To assume or not to assume blood T_1 for AIF measurement in DCE-MRI?

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Introduction In 3-D dynamic contrast-enhanced MRI (DCE-MRI), tracer kinetic modeling can be used to extract parameters related to tumor microvascular function, such as the endothelial transfer constant K^{trans}. An important step in the calculation of contrast agent concentration ([CA]) is the measurement of T_1 (1) in both the tumor tissue and blood. Many challenges to T_1 measurement, particularly in flowing blood where the arterial input function (AIF) is measured, include blood inflow effects, B_1 inhomogeneity and partial voluming (2) and so an assumed value of T_1 is often used to avoid these sources of error. In this study, we test the validity of this approach to a typical 3-D DCE-MRI study scenario where no correction is made for blood inflow or B_1 inhomogeneity and consider the effects of assuming a blood T_1 value on the measurement of the AIF and subsequent tracer kinetic parameterisations.

Data Acquisition A single patient who was enrolled in a Phase I DCE-MRI clinical trial to assess the efficacy of a novel antivascular drug was chosen as a representative data set to be retrospectively investigated. The patient was scanned at 1.5T using a Philips Intera machine (Philips Medical Systems, The Netherlands), using an axial volume protocol with the aorta running though all slices. Baseline T_1 was measured using the variable flip angle method and a 3-D Fast Field Echo (T1-FFE) sequence with the following parameters: 2°, 10° and 20° flip angles, TR/TE = 4.0/1.02 ms, FOV = 375 x 375 mm, matrix = 128 x 128, slices = 25, thickness = 4 mm. The dynamic image acquisition used the same parameters with a flip angle of 20°, 75 dynamic timepoints and a temporal resolution of 5 s. On the sixth dynamic timepoint, 0.1 mmol/kg of body weight of 0.5 mmol/ml Omniscan (GE Healthcare) was administered through a Spectris power injector (Medrad Inc.) at a rate of 3 ml/s followed by an equal volume of saline flush also at 3 ml/s.

Data Analysis Firstly, signal intensity time series from the aorta were extracted for each of the 25 slices in the volume, taking care to avoid partial volume errors. These AIFs were then converted to units of concentration (C_p) using the methods presented in (1) with the baseline blood T_1 estimated using either our measured value of T_1 at each slice location or an assumed T_1 value (1253 ms, within the blood T_1 range found in literature (3) and the blood T_1 measured at slice 18 of our volume – the point at which blood inflow effects are negligible in this DCE-MRI data set (2)). A "true" representative tumor residue curve (C_t) was simulated in MATLAB (The Mathworks, Natick, USA) using the exteded Kety model (4) with representative tumor parameter values for K^{trans} (0.1 min^{-1}), v_e (30%) and v_p (5%). Since blood T_1 at slice 18 of our DCE-MRI data was reliable, "true" C_p was regarded as the AIF from this slice. Subsequently, for each slice in the volume our "true" C_t curve was fit with the extended Kety model using the slice specfic AIF from both the measured T_1 and assumed T_1 method in turn to obtain fitted parameter estimates. The error in these fitted parameters was calculated relative to our "true" set of parameter values and used to compare the level of accuracy between the measured and assumed T_1 approaches.

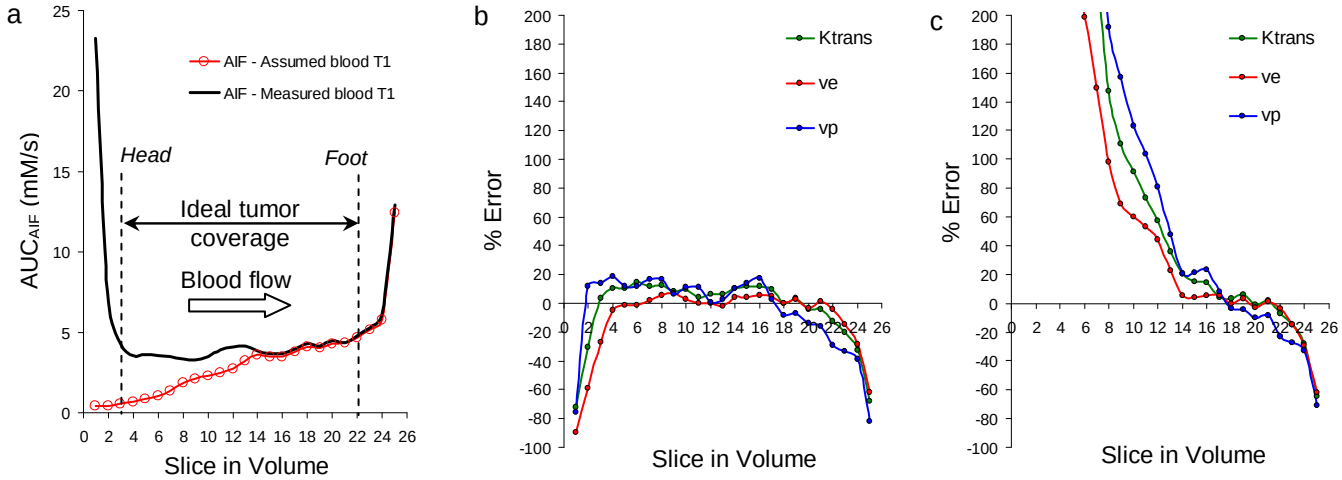

Figure 1: The area under the AIF (AUC_{AIF}) for AIFs derived using a measured T_1 (black solid line) and an assumed T_1 value (red circles) (a). The % error in K^{trans}, v_e and v_p across the imaging volume using AIFs derived using measured T_1 values (b) and an assumed T_1 value of 1253 ms (c).

Results AIFs derived using a slice-dependant measured T_1 show accurate [CA] is achieved in the central portion of our prescribed imaging volume, but errors in [CA] are seen at the volume extremities where elevated AUC_{AIF} relates to high [CA] (2). AIFs derived using the assumed T_1 value (1253 ms) show large underestimations in [CA] from slice 1 and reach accurate [CA] values from a mid-volume location (dependant on blood flow, flip angle and TR). The effect of these AIFs on tracer kinetic parameters is shown in Fig 1b and c where both K^{trans} and v_e have ± 10% error in the ideal tumor coverage region for the measured T_1 method whereas these errors range from +400% to -10% for K^{trans} and 200% to -10% for v_e using the assumed T_1 method. Much larger errors are seen with v_p, particularly in the assumed T_1 method where errors range from approx. +1000% to -20%.

Discussion & Conclusions In a typical DCE-MRI study where B_1 inhomogeneity and blood inflow is left uncorrected, the resulting errors in flip angle and signal intensity are propagated through to estimates of T_1, [CA] and AUC_{AIF}. In this situation, it has been shown that simultaneous measurement of the AIF and tissue residue curve, using a measured T_1 from the same experiment, is essential as it significantly reduces the errors in tracer kinetic parameters (5). While it is often easier to assume a literature value of blood T_1 we have demonstrated that avoiding this measurement can induce large errors in the AIF and introduce bias into tumor microvascular parameterisations. Where possible, good tumor volume coverage is desirable in DCE-MRI studies and while errors in the T_1 measurement due to B_1 inhomogeneity and blood inflow are inevitable, these are accommodated by the measurement of T_1 and an AIF and improve the accuracy of K^{trans}, v_e and v_p across a larger proportion of the imaging volume. Using an assumed value of T_1 for AIF measurement does not accommodate these errors and leads to erroneous tracer kinetic parameter estimates in a large proportion of the prescribed imaging volume. It is therefore essential to measure T_1, especially in the presence of B_1 inhomogeneity and blood inflow error.

References 1. Li KL *et al*. J Magn Reson Imaging 2000;12(2):347-357. 2. Roberts C *et al*. 2008; Toronto, Canada. Proc. of the 16th Annual ISMRM. p 1473. 3. Tadamura E *et al*. J Magn Reson Imaging 1997;7(1):220-225. 4. Tofts PS. J Magn Reson Imaging 1997;7(1):91-101. 5. Buckley DL, Parker GJ. 2004; Kyoto, Japan. Proc of the 12th Annual ISMRM.