Improved DCE-MRI Quantification of Pharmacokinetics based on an Accurate Approach for Individually Measured Arterial Input Functions

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INTRODUCTION

Accurate quantification of pharmacokinetic parameters in dynamic contrast-enhanced (DCE) MRI is known to depend on reliable measurement of the arterial input function (AIF), or plasma contrast concentration time-course. However, AIF characterization depends on accurate blood T_1 measurement, which is non-trivial and is subject to system imperfections and in-flow effects, and may be limited by additional factors such as partial volume error. In this study, we demonstrate improved pharmacokinetic estimation of blood volume (v_b) and endothelial transfer constant (K^{trans}) in rabbit muscle using individually measured AIFs that account for errors arising from B_1 field, in-flow, and partial volume. The proposed technique provides a simple means for direct AIF determination, thereby circumventing the need to adopt conventional alternatives (standard curve [1] or measured cohort-average [2]) and enabling individual differences to be easily accounted.

METHODS

Female rabbits (n=10) were imaged on a 1.5-Tesla MRI system (Signa EXCITE TwinSpeed, GE), using an 8-channel transmit/receive knee-array coil over the abdomen. Gadomer (Schering) was bolus-injected via the ear vein (0.033 mmol/kg). Pre-injection blood T_1 was measured using a 3D fast SPGR sequence (FA=2°,10°,20°) and segmented SE-EPI (60°/120°, 120°/240°) to correct for B_1 variation [3]. DCE-MRI with 3D T_1-weighted SPGR was acquired before and for 5 min after contrast injection [TR=5.2, TE=1.3 ms, FA=15°, FOV=12 cm, SL=3 mm, 256×224×16 matrix, 0.75 FOV, 1 NEX, BW=31 kHz, 14 s per dataset]. Single time-point measurements at a higher resolution (4 NEX) were taken over the next 60 minutes.

Pre-injection T_1 maps corrected for B_1 errors were computed as described in [3]. Plasma contrast concentration was determined assuming linearity with the change in $1/T_1$, a relaxivity of 16 $s^{-1}mM^{-1}$ [4], and a hematocrit of 0.2857 [5]. A region-of-interest (ROI) was manually defined on the iliac artery at least 9 cm distal from entry into image slab to eliminate in-flow effects. Only purely vascular, non-partial volume voxels were retained in the ROI (peak concentration changes within the top 25% of the maximum peak change in the first 15 s post-contrast). ROI-averaged T_1 and plasma concentrations were obtained, the latter used to determine the AIF.

Measured AIFs were fitted to a bi-exponential decay function and then applied to a two-compartment pharmacokinetic model [6] to estimate v_b and K^{trans} in resting skeletal muscle. Mean v_b and K^{trans} values were obtained in each rabbit by averaging across at least three ROIs.

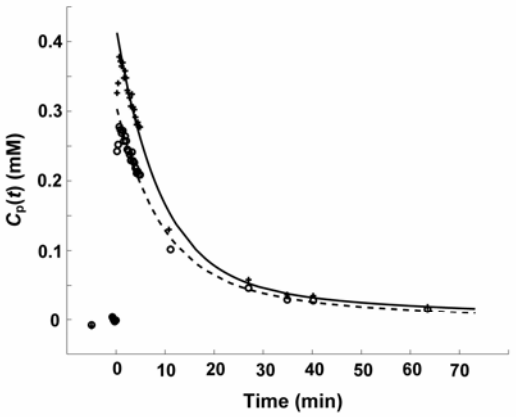

Fig. 1. AIF measurement in one rabbit using corrected (+) and uncorrected (o) pre-injection blood T_1, along with fitted biexponential decay curves.

RESULTS

Measured blood T_1 (1267±72 ms) agreed with literature reports (1262±80 ms [7], 1318±76 ms [8]). Reproducibility of uncorrected T_1 (1544±173 ms) was improved by correcting for B_1 variations (0.83 – 1.14), while correction for partial volume improved only accuracy (1408±176 ms). Figure 1 illustrates AIFs measured in one rabbit, derived from corrected and uncorrected pre-injection blood T_1's. Note that AIFs fit well to a biexponential decay function; fit parameters are compared to literature values for Gadomer clearance in rabbit (Table 1), showing better agreement for corrected AIFs. Parameters v_b (2.47±0.65%) and K^{trans} ($3.6±1.0×10^{-3}$ min^{-1}) derived in muscle from corrected AIFs were more reproducible and agreed better with literature values (Fig. 2)

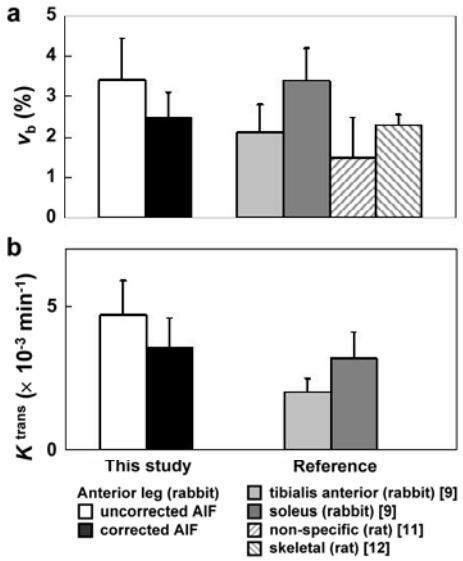

Fig. 2. Comparison of v_b and K^{trans} to literature values (mean ± SD). K^{trans} comparison based on Gadomer.

CONCLUSIONS

The proposed method enables accurate in vivo blood T_1 and AIF measurements and can be easily implemented in a range of DCE-MRI applications to improve both the accuracy and reproducibility of pharmacokinetic parameters.

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Table 1. AIF measurements of Gadomer clearance in rabbits (n=10) using corrected and uncorrected pre-injection blood T_1: literature comparison of biexponential decay fit parameters (mean ± SD).

Ref.		Pre-injection blood T_1 (ms)	Amplitudes (kg/L)		Decay rate constants (min^{-1})	
			A_1	A_2	m_1	m_2
This study	Corrected AIF	1267 ± 72	9.09 ± 2.62	2.60 ± 1.85	0.143 ± 0.040	0.034 ± 0.024
	Uncorrected AIF	1544 ± 173	6.33 ± 1.84	2.41 ± 1.21	0.139 ± 0.034	0.039 ± 0.021
[9]			28.1	2.4	0.17	0.02
[10]			23.4	1.59	0.173	0.022