Simultaneous Bayesian Estimation of Motion and Pharmacokinetic Parameters in Dynamic Contrast-Enhanced MRI for the Discrimination of Responders in Colorectal Cancer

Manav Bhushan[1], Julia Schnabel[1], Lydia Tanner[2], Fergus Gleeson[3], Sir Michael Brady[2], and Mark Jenkinson[4]

[1]Institute of Biomedical Engineering, Oxford University, Oxford, United Kingdom, [2]Department of Radiation Oncology and Biology, Oxford University, [3]Department of Radiology, Churchill Hospital, [4]Centre for Functional MRI of the Brain, Oxford University

INTRODUCTION: Patients with **colorectal cancer** often have downstaging chemo/radiotherapy prior to clinicians deciding whether to recommend resection, further chemo/radiotherapy, or surveillance/palliative care. A key factor in that decision is whether the patient is deemed to be a responder or non-responder to therapy. In extreme cases, all too frequent in practice, complete responders are sent for surgery while non-responders are subjected to chemotherapy for too long. In order to quantitatively assess a patient's (non-)response to therapy, we have developed a **Bayesian** framework for **simultaneous non-rigid motion correction (MC) and pharmacokinetic (PK) parameter estimation** in dynamic contrast-enhanced MRI (**dceMRI**). This enables comparison of the distributions of physiologically relevant parameters before and after therapy, and provides a mechanism for **discriminating between responders and non-responders** at an early stage during the treatment.

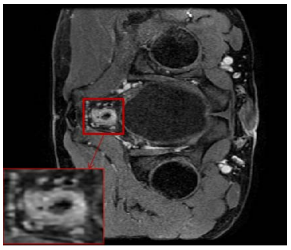

Fig 1: Axial slice of the post-contrast image volume, with tumour ROI shown in inset

METHODS: The aim is to estimate (a) the transformations that need to be applied to each image in the dataset to bring all images into alignment, and (b) the PK parameters that best explain the data.

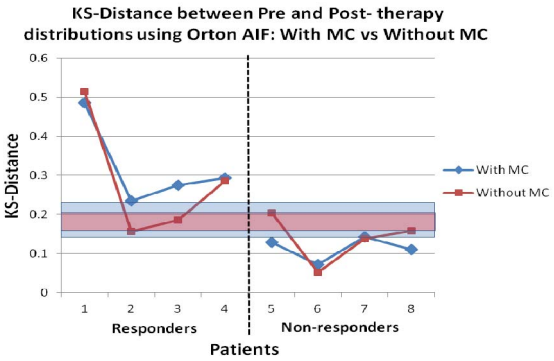

Fig 2: KS-distance using the Orton AIF. The blue band indicates the minimum (positive) gap between responders and non-responders using Motion Correction (MC). The red band indicates the minimum (negative) gap obtained without using MC.

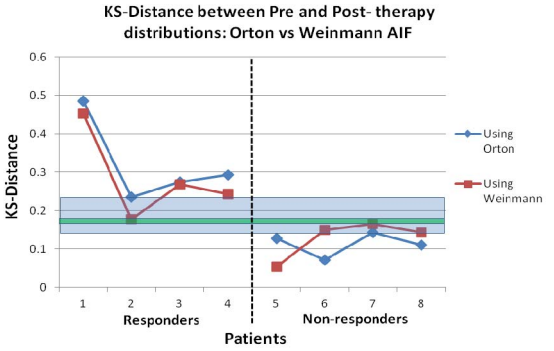

Fig 3: KS-distance using the Orton and Weinmann AIFs with motion correction. The wider blue band indicates the minimum (positive) gap between responders and non-responders using the Orton AIF, and the narrow green band indicates the minimum (positive) gap obtained using Weinmann AIF.

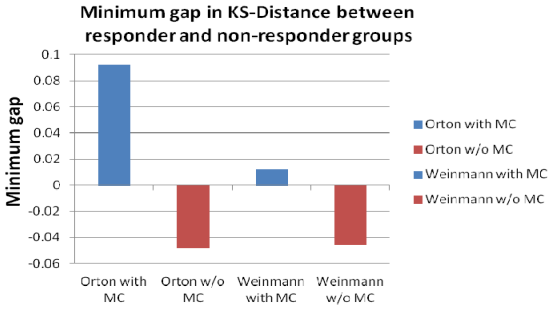

Fig 4: Minimum gap between responders and non-responders, i.e. difference between the responder with lowest KS-distance and the non-responder with highest KS-distance (between pre- and post-therapy distributions of K_{trans}), using each of the 4 methods. Blue indicates a positive gap and red indicates a negative "gap".

Similarity measure: Since traditional similarity measures are unable to deal with the time-varying contrast in dceMRI images, our algorithm is based on maximization of the **joint log-posterior probability** of the transformation and PK parameters, given the data and the known acquisition parameters. Like in most Bayesian similarity measures, two key factors lead to our similarity measure: (i) **Image formation model:** Assumes that the concentration of contrast agent (CCA) is a convolution between the Arterial Input Function (AIF) and the PK model. This implies that the MR intensity at each voxel can be expressed as a function of 2 PK-parameters. (ii) **Deformation model:** To ensure that the deformations being applied to each time-point image are smooth and invertible, we use the **logDemons** framework [1].

Generic framework: Our framework supports any PK model or AIF. In this implementation we have used the standard Tofts model [2] and experimented with two population-averaged AIFs: the Orton [3] and Weinmann [4] AIFs.

Algorithm: For each dceMRI scan, we select an ROI containing the tumour (Fig. 1 inset), and get an initial estimate of the two PK parameters at each voxel. Then we iteratively update the deformation vector (initialized zero) and the PK-parameters successively at each voxel so that the similarity measure is maximized.

Experiments: We tested the algorithm on dceMRI scans (LAVA sequence with TR=4.5ms, TE=2.2ms, flip angle=12°, 50 volumes, 12 sec/volume, voxel size=1x1x2 mm^3) obtained for 8 patients before and after 5 cycles of chemoradiotherapy. The probability distribution function (PDF) of the PK-parameter K_{trans} was determined for each scan using Orton/Weinmann AIF, and with/without motion-correction (MC). For each patient, we then calculated the Kolmogorov-Smirnov (KS) distance between the pre- and post-therapy distributions of K_{trans} and used this to classify the patient as a responder/non-responder. All 8 tumours were resected after therapy, and histopathology determined the rectal cancer regression grade (RCRG) of each tumour. This provided ground truth (4 were responders and 4 non-responders) to compare with our results.

RESULTS: We have previously shown [5] that in synthetic experiments, our algorithm recovered the deformation fields as well as the PK parameter maps used to generate the synthetic data (average voxel-wise error <0.7 mm for deformations, <0.04 for K_{ep} and <0.02 for V_e). Here we tested the method on real patient data to **quantify the benefit of using non-linear motion correction (vs no motion-correction)** and to compare the performance of the algorithm using **two different AIFs (Weinmann vs Orton AIF).**

Fig 2 shows the KS distance between the pre- and post-therapy distributions of K_{trans} obtained for all 8 patients using MC and without using MC. In Fig 3 we show the comparison between the Orton and Weinmann AIFs. Since the KS-distance is expected to be high for responders and low for non-responders, we have displayed the minimum gap in KS-distance between the group of responders and the group of non-responders in Fig 4. For a good classification method, this minimum gap should be high and positive.

CONCLUSIONS: For both AIFs, the algorithm using **non-linear motion-correction gave better discrimination between responders and non-responders** than the one without motion-correction and the **Orton AIF gave a better discrimination** than the Weinmann AIF when combined with motion-correction. We are now extending our framework to include other clinical factors and robust estimation of the T_{10} map.

REFERENCES: [1] Vercauteren et al., MICCAI, 2008; [2] Tofts et al, Magn. Reson. Med. 1991; [3] Orton et al, Phys. Med. Biol. 2008; [4] Wienmann et al, Physiol. Chem. Phys. Med. NMR, 1984; [5] Bhushan et al., MICCAI, 2011.