation of a log-likelihood function that, as described above, incorporated the Rice probability density function [REF]. Reference and dynamic data were optimised simultaneously, resulting in 6 free parameters in the data model (K^{trans}, v_e, $T_{1,native}$, $T_{2,native}$, $M_{0,ref}$ and $M_{0,dyn}$). By optimising the complete set of dynamic and reference data simultaneously, dynamic T_1 values are implicitly constrained by the pharmacokinetic model and are significantly weighted by the reference measurement. As all parameters have support over positive values only, optimisation was performed over their natural logarithms. A literature-derived, bi-exponential arterial input function (AIF) was used for all studies, of the form $a_1e^{-m_1t} + a_1e^{-m_1t}$, with a_1= 2.55 mM, a_2= 1.2 mM, m_1= 4.8 /min and m_2= 0.06/min [6]. r_1 and r_2 were fixed at 4.1 s/mM and 3.8 s/mM, respectively (unpublished data).

Results and Discussion: Figure 1 shows example signal magnitude data from an example pixel, with the optimised data model overlaid. As can be seen, the reference signal magnitude initially decreases, then increases towards an equilibrium value, reflecting the transition from negative to positive signal intensity via a signal null. Around the signal null, the signal-to-noise ratio is by definition low, which emphasises the need to implement a maximum likelihood approach in place of a least-squares algorithm, as the noise in this region will be significantly non-Gaussian [2]. Across the cohort, the mean K^{trans}, v_e, $T_{1,native}$, $T_{2,native}$ were 0.064±0.008/min, 0.068±0.009, 1195±16/ms and 88±2/ms, respectively. Each of these values is in keeping with those previously published [7,8]. Mean peak Gd-DTPA concentration and $IAUGC_{90}$ (initial area under the Gd-DTPA curve) were 0.070±0.007mM and 0.058±0.006mM.min, respectively. This resulted in an average minimum T_1 and T_2 of 3.5±10.9ms and 3.3±1.7ms (an average decrease of 99.7% and 96.1%). This significant decrease in T_2 illustrates the requirement to incorporate changes in both T_1 and T_2 when using IR-TrueFISP to estimate tissue pharmacokinetics. Figure 2 shows parameter maps from a single example tumour.

Conclusions: Dual-relaxation DCE-MRI using IR-TrueFISP is a promising acquisition and analysis approach that provides physiologically realistic pharmacokinetic and native tissue MR parameter estimates. Further work is required to evaluate whether the proposed robust analysis approach results in improved parameter accuracy, as has been noted in similar optimisation approaches in other contexts [9]. Furthermore, inclusion of fractional blood volume, water exchange and a study-specific AIF into the analysis could provide further accuracy.

Acknowledgements: This work was supported by Cancer Research UK (C1060/A5117), NHS funding to the NIHR Biomedical Research Centre, The Royal Society and the Medical Research Council (G0700014)

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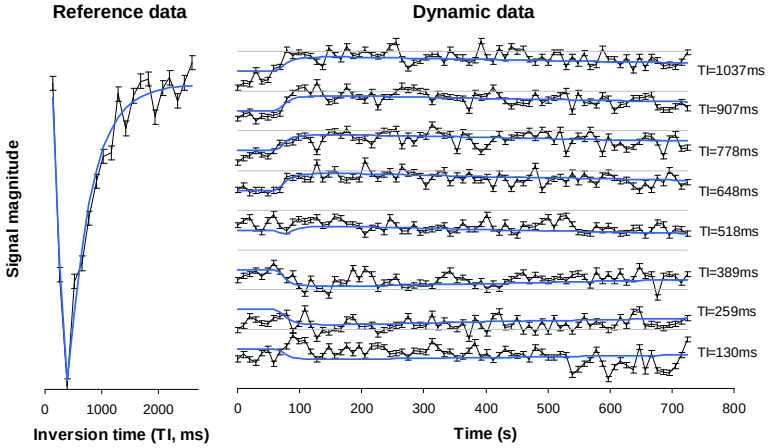

Figure 1: Reference and dynamic IR-trueFISP data from a single example pixel (black) with fitted data overlaid (blue). Error bars are given by the square of the Rician noise variance. Note that dynamic data with differing TI have been arbitrarily offset from one another for clarity.

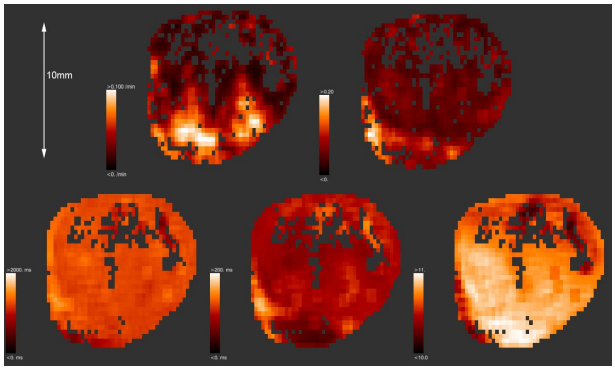

Figure 2: Parameter maps from an example PC3 orthotopic prostate tumour: (left to right, top to bottom) K^{trans}, v_e, $T_{1,native}$, $T_{2,native}$, $\ln(M_{0,dyn})$.