SOURCES OF ERRORS IN PHARMACOKINETIC ANALYSIS OF DCE-MRI

Hallack A.[1], Chappell M. A.[1], Anderson E. A.[2], Gleeson F. V.[2], Gooding M. J.[3] and Schnabel J. A.[1]

[1]Institute of Biomedical Engineering, University of Oxford, Oxford, UK
[2]Department of Radiology and Oncology, University of Oxford, Oxford, UK
[3]Mirada Medical, Oxford, UK
Email: andre.hallackmirandapureza@eng.ox.ac.uk

Introduction

- Pharmacokinetic analysis of dceMRI has shown potential as a tool to predict and assess tumour treatment response
- Quantitative PK analysis can reveal more information from tumour micro-vasculature and increase the reproducibility of dceMRI studies
- It requires the estimation of the pre-contrast relaxation time (T_{10}) to convert signal intensity to contrast agent (CA) concentration curves
- T_{10} maps may be computed from a sequence of Spoiled Gradient Echo (SPGR) volumes with variable flip angles
- This method for T_{10} estimation assumes that no motion is present during the SPGR acquisitions

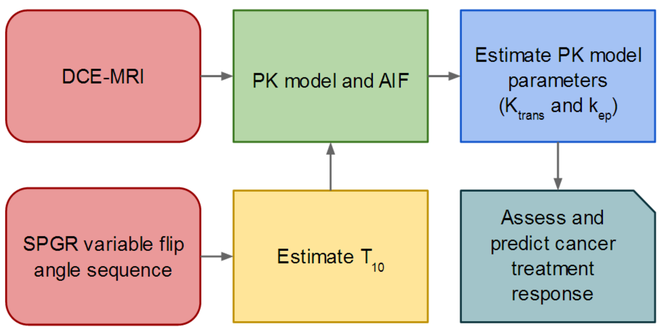

Fig. 1: PK model parameter estimation in dceMRI studies

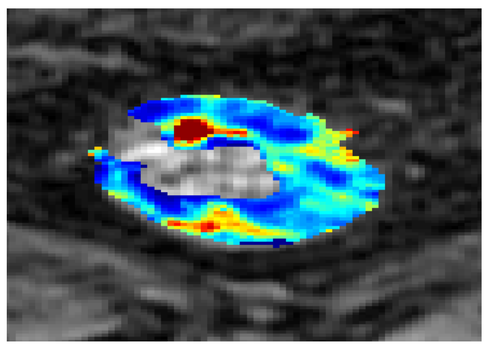

Fig. 2: K_{trans} map of colorectal tumour

Aim

Evaluate the effects of motion within variable flip angle SPGR sequences on T_{10} and subsequent PK model parameter (K_{trans} and k_{ep}) estimation

T10 Estimation

- Signal intensity in SPGR acquisitions relate to the relaxation time and equilibrium magnetization ($T_1$and M) by [1]:

$$S = M\sin(\alpha)\left[\frac{1-\exp(-TR/T_1)}{1-\cos(\alpha)\exp(-TR/T_1)}\right]$$

where α is the flip angle and TR the repetition time
- T_{10} and M_0 maps can be obtained from a sequence of variable flip angles by fitting the signal intensities curves over the several volumes

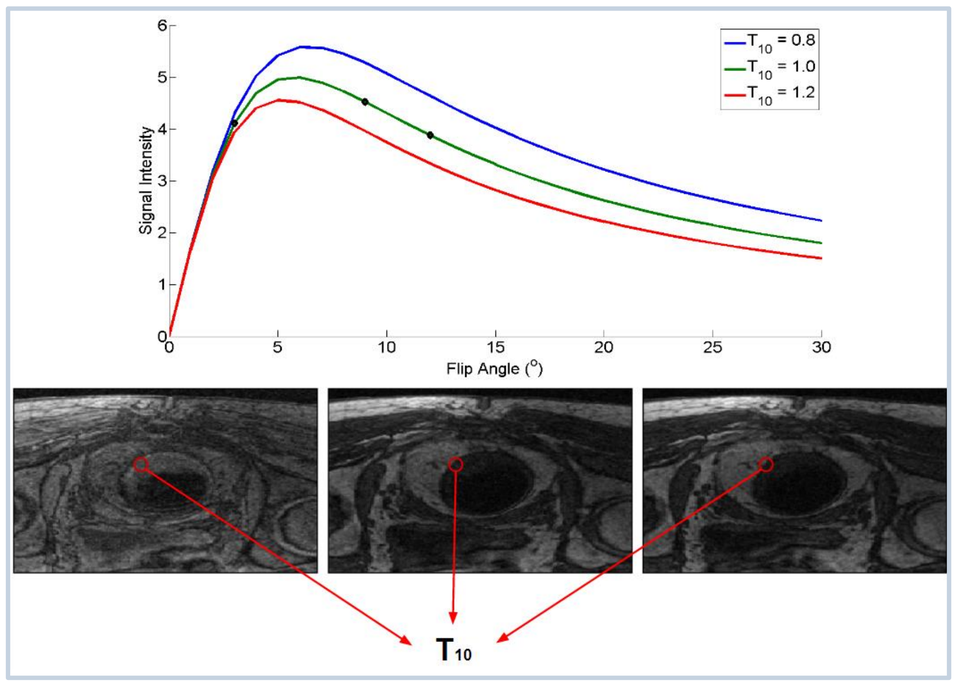

Fig. 3: T_{10} estimation by fitting a the signal intensity curve over three variable flip angle SPGR acquisitions

PK Modelling

- The CA enhancement on the extravascular extracellular space can be modelled by the Tofts model [2]:

$$C_e(t) = K_{trans}C_p(t) \otimes \exp(-k_{ep}t)$$

- C_p is the arterial input function (AIF). We used the Orton AIF [3], a population model
- The CA causes a shortening of the relaxation time which then relates to change in the dceMRI intensities:

$$\frac{1}{T_1} = \frac{1}{T_{10}} + r_1 C_e$$

- K_{trans} and k_{ep} are the desired model parameter estimated by fitting them to the dceMRI signal enhancement curves

Estimating motion in flip angle sequences

- 21 colorectal SPGR sequences with 3 or 4 acquisitions volumes each (3º, 9º, 12º and/or 15º flip angles)
- Rigid registration using Groupwise Normalized Mutual Information [4] was applied to each sequence
- The mean displacement found by the registration provided an estimation of the motion present within these acquisitions:

	Mean	Std Dev	Min	Max
Recovered Motion	0.43mm	0.34mm	0.00mm	0.90mm

Evaluating the effects of simulated motion on T10 estimation

- 21 T_{10} and M_0 maps were computed from clinical data and considered as ground truth data
- These maps were used to generate synthetic SPGR variable flip angle sequences
- Random B-Splines free-form deformation [5] was applied to the volumes within these sequences
- $\hat{T}_{10}$ was estimated from the motion corrupted sequences and compared to the ground truth maps

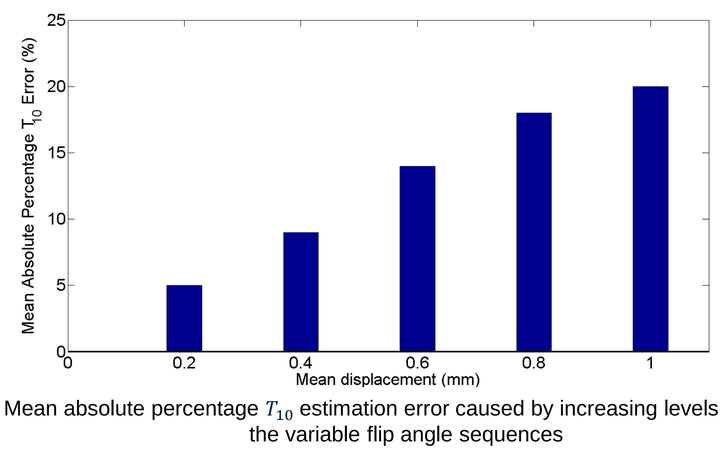

Fig. 4: Mean absolute percentage T_{10} estimation error caused by increasing levels of motion within the variable flip angle sequences

Evaluating the effects of inaccurate T10 on PK parameter estimation

- dceMRI signal intensity curves were generated using the Tofts model and the Orton AIF with T_{10}=1.0s and a range of PK model parameters
- $\hat{K}_{trans}$ and $\hat{k}_{ep}$ were estimated from the signal intensity curves using inaccurate $\hat{T}_{10}$ parameters and compared to the ground truth

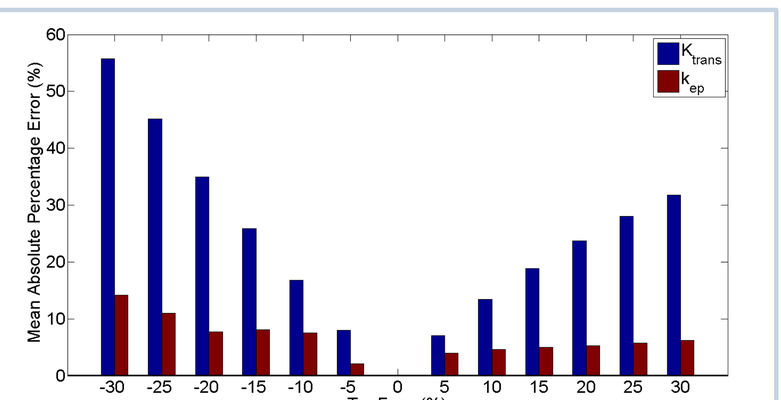

Fig. 5: Average K_{trans} and k_{ep} errors for different levels of T_{10} deviation

Summary

- Errors in T_{10} estimation are propagated and amplified to subsequent K_{trans} estimation
- k_{ep} is much more robust to T_{10} deviations
- An average displacement of 0.43mm was observed between volumes in variable flip angle SPGR sequences, and this motion is expected to cause 10% T_{10} estimation error leading to 16% mean K_{trans} estimation error

Acknowledgements

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[1] S. C. L. Deoni et al., “Rapid combined T1 and T2 mapping using gradient recalled acquisition in the steady state”, Magn. Reson. in Med., vol. 49, pp. 515-26, Mar. 2003.
[2] P. S. Tofts et al., “Estimating kinetic parameters from dynamic contrast-enhanced T1-weighted MRI of a diffusable tracer: standardized quantities and symbols”, J. Magn. Reson. Imaging, vol. 10, pp. 223–32, 1999.
[3] M. R. Orton et al., “Computationally efficient vascular input function models for quantitative kinetic modelling using DCE-MRI”, Phys. Med. Biol., vol. 53, pp. 1225–39, Mar. 2008
[4] K. K Bathia et al., “Groupwise Combined Segmentation and Registration for Atlas Construction”, MICCAI, pp. 532–40, 2007.
[5] D. Rueckert et al., “Nonrigid registration using free-form deformations: application to breast MR images”, IEEE. Trans. Med. Imag., vol. 18, pp. 712–21, Aug. 1999.