MR Estimation of Arterial Input Function (AIF) in Dual Gradient Echo Sequences Using an Adaptive Model Trained by Standard Radiological AIF

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Introduction:

Contrast agents (CAs) are widely used as indicators to study quantitative perfusion and blood-brain barrier (BBB) permeability by MRI in order to characterize cerebral pathology [1]. The models employed are input-response models, thus the arterial input function (AIF), *i.e.*, the arterial concentration-time trace of the CA, is critical to producing unbiased estimates of mean transit time (MTT), cerebral blood flow (CBF), cerebral blood volume (CBV), vascular transfer rate constant (K^{trans}), vascular volume (v_D), and extracellular-extravascular space (v_e) in dynamic susceptibility (DSC) and dynamic contrast-enhanced (DCE) studies [1, 2]. While a variety of approaches have emerged to predict the AIF profile from fast MRI techniques such echo planar imaging (EPI) and dual-gradient echo (DGE), restricted water exchange, competing T_2* contrast mechanisms, and moving blood can significantly undermine correct quantification of the AIF. Our group has previously measured the AIF for 13 Wistar rats at relatively high temporal resolution by counting β emissions in a well counter from a series of timed arterial blood samples that were collected after an intravenous bolus injection of radiolabeled Gd-DTPA CA (time–activity curve) [3]. The measured AIF profiles were then calibrated to the blood relaxivity to construct a standard radiologically based AIF (SRAIF). In this study an adaptive model was used for predicting the time trace of AIF from DGE signal components measured in the normal area of rat brains. It was hypothesized that, given a set of physically meaningful extracted features from DGE sequences, an artificial neural network (ANN) could be trained to estimate the time trace of SRAIF.

Material and Methods:

To train and test the ANN, 13 SRAIF curves were used to construct an averaged SRAIF, and DGE experiments in 12 animals with U251 brain tumor were employed as an MRI sample. As shown in Figure-1, in MRI procedures, DGE images were acquired (two gradient echoes at 3.4 and 6.8 ms, ~18° pulse, TR=60 ms, 3 slices of 2 mm thickness, FOV= 32 mm, 128x64, 4 seconds per image set) with the CA injection (140μmol/kg gadolinium-DTPA, bolus in about 4sec)) at time 44 Sec. As shown in equations 1-8, using a feature set (μ_1, μ_2, μ_3, and μ_4) that was physically meaningful and independent from system gain extracted from 7T Dual Gradient Echo signals, an ANN was trained and tested with the averaged SRAIF curve as the gold standard.

$$H_1 = -\frac{1}{TR}\ln\left[\frac{\frac{n_S}{1}\left(\frac{TE2}{TE2-TE1}\right)}{\frac{n_S}{2}\left(\frac{TE1}{TE2-TE1}\right)}\right] \quad (1)$$

$$H_2 = -\frac{1}{(TE1-TE2)}\ln\left[\frac{\frac{n_S}{1}}{\frac{n_S}{2}}\right] \quad (2)$$

$$\Delta H_1 = H_1(Post) - H_1(Pre) \quad (3)$$

$$\Delta H_2 = H_2(Post) - H_2(Pre) \quad (4)$$

$$\mu_1 = \frac{\Delta H_1^{DGE}}{H_1^{DGE}{}_{(Pre)}} \quad (5)$$

$$\mu_2 = \frac{\Delta H_2^{DGE}}{H_2^{DGE}{}_{(Pre)}} \quad (6)$$

$$\mu_3 = -\frac{\Delta H_1^{DGE}}{H_1^{DGE}{}_{(Post)}}\ln\left[\frac{\frac{n_S}{1}}{\frac{n_S}{2}}\right] \quad (7)$$

$$\mu_4 = -\frac{\Delta H_2^{DGE}}{H_2^{DGE}{}_{(Post)}}\ln\left[\frac{\frac{n_S}{1}}{\frac{n_S}{2}}\right] \quad (8)$$

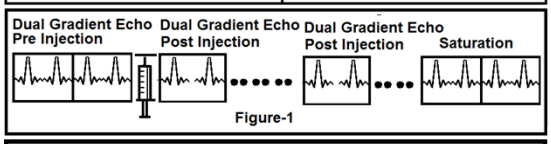
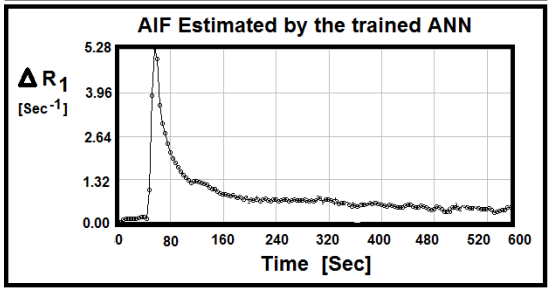


Figure-1

The feature set was constructed from first and second components of the DGE signal ($^{n}_{1}S$ and $^{n}_{2}S$, *n*=1-150) at all time points before and after CA administration. The average curve of the SRAIF at time points corresponding to the feature set served as the training set for the ANN. An ANN with multi-layer perceptron (MLP) architecture was trained by a small value (~0) for the first part (before the CA administration) of the DGE experiment and the average SRAIF curve for the time points after CA administration. The ANN was then trained and validated using K-folding cross validation method, also optimized by maximizing the Area Under Receiver Operator Characteristic (AUROC) [4], and validated by 3150 samples from 12 animals with 50 folds and 63 samples in each randomly split fold.



Results and Discussions:

The ANN: 4:8:1 was optimal at AUROC=0.87. Thus, the trained ANN (4:8:1) was applied to the DGE images from the 12 animals to generate a time course of AIF, including the pre- and post-injection time points. Figure 2 shows an AIF curve generated by the trained ANN from normal area of the brain. The AIFs estimated by the ANN from the normal area of the brains were highly correlated (*r=0.86, p<0.0001*) with the SRAIF.

It can be concluded that the AIF time course estimated by the ANN was stable with no sign of peak saturation and a reasonable rise time. The ANN appears to be generating estimates of AIFs that are close to known values of the AIF measured by radiographical methods at different time points. Thus, this pilot study demonstrates the feasibility of applying an ANN for estimating the AIF from the signal components measured from normal tissue using fast imaging techniques which has long presented a problem for studying of vascular physiology particularly in small animals. The ANN approach described herein may well solve the problem by deconvolving the AIF signal from the normal tissue-response.

References

[1] Nestorov,I., Expert Opin Drug Metab Toxicol.,2007;3:235-249.
[2] Tofts P. et al. MRM, 1991;17:357-367.
[3] Nagaraja TN. et al. Magn Reson Med 2010;63:1502-1509.
[4] Bagher-Ebadian H, et al, ISMRM 2008, pp. 3260.