An improved reference tissue approach for measuring the arterial input function in DCEMRI; comparison of late-phase reference tissue and plasma contrast media concentrations.

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Introduction: Analysis of dynamic contrast enhanced MRI (DCEMRI) data requires knowledge of the arterial input function (AIF), which accounts for variations in contrast media injection, cardiac output, and vascular function. The AIF can be determined from a major artery, a pre-defined 'population' function, or a reference tissue. However, the direct measurements from artery are subject to significant systematic errors due to the very high contrast concentration at early times after injection, and partial volume effects. The 'population' AIF does not account for significant variability between patients and contrast media injections. The reference tissue method uses the literature value of the volume transfer constant (K^{trans}) and the contrast media distribution volume (v_e) as starting points, and these may differ significantly from the true value. Here we introduce a new method to better estimate K^{trans} and v_e for a reference tissue, and thereafter to derive the entire AIF. First, a homogeneous population of reference tissue pixels with, slow blood flow (low K^{trans}) is selected. In these tissues, contrast media concentration (C(t)) remains significantly different from the plasma concentration ($C_p(t)$) between ~1 minute and ~5 minutes after injection. During this period, $C_p(t)$ can be measured accurately and at high resolution to avoid partial volume effects. By applying the two-compartment model (TCM [1]) to $C_p(t)$ and C(t), K^{trans} and v_e can be estimated. Instead of using the literature values, the estimated K^{trans} and v_e can be used to determine the early part of the AIF, as in the original reference tissue approach [2].

Methods: The DCEMRI data were acquired with a 9.4 Tesla scanner from a rat illiac artery. The T_1-weighted gradient echo images (TR/TE=40/3.5 ms, FOV=6 cm, array size=128^2, slice thickness=1 mm, flip angle=30°) were acquired before and after Gd-DTPA (dose = 0.10 mmol/kg) injection. Temporal resolution was 5 seconds during the first 10 minutes after injection, and subsequently 10 seconds for another 20 minutes. Contrast media concentration in the artery ($C_a(t)$) and nearby leg muscle (C(t)) was converted from the MRI signal intensities first. To obtain the AIF $C_p(t)$ from $C_a(t)$, we used $C_p(t) = C_a(t)/(1-Hct)$ with Hct = 0.45, to correct for the hematocrit (Hct). Under the assumption that muscle was well approximated by the TCM: $dC(t)/dt = K^{trans}\left(C_p(t) - C(t)/v_e\right)$, we estimated muscle's K^{trans} and v_e as follows: (i) at long times after injection (> 30 min), when dC(t)/dt ~ 0, $v_e \sim C(t)/C_p(t)$ at t = 30 min; (ii) using v_e from step (i), we searched for the value of K^{trans} that minimizes $\left|dC(t)/dt - K^{trans}\left(C_p(t) - C(t)/v_e\right)\right|$ over the period from approximately one minutes to five minutes after injection, when $C_p(t) > C(t)/v_e$.

Results: Fig. 1 shows $C_a(t)$ (open circle) and C(t) (black line) measured from MRI. Obviously, due to ~5 s temporal resolution the peak of $C_a(t)$ was missed which was not going to used in the calculations. To minimize effects of motion and noise, we fit the experimental curves by two different empirical mathematical models, one for $C_a(t)$ (red line) and one for muscle C(t) (green lines). Excellent fits to experimental data were obtained. After applying our technique to fitted curves, the estimated $\mathbf{K^{trans}}$ and $\mathbf{v_e}$ were **0.12**(min^{-1}) and **0.23** for muscle, respectively. These are close to the literature values for muscle.

Discussion: The results demonstrate that K^{trans} and v_e can be calculated from the difference in contrast media concentration between a reference tissue with modest blood flow, and an artery, following the first and second passes of the contrast agent bolus. At these times, the arterial concentration is relatively low and therefore can be measured accurately, and with high spatial resolution and signal-to-noise ratio. The K^{trans} and v_e measured using this approach were close to the literature values. The AIF, including the first and second passes, is then calculated from the accurately measured the K^{trans} and v_e, in the reference tissue. The only assumption required is that contrast dynamics in the reference tissue are well approximated by the TCM; this assumption is well justified for muscle. The method described here can be incorporated into the double reference tissue developed by Yang et al [3] to further improve AIF estimation. This is an especially useful technique to estimate a *local* AIF in tissue near specific lesions.

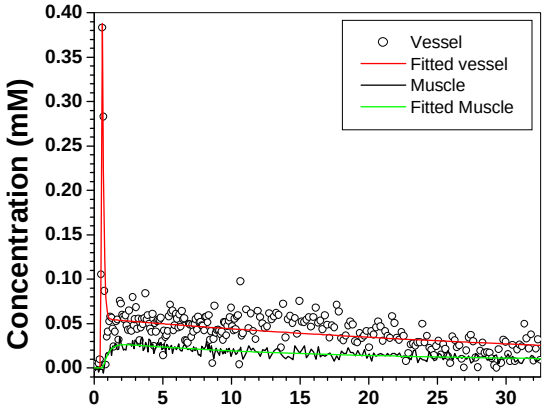

Figure 1.

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References: [1] Tofts et al., JMRI 1999. [2] Kovar et al., JMRI 1998. [3] Yang et al., MRM 2004.