Evaluation of reproducibility of measured arterial input functions and DCE-MRI derived model estimates obtained using either pre-bolus individual AIF's or population derived AIF's

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Introduction. Dynamic contrast-enhanced (DCE) MRI is emerging as a cancer imaging tool for diagnosis and assessing treatment response [1], obtained by sequential analysis of the temporal distribution of the contrast agent within the imaged tumour. The pharmacokinetic (PK) modelling of such a temporal distribution demands a reliable measure of the arterial input function (AIF). To achieve optimal estimates of the PK parameters, it may be preferred to measure patient-specific AIFs as an alternative to the usual population-based averaged AIF. This study explores this assumption by using individual AIFs measured from pre-bolus data [2] compared with results obtained from a population AIF [3]. First, the heterogeneity of the measured pre-bolus AIFs was explored over 3 segments of the aorta in order to define the most reproducible region. Second, a PK analysis based on the extended Kety model [4] tested the two different approaches.

Methods. <u>Acquisition.</u> Twenty-one DCE datasets for abdominal/ pelvic tumours were acquired on a 1.5 T Siemens Avanto, following a pre-bolus acquisition (1/10th of the standard dose i.e. 0.02 ml/kg Magnevist contrast agent). Both contrast doses were delivered by power injector at 3 ml/s, followed by 20 ml of saline. The pre-bolus protocol was: 2D FFE sequence, single slice coronal orientation, TR/TE = 5.5/1.21 ms, FOV = 440 mm, 128×128 matrix, temporal resolution 0.7 s/image, 60 pre-contrast images at 3° and 170 dynamics at 20°. The corresponding parameters for the 3D DCE acquisition were: TR/TE = 3.05/0.89ms, FOV = 380 mm, 104×128 matrix, temporal resolution 3s/ volume (14 partitions) pre-contrast images at 3° and
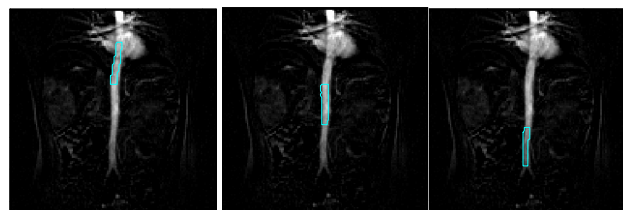

Fig1. Vertical segmentation of the aorta into 3 regions.

40-80 dynamics at 16°. To assess reproducibility, all patients were scanned twice, 7 days apart, prior to treatment.

<u>AIF measuring and PK analysis</u>. The descending aorta was extracted from the pre-bolus data, from diaphragm dome to pelvic bifurcation, manually drawn on subtracted images for each patient. Each individual aorta was automatically segmented into 3 equal vertical regions (see Fig.1), approximately corresponding to: 1 diaphragm-celiac bifurcation; 2 supra-renal; 3 infra-renal. A 4-parameter model was used to estimate the pre-bolus AIF and the full-dose AIF was obtained by convolution with a rectangular function accounting for the duration of the injection corresponding to the main DCE sequence [5]. The PK analysis was also run using a population AIF [3] and using the individual AIF estimates from the three vertical regions – all analyses used the same 4-parameter model representation [6]. Reproducibility coefficient r as derived from Bland-Altman analysis and defined in [7] was reported.

Results and discussions. Different forms and lengths of the aorta were observed among the patients. Capturing the entire aorta within a single slice positioned coronally was challenging and induced data variability. Due to the close vicinity with the heart, 12 of 21 AIF's measured from the upper aorta were significantly affected by pulsatile effects. Unsurprisingly, this segment was the least reproducible region of the AIF measurement.

Overall, the most reproducible pre-bolus AIF measure was within the middle segment (supra-renal aorta) for 3 out of 4 parameters characterizing the AIF (see an example in Fig.2). One estimate, m1, which defines the width of the peak enhancement, was more reproducible when using data from the infra-renal aorta. Due to the greater AIF variability among patients (mainly because of the coronal acquisition), the best reproducibility of the K^{trans} measure was obtained when using the population AIF (r=0.11). Exactly the same reproducibility was obtained when using an average AIF data set extracted from our cohort. The results from the pre-bolus AIF analysis translated to the PK analysis, suggesting again the supra-renal aorta as a better choice for reproducibility (r=0.27) over the lower aorta (r=0.42).

Conclusion. Employing a pre-bolus coronal acquisition to extract individual AIF's for PK analysis reduces the reproducibility of PK analysis. Both population AIF's offered better reproducibility. Our results suggest that a single-slice coronal acquisition is not the right way to acquire pre-bolus data. Further work is needed to develop more robust acquisition protocols to comprehensively test the pre-bolus concept for measuring AIFs.

References. 1. Padhani AR *Clin Radiol* 2001, 56:607–20; 2. Köstler H *Mag Res Med* 2004, 52(2):296-9; 3. Parker GJ *Mag Res Med* 2006, 56:993-1000; 4. Kety SS *Pharmacol Rev* 1951, 3:1–41; 5. Orton M, *Phys Med Biol.* 2008; 53(5):1225-39; 6. Orton M, *Proc. Intl. Soc. Mag. Reson. Med.* 17 (2009); 7. Koh DM, *Eur Radiol* 2009, 19: 2728–38.
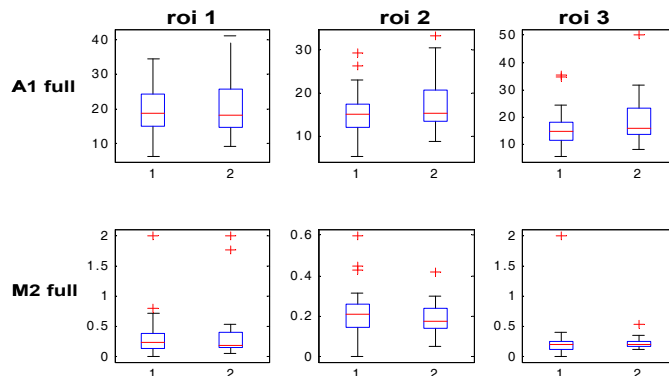
Fig2. Boxplots of amplitude peak and washout curve parameters showing inter-patient variability.

Reprod. coeff. r	Param.	Roi 1	Roi 2	Roi 3	Pop.
AIF estimates	a1 full	0.31	0.22	0.32	-
	m1 full	0.17	0.16	0.13	-
	a2 full	0.83	0.18	0.46	-
	m2 full	1.31	0.79	1.09	-
PK analysis	Ktrans	-	0.27	0.42	0.11

Table1. Reproducibility coefficients r [as defined in 7] of measured AIF parameters and the associated PK analysis, respectively.