An experimentally-derived functional form for a population-averaged high temporal resolution arterial input function

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Introduction An accurately measured arterial input function (AIF) is desirable for kinetic modelling using contrast agents. However, in many settings it is not possible to perform such a measurement reliably, either due to data acquisition constraints or due to the lack of a suitable artery within the imaging field of view from which to obtain an AIF. One pragmatic solution to this problem is to use the same assumed AIF for all patients in a study[1]. To date, only a low temporal resolution assumed AIF has been proposed, based on invasive blood sampling in 5 volunteers[1,2]. This AIF has been shown to lead to significant errors in the accuracy with which kinetic parameters such as K^{trans}, v_e, and v_b can be quantified[3]. Here we present a population-averaged AIF derived from 113 individual AIFs measured in the abdomen or pelvis of patients at a significantly higher temporal resolution than previously reported. A functional form for this population AIF is suggested, providing a standardised AIF of greater accuracy than has been available previously.

Patients 23 patients with advanced cancer demonstrating abdominal or pelvic masses were enrolled in a multi-visit dynamic contrast-enhanced (DCE)-MRI study to assess the efficacy of a novel anti-vascular treatment. 21 of the patients were scanned 5 times, with 2 patients receiving 4 scans, giving a total of 113 DCE-MRI sessions. At each visit, each patient underwent a DCE-MRI protocol consisting of a baseline volume variable flip angle gradient echo T_1 measurement followed by a series of spoiled gradient echo T_1-weighted volumes covering the period of gadodiamide contrast agent administration (Omniscan, Nycomed).

DCE-MRI Protocol All data were acquired on a 1.5T Philips Intera system using the whole body coil (Q body coil) for transmission and reception. The baseline T_1 measurement consisted of 3 axial spoiled Fast Field Echo (gradient echo) volumes with flip angles 2, 10, 20 degrees, respectively and 4 NSA. The dynamic series consisted of 75 consecutively-acquired axial volumes with a flip angle of 20 degrees, 1 NSA, and a temporal resolution of 4.97 s. All studies maintained the same number of slices (25), field of view (375 mm × 375 mm), matrix size (128 × 128), TR (4.0 ms), and TE (0.82 ms). Elliptical k-space sampling, partial Fourier encoding, overcontiguous slice spacing, and partial echo acquisition were used to improve temporal resolution. Slice thickness was 4 mm for small target lesions or 8 mm for larger lesions, giving volume coverage of 100 mm or 200 mm, respectively.

Contrast Agent Administration 0.2ml/kg of Omniscan 0.5mmol/ml (Gd-DTPA-BMA; gadodiamide) was administered intravenously via the antecubital vein at the beginning of the 6th dynamic volume using a Spectris power injector (Medrad, Inc) at a rate of 3 ml/s, followed by an equal volume saline flush, also at 3 ml/s.

AIF Extraction A previously described automated AIF extraction method was employed[4]. Operator interaction was limited to identification of the slice from which to extract the AIF. The optimum slice is one that is sufficiently distal to allow adequate saturation of the flowing blood signal, but not within the outer slices of the axial volume, where significant RF inhomogeneity is present. AIFs were extracted from either the descending aorta or iliac arteries, depending on volume location (which was dictated by target tumour location). Signal intensity was converted to concentration of contrast agent by employing the standard relationship between a spoiled gradient echo signal and T_1[5]. A contrast agent relaxivity of 4.5 $s^{-1}mM^{-1}$ was assumed. Figure 1 shows an example of AIFs extracted from a single individual over 5 visits.

Population AIF and Functional Form Each AIF was manually shifted in time to ensure that the AIF first pass peak occurred at the same time point. Figure 2 shows the population-averaged blood concentration $C_b(t)$ drawn from the 113 DCE-MRI sessions. To provide a functional form of the AIF we fit a mixture of 2 Gaussians plus an exponential modulated with a sigmoid function:

$$C_b(t) = \sum_{n=1}^{2} \frac{A_n}{\sigma_n\sqrt{2\pi}} \exp\left(-(t-T_n)^2 / 2\sigma_n^2\right) + \alpha \exp(-\beta t)/\left(1+\exp(-s(t-\tau))\right)$$

where A_n, T_n, and σ_n are the scaling constants, centres, and widths of the n^{th} Gaussian, α and β are the amplitude and decay constant of the exponential, s and τ are the width and centre of the sigmoid. The fitted values for each parameter are given in the table. The resulting model fit is shown in Fig. 3.

Discussion Using an automated AIF extraction technique we have generated AIFs successfully from 113 patient visits, providing a representative population of AIFs. The average AIF over this population shows the expected features of a first pass and a recirculation peak, followed by a prolonged washout, and is compatible with previously reported values of blood contrast agent concentration[2,6]. We have successfully modelled this population AIF and provide a functional form that may be used in place of previous low temporal resolution standard input functions, with a likely benefit in accuracy of kinetic modelling output parameters.

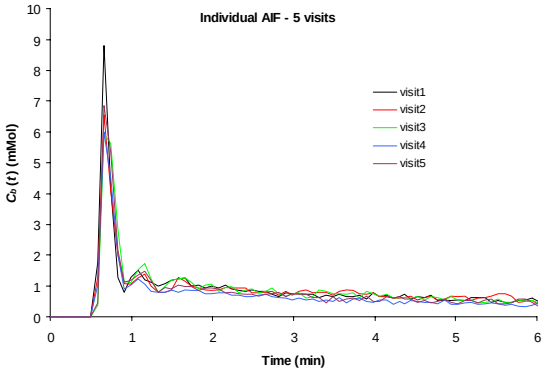

Fig. 1. Automatically-extracted AIFs from one patient over 5 visits.

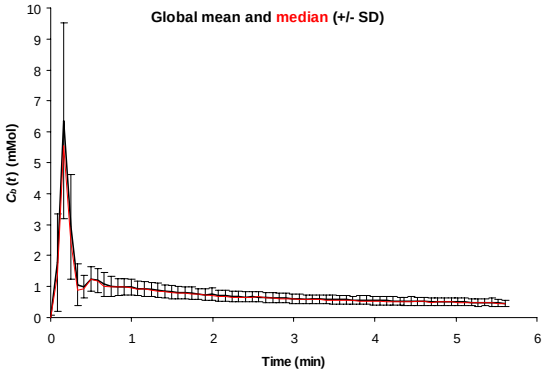

Fig. 2. Global mean AIF (black) and global median AIF (red). Error bars depict +/- 1 SD across the population of 113 AIFs.

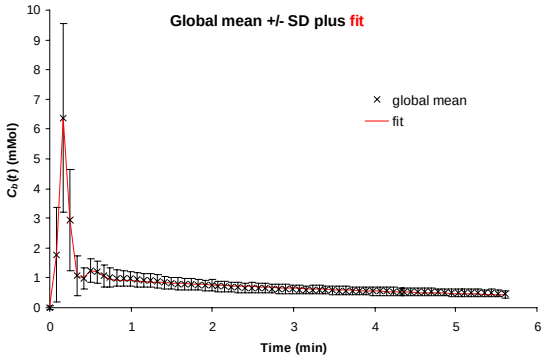

Fig. 3. Global mean (crosses) and model fit to data (red). Error bars depict +/- 1 SD across the population of 113 AIFs.

A_1	A_2	T_1	T_2	σ_1	σ_2
0.833 mMol.min	0.336 mMol.min	0.171 min	0.364 min	0.055 min	0.134 min
α	β	s	τ		
1.064 mMol	0.166 min^{-1}	37.772 min^{-1}	0.482 min		

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Acknowledgements We are grateful to Yvonne Watson, Karen Davies, and Lynn Broughton for assistance in protocol development and patient scanning.