Dual Blood Supply Model and Analysis for Liver DCE-MRI Studies

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Introduction The use of Dynamic Contrast-Enhanced MRI (DCE-MRI) in the early stage evaluation of novel therapeutics is increasing[1]. Objective evaluation of DCE-MRI data requires the use of pharmaco-kinetic (PK) models to report agreed vascular parameters[2]. Existing PK models rely on a single input function (IF) supplying the tissue with contrast agent. We implemented a dual input model for evaluation of liver lesions which accounts for both arterial and portal contributions to blood supply[3]. It has been implemented in our software platform MRIW[4] to perform clinical trial DCE-MRI analysis. We demonstrate that Hepatic Perfusion Index (HPI) can be successfully modelled in addition to the conventional parameters K^{trans}, v_e and k_{ep}.

Theory A primary requirement of DCE-MRI is the accurate conversion of signal intensity variations into contrast agent concentrations. This conversion is performed using T1-weighted data obtained using a calibrated image ratio. MRIW fits the concentration-time curve data with a PK model which allows mixing of arterial and portal IF's using HPI as a partitioning term. The two IF's are specified in raised-cosine form[3] separately to reflect the different bolus shape found in the different feeding vessels. The portal IF is delayed relative to the arterial by a fixed value. On completion of model fitting a wide range of parametric images are available for evaluation, including K^{trans}, k_{ep}, v_e, HPI, arterial and portal perfusion, mean transit time (MTT) and IAUGC. MRIW supports model-based input function (IF) estimation using a range of input model forms[5], which are required for modelling with individualised IFs. Alternatively, population-based IFs can be used. Regions of Interest (ROI) are defined via a Graphical User Interface (GUI) to localise analysis where required.

Method Sets of three image slices (256x256) were acquired transaxially through the liver in continuous shallow breathing using a 2D-FLASH sequence. The reference scan (TR/TE/alpha = 20ms/4.7ms/3°) was proton density weighted. The dynamic scans (TR/TE/alpha = 10.2ms/4.7ms/35°) were acquired serially every 7.8s for 6.5 minutes with 0.1mmol/kg of Magnevist administered intravenously after 30s. Population-based IF's obtained from local clinical trial data were then used as inputs for the PK model when analysing the liver ROI.

Results The HPI map in fig. 1 clearly shows the delineation between the large, arterially supplied metastasis and the surrounding liver tissue, which shows mixed arterial/portal supply. The "non-involved" liver was found to have an HPI of 7-20% and an MTT of 15-25s in line with previously reported CT results[6]. The metastasis had an HPI of 1 and an MTT of 40-90s.

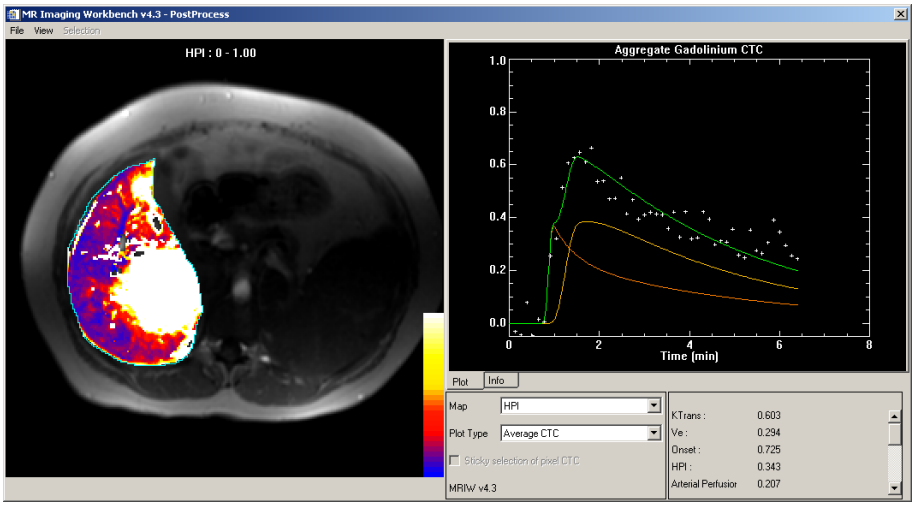

Figure 1. An HPI (0-1) map of a liver metastasis. This clearly delineates the arterially fed malignancy from the mixed arterial/portal feed of the rest of the organ. The plot on the right shows the arterial (orange) and portal (yellow) contributions to the overall fitted curve (green).

Post-Processing The post-processing environment in MRIW is highly interactive, giving the user easy to use tools for exploring the model results. Both whole-ROI and individual pixel results are available with raw data and fitted results plotted together for easy visualisation of uptake curve shape and goodness of fit. The heterogeneity of parameter distribution, and characteristic uptake curve shapes, in tumours can be explored using a dynamic model update on a pixel by pixel basis. Individual pixel results can be output for further evaluation in addition to various other forms of output available from the software: summary statistics, parametric images, histograms and per-pixel model results can be exported for further analysis in external packages.

The dual input liver model also permits calculation of liver specific parameters such as arterial (K^{trans} * HPI) and portal (K^{trans} * (1-HPI)) perfusion. Accuracy of conversion from signal intensity to T1, and by inference contrast agent concentration, was verified by comparison of calculated T1 maps to known tissue T1's. The software affords the flexibility of analysing the data repeatedly using a range of models at different evaluation sessions by making use of XML data descriptor files. This guarantees reproducible data evaluations which are essential for good clinical practice and audit trail in clinical trials. XML data descriptor files also allow the software to operate in batch mode and be integrated with a database. MRIW is cross-platform and will operate on operating systems for which the IDL Virtual Machine[7] is available (MS Windows 2000/XP, Mac OS X, GNU/Linux, Solaris).

Conclusion We have implemented a PK model incorporating the dual blood supply of the liver for use in the evaluation of clinical trial DCE-MRI data. This has been integrated into our MRIW software. This work was supported by Cancer Research UK (C1060/A5117) and EPSRC grants GR/T20434/01 and GR/T20427/01 (P).

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