Evaluating sources of uncertainty on DCE-MRI parameter estimates when using different AIFs

Mihaela Rata[1], Matthew R Orton[1], Christina Messiou[1], Helen Young[2], Nandita de Souza[1], David J Collins[1], and Martin O Leach[1]

[1]*Radiotherapy and Imaging Department, CR-UK and EPSRC Cancer Imaging Centre, Institute of Cancer Research and Royal Marsden Hospital, Sutton, Surrey, United Kingdom,* [2]*Early Clinical Development, AstraZeneca, Macclesfield, Cheshire, United Kingdom*

Target: Physicists and clinicians using dynamic contrast-enhanced MRI in oncology

Introduction. Dynamic contrast-enhanced (DCE) MRI method is a technique employed in the assessment of tumour response to novel antiangiogenic therapy[1]. The technique is based on the analysis of the temporal bio-distribution of a MR contrast agent within the imaged tumour. Pharmacokinetic (PK) modelling of such data requires a reliable measure of the arterial input function (AIF) in order to obtain robust estimates of physiological parameters characterising tumour vascular properties. It was previously shown[2] that DCE-CT acquisitions can measure individual AIFs more accurately than DCE-MR, mainly due to the higher temporal resolution and insensitivity to flow of the CT technique. Following this result, we explore here the impact on main PK estimate of various sources of uncertainty affecting a DCE-MR acquisition. Three experiments were performed to separate sources of uncertainties.

Materials and Methods. MR Acquisition. Twenty-four DCE-MRI data were acquired with the following protocol: 1.5 T Siemens Avanto, 0.2 mg/kg Magnevist followed by 20 ml saline, both at 3ml/s; 3D FFE sequence with TR/TE = 3.05/0.89 ms, FA = 16°, 14 slices, thickness=5 mm, NSA = 1, IPAT = 2, FOV = 308x320 mm, 208x256 matrix. Dynamic scans were preceded by a calibration scan with the same parameters except FA = 3°, NSA = 8 to enable contrast quantification. Patients were imaged twice, 7 days apart, prior to treatment, for repeatability purposes. Patients with abdominal tumours (16/24) were imaged coronally using a sequential breath-hold technique optimised for liver lesions; two image volumes were acquired during each 6s breath-hold, followed by a 6s breathing gap, 40 volumes were acquired over a 4 minute period. Non-abdominal tumours (8/24) were imaged axially with a free breathing technique; 80 image volumes acquired continuously at 3.3 s/vol for 4.3 min.
CT Acquisition. Corresponding DCE-CT data were acquired axially with the following set-up: GE Lightspeed; Omnipaque 300; 0.5ml/kg followed by 20 ml saline both at 3-5ml/s; 5s-delay followed by breath hold cine covering 4x5mm, at 0.5 s/volume in centre of lesion of interest over 55s at 120 kV, 60 mA; following this, twelve breath-hold acquisitions at 10s intervals. CT data were acquired on the same day up to four before MR scanning.
Analysis.Three experiments (see **Table 1**) were investigated in order to separate variability sources of the PK estimate. The individual CT-AIF was measured from aorta/suitable vessel from DC-CT acquisitions[3], while the popCT-AIF value was averaged over our cohort of CT-AIFs. The extended Tofts model was applied to the MRI tumour data over four slices and the median K^{trans} was reported for each visit.
Repeatability was assessed using the coefficient of variation (CoV).

Data	*Experiment 1*		*Experiment 2*		*Experiment 3*	
	baseline 1	**baseline 2**	**baseline 1**	**baseline 2**	**baseline 1**	**baseline 2**
AIF	CT1	CT2	popCT		CT1	CT2
DCE	MR1	MR2	MR1	MR2	MR1	
Uncertainties	AIF var & CT-MR var & MR tissue var		CT-MR var & MR tissue var		AIF var & CT-MR var	

Table 1. Design of experiments.

Results. An example of typical population or individual CT-derived AIFs is shown on the left panel of **Figure 1**. The coefficient of variation for the DCE-MR parameter is displayed on the right panel. Overall, the split PK analysis between axial/coronal MR data indicated a better repeatability for the K^{trans} parameter when the acquisition plan is coronal (7% difference). The impact of AIF biological variability on K^{trans} estimate (measured by experiment 3, for all data) was less than 10%.

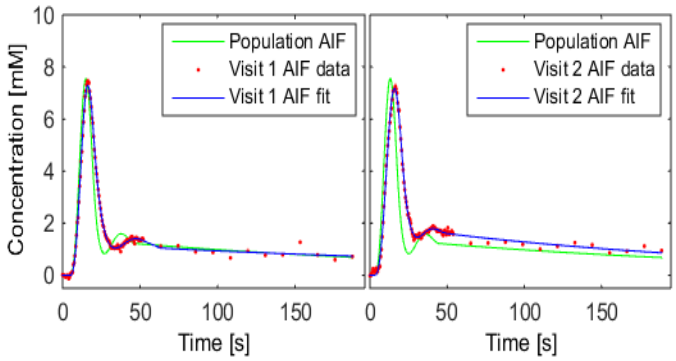
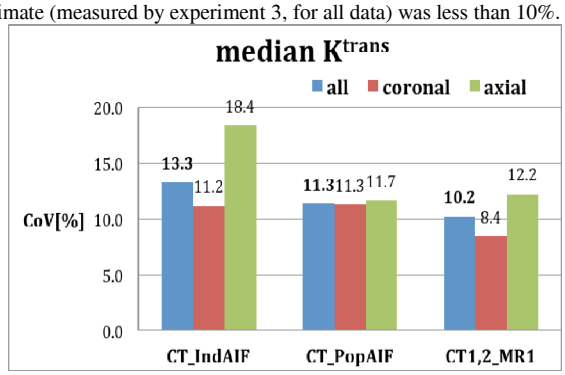


Figure 1. Left: An example of typical CT-derived AIFs.



Right: CoV of the K^{trans} parameter for all experiments.

Discussion. These results suggest that the CoV for K^{trans} when using the best possible measurement of AIF (i.e. the CT-derived one) is still worse when compared with a population derived AIF (experiment 1 vs. 2, all data), although only by a small difference of 2%.
The experiment no. 3 artificially removed the MR tissue variability by applying individual CT-measured AIFs from both baselines to the same DCE-MR datasets (i.e. baseline 1 only). Henceforth, the measured variability sums up just the intrinsic AIF variability and the physiologic variability between CT and MR measurements. These 2 factors effects cannot be further resolved; hence we can report only that the individual AIF variability is within 0%-10% range of K^{trans} repeatability. That means that a perfect measure of AIF (e.g. generated by future technology development) could potentially improve a K^{trans} repeatability up to 10%. Similar values were obtained when same individual AIFs were applied to the other MR datasets (baseline 2, data not shown here).
All CT-AIFs were measured axially, while DCE-MR data were axial/coronal acquisitions. The better K^{trans} repeatability for the coronal plan indicates the benefits of a controlled breathing over a free breathing approach (i.e. the axial acquisition).
Conclusion. The best CoV of measured K^{trans} is still obtained when using a population AIF. For best results the MR coronal acquisition plane is preferred. A perfect measure of AIF may yet improve a K^{trans} repeatability up to 10%. A complete discrimination of uncertainties affecting the K^{trans} estimate is not available with the actual datasets.

References. [1] Padhani AR, *et al*., *Clin Radiol.* 2001, 56:607–20; [2] Rata M, *et al., Proc. Intl. Soc. Mag. Reson. Med.* 22 (2014) 1098; [3] Orton MR, *et al*., *Proc Intl Soc Mag Reson Med.* 18; 1726.

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