Joint estimation of precontrast $T_1$ and DCE-MRI perfusion and permeability parameters significantly improves precision of parameter estimates

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TARGET AUDIENCE Imaging scientists who use DCE-MRI to study perfusion and permeability, particularly in preclinical and clinical studies of cancer.

PURPOSE DCE-MRI can be used to spatially map estimates of biophysical parameters related to tumour perfusion and capillary permeability [1]. These parameters are commonly used in pre-clinical and clinical trials of novel anti-vascular and anti-angiogenic agents as they can provide early quantitative measurements of treatment efficacy [2]. Improving the precision of parameter estimates is important ethically and economically, as greater precision can help minimise the number of animal or human subjects required. We present a novel method for estimating DCE-MRI perfusion and permeability parameters from data acquired using a typical DCE-MRI protocol. The kebabon, and cut the other... 

THEORY DCE-MRI involves the acquisition of a series of images during the administration, uptake and washout of a contrast agent. Biophysical parameters related to tumour perfusion and capillary permeability may be estimated by fitting a tracer kinetic model, such as the two-compartment exchange model (2CXM: Eqn. 1), to measured signal-time curves via the spoiled gradient echo equation (Eqn. 2): 

$$C(t) = F_p A e^{-K_e t} + (1 - A) e^{-K_p t}$$ \hspace{1cm} (1)

$$S(T_1, M_0, C_t) = M_0 (\sin(\alpha t) e^{-T R C T R} + V_f e^{-T R C T_R})$$ \hspace{1cm} (2)

where $C_t$ is the modelled contrast agent concentration, $F_p, A, K_e$ and $K_p$ are the 2CXM parameters, $AIF$ is the arterial input function, $S$ is the modelled MR signal, $T_1$ is the pre-contrast $T_1$, $M_0$ is the equilibrium longitudinal magnetization, $t$ is the $T_1$ relaxivity of the contrast agent, and $\alpha$ and $TR$ are the flip angle and repetition times of the MR sequence. Conventionally, $T_1$ and $M_0$ are estimated prior to model fitting using a dedicated MR experiment. This can be done using a variable flip angle (VFA) experiment by fitting Eqn. 2 (with $C(t) = 0$) to signal intensities acquired at each of a number of flip angles. The estimates of $T_1$ and $M_0$ are then substituted into Eqn. 2 as fixed parameters, and $C(t)$ is varied (by performing an optimization) to fit the modelled signal to the measured dynamic data. In this approach $T_1$ and $M_0$, and the 2CXM parameters, are estimated sequentially. Measurement error in the VFA experiment will propagate through to error in $T_1$ and $M_0$, estimation, to errors in calculation of $C(t)$, to errors in estimates of the biophysical parameters of ultimate interest. Here we present an alternative approach, which recognises that while DCE-MRI sequences are not designed to measure ground truth using joint versus sequential estimation.

RESULTS Table 1 shows that joint estimation leads to significant improvements ($p < 0.05$) in the precision of all 2CXM parameters in the motion-free data. Joint estimation of $F_p$ and $v_p$, in the registered motion-corrupted data are significantly more precise than for sequential estimation. Figure 1 shows better agreement with ground truth using joint versus sequential estimation.

CONCLUSION Joint estimation improves the precision of all tumour perfusion and permeability measurements in motion-free data, and of $F_p$ and $v_p$, in registered motion-corrupted data. Improved registration should result in significantly more precise estimates of $F_p$ and $v_p$, also. In the context of DCE-MRI studies of cancer, joint estimation may help reduce required sample sizes, conferring both ethical and economic benefits.


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