Construction of a Model-Based High Resolution Arterial Input Function (AIF) Using a Standard Radiological AIF and the Levenberg-Marquardt Algorithm

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Introduction: Estimating the arterial input function (AIF) of a contrast agent (CA), the time-concentration curve in plasma, has long presented a problem in MR dynamic contrast enhanced (DCE) and dynamic susceptibility (DSC) studies. The AIF is used in estimating mean transit time (MTT), cerebral blood flow (CBF), cerebral blood volume (CBV), transfer rate constant (K^{trans}), vascular volume (v_D), and extracellular-extravascular space (v_e) in DSC and DCE studies [1, 2]. Inaccurate estimation of the AIF for use in permeability and perfusion analyses could substantially increase bias in the estimated hemodynamic and permeability maps. While a variety of approaches have emerged to accurately predict the AIF, many of them are too complex to be implemented in practice [2]. In addition, in such fast MRI techniques as echo planar imaging (EPI) and dual-gradient echo (DGE), restricted water exchange, competing T_2* contrast mechanisms, and moving blood significantly undermine a description of the AIF. A model-based AIF can address most of these deficiencies [3, 4]. A successful model based on the blood-circulatory system for the construction of an algorithm for estimating the CA time-concentration curve in arterial plasma after an intravenous bolus injection has been previously suggested [5, 6]. A set of time courses of radiolabeled Gd-DTPA CA concentrations in arterial plasma (time–activity curve) after an intravenous bolus injection has been recently measured by counting β emissions in a well counter for 13 Wistar rats [7]. The measured AIF profiles were averaged and calibrated to blood relaxivity to construct a reference curve (ΔR_1) from the standard radiological AIF (SRAIF). In this study, the time-concentration curve of the calibrated SRAIF was used to estimate a set of parameters for constructing a blood-circulatory model AIF in a high temporal resolution which can be adapted to any MR DSC and DCE studies.

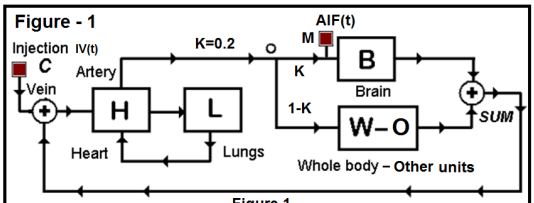

Figure 1

$$P_1(S) = k.\frac{[\eta_H.e^{-\tau_H.S}][\eta_L.e^{-\tau_L.S}][\eta_H.e^{-\tau_H.S}+C^0]}{[\eta_H+S]^2[\eta_L+S]} \quad (1)$$

$$P_2(S) = FP(S)\left[\frac{\eta_B.e^{-\tau_B.S}}{\eta_B+s}+(1-k)\frac{\eta_{WO}.e^{-\tau_{WO}.S}}{\eta_{WO}+s}\right]D(S) \quad (2)$$

where $D(s)$, η_H, η_L, η_B and η_{WO} are defined as:

$$D(S) = \frac{[\eta_H.e^{-\tau_H.S}+C^1][\eta_L.e^{-\tau_L.S}+C^2][\eta_H.e^{-\tau_H.S}+C^3]}{(\eta_L+s)(\eta_H+s)^2} \quad (3)$$

$$\eta_H = \left(\frac{F^2\tau_H}{{}^HV_r^2}\right), \eta_L = \left(\frac{F^2\tau_L}{{}^LV_r^2}\right), \eta_B = \left(\frac{F^2\tau_B}{{}^BV_r^2}\right), \eta_{WO} = \left(\frac{F^2\tau_{WO}}{{}^{WO}V_r^2}\right) \quad (4)$$

$$C^0 = C_H^{out}(2\tau_H+\tau_L) \qquad C^2 = C_L^{out}(3\tau_H+2\tau_L+\tau_B)$$

$$C^1 = C_H^{out}(3\tau_H+\tau_L+\tau_B) \qquad C^3 = C_H^{out}(4\tau_H+2\tau_L+\tau_B) \quad (5)$$

Materials and Methods: As shown in the figure-1, the response of the blood circulatory system for a rectangular IV bolus injection function at the measurement site **M**, is defined by first and second passages ($P_1(S)$, and $P_2(S)$) of the bolus in Laplace space [5, 6]. Three parameters define each compartment (volume-***V***, flow-***F***, and time lag-***t***) in four ratios (see Figure-1, Eq. 4). The subscripts in all of the equations denote compartments (Heart, Lungs, Brain, and whole body-other organs). We have already shown that these four parameters (η_H, η_L, η_B, and η_{W-O}) are adequate to model an AIF signal [5, 6]. In experiments the four parameters of the model are estimated using a multi-dimensional fitting of the model to the MR signals. In this study, a Levenberg-Marquardt multi-dimensional fitting algorithm [8] was employed to estimate the blood-circulatory model parameters (η_H=0.2721 with 95% confidence bounds of 0.2504-0.2810, η_L=4.4232 with 95% confidence bounds of 4.4122-4.4632, η_B=19.8267 with 95% confidence bounds of 19.2346-19.9132, and η_{W-O}=1.0806 with 95% confidence bounds of 0.9937-1.1131) with 95% confidence bounds using a calibrated SRAIF curve to blood relaxivity as the gold standard of fitting. The concentration-time profiles for the blood circulatory model and the SRAIF were strongly in agreement ($r=0.96$, $p<0.00001$) and both constructed for 600 sec with a bolus injection (with duration of 4 sec) 36 seconds after the experiment was started.

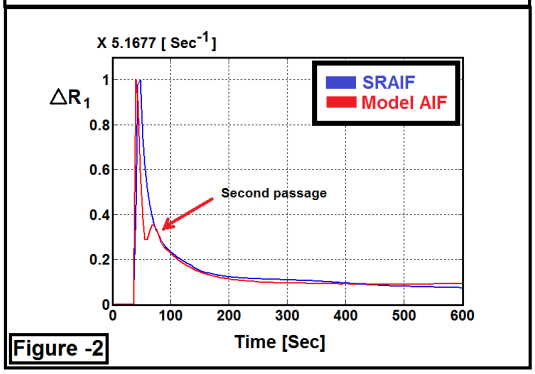

Figure -2

Results and Discussion: Figure 2 shows the longitudinal relaxation rate change (ΔR_1) versus time for the SRAIF (blue) and the blood-circulatory model AIF (red), constructed using the estimated parameters for a time course of 600 sec. Note that the AIF constructed by the circulatory-model can be generated for any arbitrarily high temporal resolution, to match the temporal resolution of the MR imaging. The blood-circulatory model is also capable of modeling the second passage of the CA concentration, which is missed by the SRAIF due to the low temporal resolution of the radiological measurement. Since AIFs are the driving signals in the DSC and DCE input-response studies, the model generates AIFs with sharper peak and quicker rise time in addition to producing the second passage peak, compared to the SRAIF, which can substantially reduce biasing effects associated with time lag and signal saturation in quantitative analyses. Thus, the model based AIF approach described herein may well address deficiencies associated with conventional methods in estimation of AIF, regardless of imaging technique.

References:

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