Estimating the Arterial Input Function Using Two Reference Tissues in DCE-MRI Studies: Clinical Validation

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Introduction: Direct measurement of the contrast agent Arterial Input Function (AIF) in a major artery by MRI is subject to significant errors due to T_2^* effects, and the rapid flow of blood in the artery. To more accurately estimate the AIF $C_p(t)$, we proposed a double reference tissue method (DRTM) which assumes that the AIFs of two reference tissues have the same shape and that physiological models with two or more compartments and unknown kinetic parameters can describe their concentration vs. time curves, $C_t(t)$ (1). For example in the two compartment model, $C_p(t) = [C_t(t) + 1/K_{ep}\, dC_t/dt]/v_e$ **Eq.[1]**, where v_e is the fractional distribution volume of the contrast agent, and K_{ep} is the ratio of the transfer constant K^{trans} to v_e (2). Utilizing a two compartment model for both reference tissues, the assumption that the two AIFs share the same shape enables us to establish a relation between the two tissues, $C_t^B(t) = (v_e^B/v_e^A)K_{ep}^B\{C_t^A(t-l)/K_{ep}^A + (1-K_{ep}^B/K_{ep}^A)\int_0^t C_t^A(\tau - l)\exp[-K_{ep}^B(t-\tau)]d\tau\}$ **Eq.[2]**, where superscript A and B denote the two reference tissues and l is the difference in contrast agent bolus arrival time between the two tissues. First we obtain a smooth estimate of $C_t^A(t)$ and its first derivative with a local polynomial smoothing method. We then use Eq.[2] to fit $C_t^B(t)$ thereby estimating the kinetic parameters of both tissues. Finally the estimated kinetic parameters of tissue A are entered into Eq.[1] to obtain its local AIF. Previous simulation studies suggested that reliable estimates of the AIF could be obtained despite measurement noise and despite different AIF shapes of the two tissues due to differences in contrast agent dispersion (1). The purpose of the present work is to evaluate whether the DRTM is effective when applied to patient data.

Materials and Method: We evaluate the DRTM with 12 sets of DCE-MRI data from patients with melanoma or colon cancer (3). T1 weighted images were scanned with 1 second time resolution for 7 minutes after bolus injection of 20ml Gd-DTPA. All the scans have liver and skeletal muscle in the field of the view, and spleen is also available in 5 scans. Normal liver or spleen is used as reference tissue A, muscle as reference tissue B, and a two compartment model was used to determine K_{ep} and the AIF.

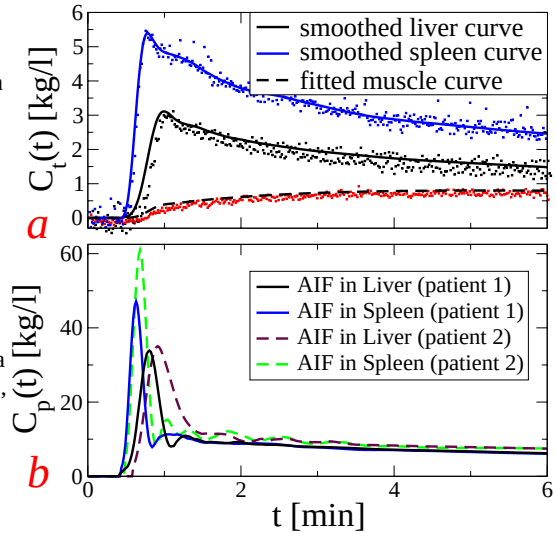

Figure 1: (**a**) Normalized Concentration vs. time curves in patient 1. (**b**) Fitted AIFs of liver and spleen in patient 1 (data shown above), and in patient 2.

Results: Fig. 1(**a**) shows that local polynomial smoothing excellently smoothes the noisy data of liver and spleen and the DRTM gives a good fit to the muscle concentration curve. All the AIFs estimated with the DRTM have similar shapes but different dispersions (Fig. 1(**b**)). They closely resemble published AIFs determined directly from the aorta (4). The 5 AIFs determined for spleen are relatively narrow and show the second pass of the bolus. The 12 AIFs estimated from liver have larger dispersion. Although the calculated AIFs have similar shapes, K_{ep} has large between patient variability especially in liver (Fig. 2) that nevertheless falls within the previously reported range (5). For the patients with both liver and spleen data available, the K_{ep} in liver can be estimated directly by using liver as tissue A, *and* can also be estimated by fitting $C_t(t)$ of liver with the AIF estimated using spleen as tissue A. Figure 2 shows that the difference in the two estimates of K_{ep} in liver (or similarly in spleen) is very small (< 5%) in all 5 cases. This self consistency test is strong evidence that the AIFs obtained from the DRTM are valid.

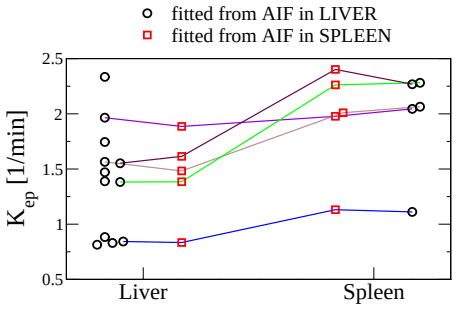

Figure 2: Fitted K_{ep}, data from the same patient are connected with a straight line.

Conclusions: The DRTM provides internally consistent AIFs that are very similar to published AIFs calculated directly from the aorta. Thus, preliminary clinical application of the DRTM confirms the suggestion of simulation studies that it can provide a reliable estimate of the local AIF and the kinetic parameters of the reference tissues.

References: **1**. Yang C *et al*, MRM 2004; 52:1110. **2**. Tofts PS *et al*, JMRI 1999; 10:223. **3**. Medved M *et al*, JMRI 2004; 20:122. **4**. Li KL *et al*, JMRI 2000; 12:347. **5**. Padhani AR et al, NMR Biomed 2002; 15:143.