Estimation of Reference Tissue based Arterial Input Function using Neural Network

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Introduction:

Arterial input function (AIF) plays an important role in analysis of dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) data. Accurate measurement of AIF is crucial in pharmacokinetic model analysis for cancer detection and monitoring of treatment response. However, it is often difficult to find a suitable artery in the field of view (FOV). Even for the cases with a large artery visible in the FOV, it is uncertain how adequately the measurement from a large artery can represent the actual vascular signal in the region of interest. Reference tissue approach [1-4] has been suggested as a means to estimate the capillary vascular signal under the assumption that the contrast enhancement kinetics in the reference tissue can be modeled as a two compartment model with fixed parameters. However, estimation of the AIF from the reference tissue remains a challenge due to noise and relatively weak contrast enhancement in the preferred reference tissues, such as muscle. In this study, we investigated a novel method to estimate AIF from a reference tissue using a neural network and assessed the performance of the proposed method in comparison with previously reported methods using clinical and preclinical DCE-MRI data.

Materials and Methods:

A retrospective analysis was conducted with DCE-MRI data acquired from three patients with suspicious prostate lesions who underwent multiparametric MRI studies as part of routine MRI exam using a whole body Siemens 3T TIM Trio system. A 3D turbo FLASH pulse sequence was used with the following imaging parameters: TR/TE = 2.84/1.04 ms, flip angle = 16 deg, image resolution = 0.94 x 0.94 mm, slice thickness = 3 mm, 24 slices, which provided a temporal resolution of 5.5 s/frame. Following acquisition of baseline preinjection images for 30 s, a single dose of Gd-DTPA (Magnevist, Bayer) with concentration of 0.1 mM/kg body weight was injected at 3 mL/second into an antecubital vein, during which scanning was continued for another five minutes.

For mouse data, six- to eight-wk-old BALB/c mice (n = 6) were scanned using a 7T horizontal bore magnet with a volume transmit and receive coil. General anesthesia was induced by 1.5% isoflurane in air. The animal was mounted on a cradle with respiratory and temperature monitoring probes. The animal body temperature was maintained at 32 ± 2 ºC during the scan. A 3D FLASH sequence was used to minimize the flow effect (TR = 13.4 ms, TE = 3.0 ms, flip angle = 50º, image matrix = 64 x 64 x 10, resolution = 0.7 x 0.7 x 1.5 mm, temporal resolution = 4.7 s). This sequence was run to acquire 150 single average 3D images for 11.8 min. A bolus of 10 mM Gd-DTPA in saline, corresponding to dose 0.1 mmole/kg, was injected through a tail vein catheter starting after the acquisition of 13 pre-contrast images (~ 1 min). This study was approved by the institutional animal care and use committee.

The Gd concentration in the artery, $C_p(t)$, can be estimated from that of a reference tissue, $C_{tis}(t)$, using the following equation: $C_p(t) = C_{tis}(t)/V_e + 1/K^{trans} \times dC_{tis}(t)/dt$ where K^{trans} and V_e denote transfer constant and interstitial space volume, respectively. Presumed literature values for transfer constant and interstitial space volume were used. In this case, they were assumed to be K^{trans}=0.11 (min^{-1}) and V_e=0.20 respectively [1]. A multiple layer neural network (NN) with 2 by 2 neurons in each hidden layer was used to fit tissue concentration curve and consequently obtain differential of tissue concentration curve by difference approximation. The proposed NN method was compared with two previously reported reference tissue approaches; raw data approach [1] and the empirical mathematical model (EMM) [2].

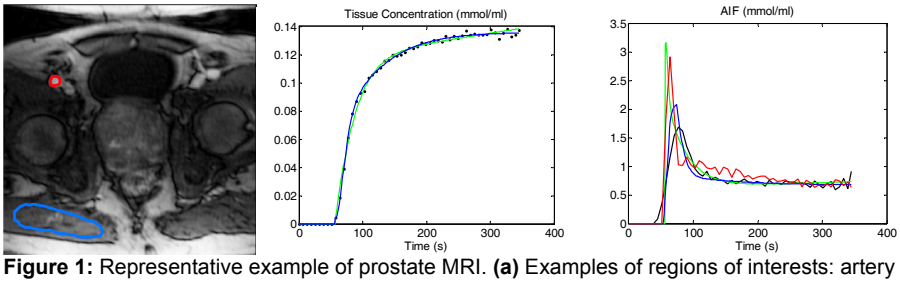

Figure 1: Representative example of prostate MRI. **(a)** Examples of regions of interests: artery (red) and muscle (blue), **(b)** Muscle data (black dots) with two models: EMM (green) and NN (blue), **(c)** AIF estimation by three methods, raw (black), EMM (green), and NN (blue), with measured AIF (red).

Table 1. Variability of the estimated (raw, EMM, and NN) and measured AIF in terms of residual sum of square (RSS) between data from 10 slices and the average.

Subject	RSS (Mean±SD)			
	Raw	EMM	NN	Measured
1	0.482±0.167	1.538±0.943	0.430±0.199	0.620±0.361
2	0.562±0.254	1.500±0.516	0.580±0.264	1.0187±0.535
3	0.476±0.134	0.804±0.297	0.388±0.174	1.454±1.085

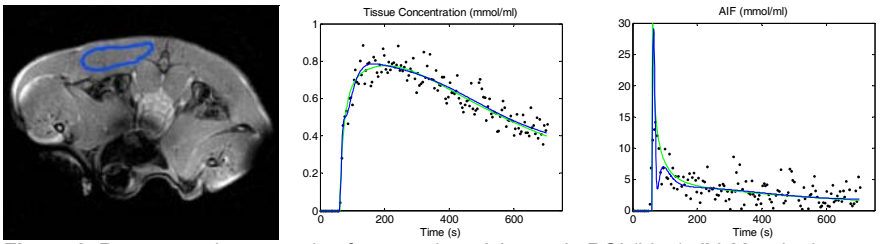

Figure 2: Representative example of mouse data. **(a)** muscle ROI (blue) **(b)** Muscle data (black dots) and two model fits: EMM (green) and NN (blue). **(c)** AIF estimation by three methods: raw (black dots), EMM (green) and NN (blue).

Results and Discussion:

Fig 1 demonstrates one example of AIF estimation in DCE-MRI data of the pelvic region. The AIF from EMM has faster enhancement than the measured AIF, and the AIF from the raw muscle data show ripples in the wash out phase. In contrast, the AIF from the proposed NN method appears to have a reasonable delay and dispersion, and smooth curve close to that from the raw muscle data. This estimation was repeated 10 times using 10 mid slices in each patient to assess the variability of each method as shown in Table 1. Measured and EMM-AIF have relatively large SD, compared to the raw and NN-AIF. Fig 2 shows the AIF estimation in mouse DCE-MRI data. Since the noise in the muscle data was high, it was not possible to use raw-AIF method as shown by black dots in Fig.2c. The second peak of the NN-AIF appeared to be a recirculation effect, demonstrating the flexibility of the proposed NN method. Similar results were observed with the other mice, indicating that the NN method can be used to estimate AIF when its direct measurement is not possible.

Reference: [1]. Kovar D.A. et al., *JMRI* 1998;8:1126-1134. [2]. Fan X. et al., *MRM* 2004;51:487 – 494. [3]. Yang C. et al., *MRM* 2004;52:1110–1117. [4] Yang C.et al., *MRM* 2007;58:1266–1275.