A Blood Circulatory Model to Estimate the Arterial Input Function in MR Brain Perfusion Studies

H. Bagher-Ebadian[1,2], K. Jafari-Khouzani[3], H. Soltanian-Zadeh[3,4], and J. R. Ewing[1,5]

[1]Neurology, Henry Ford Hospital, Detroit, MI, United States, [2]Physics & Nuclear Engineering, Amir-Kabir University of Technology, Tehran, Iran, [3]Radiology, Henry Ford Hospital, Detroit, MI, United States, [4]Control and Intelligent Processing Center of Excellence, University of Tehran, Tehran, Iran, [5]Physics, Oakland University, Rochester, MI, United States

Introduction: The arterial input function (AIF) plays an important role in estimating relative Cerebral Blood Flow and Volume (*rCBF* and *rCBV*) in MRI perfusion studies. Thus, a mathematical model of Contrast Agent (CA) concentration in the circulatory system as a function of time is of interest since it may allow the description of the AIF based on the Intravenous (IV) injection function [1]. In order to be useful, a model needs to be easy to assemble, and relevant [2]. While a variety of approaches have emerged to predict blood concentration-time profiles, many of them are too complex to be implemented in practical experiments [2]. As for models that fulfill the requirement of usability, compartmental approaches based on compartmental-venous equilibration and mass balance are the simplest and most widely used [3-4]. In this study, as a building block, the concentration-time profile in the circulatory system for each compartment was modeled by simple physical and pharmacokinetic assumptions using the Fick equation and Kety's model [4]. A complete model of the CA concentration as a function of time in the circulatory system was then constructed by combining those building blocks using typical flow and volume parameters for the various compartments. Using a model of the IV bolus injection, its results were compared to MR perfusion (T_2^*) signal.

Materials and Methods: In this study, four large tissue compartments - heart, lungs, brain, and the whole body absent the heart, brain, and lungs – were used to model the circulatory system (Figures 1-a and 1-b). As shown in this figure, CA as an arbitrary function of time was injected intravenously at the site of injection (C), assumed to be a large vein with a short path to the heart, and CA concentration was recorded temporally at the point of measurement (M). Each compartment (building block) was considered as a unit with discrete inlets and outlets (Figure 1). It is assumed that once the blood with certain amount of concentration enters the unit (***C*****$_{in}$**), it is diluted (by the blood pool and the tissue of the compartment) in a "well-stirred" form in a short period of time (τ) and leaves the unit with a different concentration (***C*****$_{out}$**) and transport lag of τ. Therefore, an ordinary differential equation can model each unit considering the following assumptions: (1) The inlet and outlet flows (***F***) are equal. (2) The compartmental concentration ***C*****$_r$**(t) is proportional to ***C*****$_{out}$** (Kety's model) via the partition coefficient, λ: **$C_r = \lambda C_{out}$** (equation 3). Thus, a substance confined to the vascular space will travel through the compartment and will appear in the outlet after a transport lag, and with a different concentration. Equation (4), which is the building block equation of the model, relates inlet (***C*****$_{in}$**) and outlet (***C*****$_{out}$**) concentrations for each compartment. In this study, the circulatory system consisting of heart (**H**), lungs (**L**), brain (**B**) and whole body without other organs (**W-O**), with administration and measurement sites of ***C*** and ***M*** (Figure 1-b) was modeled using equation (4). In this study, the response of the system at the measurement point ***M***, was simulated for a rectangular IV bolus function using Simulink-MATLAB-7.0. Three parameters defined each compartment (volume, flow, and time lag) in four ratios: $[(V_r^2/\tau F^2)_H, (V_r^2/\tau F^2)_L, (V_r^2/\tau F^2)_B$, and $(V_r^2/\tau F^2)_{W-O}]$ (subscripts denote compartments) for the four compartments, using parameters typical of an adult human. Simulation was long enough (75 Sec) to generate all orders of bolus passages (first, second, etc.), and long compared to the duration of injection (5 sec). A simulated concentration-time curve was generated at site ***M,*** and then compared to a temporal T_2^* signal in an MR brain perfusion study (Figure-2).

$$F[C_{in}(t-\tau) - C_{out}(t)] = \frac{dQ_r}{dt} \quad , C_r = \frac{Q_r}{V_r} \qquad (1)$$

$$C_r(t) = \lambda C_{out}(t) \ , \ \lambda = V_r/F.\tau \quad \text{Kety's model} \qquad (2)$$

$$F[C_{in}(t-\tau) - C_{out}(t)] = \lambda V_r \frac{dC_{out}(t)}{dt} \qquad (3)$$

$$C_{out}(t) + \left(\frac{V_r^2}{\tau F^2}\right)\frac{dC_{out}(t)}{dt} = C_{in}(t-\tau) \qquad (4)$$

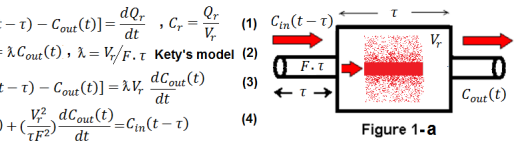

Figure 1-a

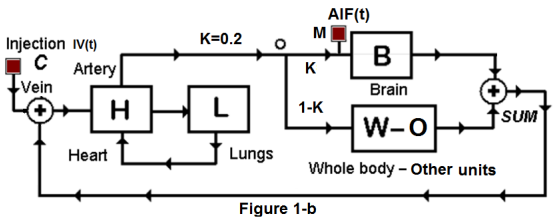

Figure 1-b

Results and Discussion: The proposed model of the temporal behavior of the CA concentration at site ***M***, compared to an AIF constructed from a T_2^*-weighted signal in MR brain perfusion is shown in Figure 2. This result indicates a good agreement between the model estimation and experimental AIF (r=0.79, p<0.0001). Note that, since the peak of the measured AIF is often underestimated [5], the model curve, if appropriately scaled, may provide a better representation of the true shape of the AIF than does the measured curve alone. Note the agreement between the recirculation pass of the bolus in the experiment and model at 40 second. There are about 1.5 seconds of delay between the model (carotid site) and the experiment (inside brain) which is due to the difference in sites of measurement. The proposed model in Figure 1-b needs only 4 parameters to generate a CA concentration profile, and may be more accurate and easier to implement compared to the methods that fit gamma-variate functions to the perfusion curves. These latter cases suffer from convergence problems and lengthy processing times for estimating the AIF [6]. Since all model parameters are defined regardless of the signal type and imaging parameters, this model can be easily translated to animal studies and can also be used in other techniques (e.g., CT). This model is a good candidate to be used to define a cost function for detection of the AIF in MR brain perfusion studies. If necessary, it can be refined using further physiological information for a larger number of organ compartments (e.g., muscle, gut, etc.) and their interactions with the circulatory concentration time profile.

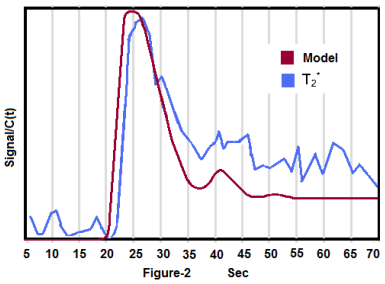

Figure-2

References:

[1] Nestorov,I., Expert Opin Drug Metab Toxicol.,2007;3:235-249
[2] Rowland, M. et al., J Pharmacokinet Biopharm.,1973;1:123-136
[3] Pang, KS. et al., J Pharmacokinet Biopharm.,1977;5:625-653.
[4] Carl A. et al., Circ. Res. 27;739-764, Nov. 1970
[5] Conturo et al, JMRI 22: 697-703
[6] Chan, A. et al., IEEE Symp. Bio. Img 2004, vol.2 (15): 1067–70