A Simulation to Tissue Homogeneity Model for Capillary of Brain By Statistical Method

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Abstract- **Analytical methods for solving adiabatic equations with non-uniform permeability and real Arterial Input Function (AIF) are complicated. We consider crossing of contrast agent through the capillary and BBB as intrinsically statistical processes. Therefore, it is simulated by a stochastic method (Monte Carlo Method). In our model, capillary is divided into multiple sections as in Patlak model and contrast agent moves from one section to other sections. For capillary input, AIF is made by Monte Carlo Method from real data. Without solving an equation, we derive the concentration of contrast agent as a function of time and distance in the capillary for normal (not permeable due to BBB) and abnormal capillary with uniform and non-uniform permeability.**

Keywords **- Blood Brain Barrier (BBB), Arterial Input Function, Contrast agent, Permeability, Monte Carlo Method.**

I. INTRODUCTION

Measurement of physiological parameters such as permeability of blood brain barrier (BBB) is an important area of research in MRI. Tissue homogeneity model describes BBB in two compartments: intravascular and extravascular, which are separated by permeable BBB [1,2,3]. The quantity of contrast agent inside and outside of capillary (intravascular and extravascular space) depend on permeability of BBB. The amount of enhancement of a region of tissue above normal tissue will be estimated by [amount of contrast concentration in abnormal tissue]-[amount of contrast concentration in normal tissue]. It is this enhancement of the MRI image near an abnormal tissue that clinicians will use to identify and estimate the extent of the abnormal tissue. To investigate the effect of exchange during bolus injection of a contrast agent, it is necessary to model the concentration of contrast agent within the capillary of BBB both as a function of time and position [2].

II. METHODOLOGY

One of the important models describing BBB is tissue homogeneity model (TH). TH model describes BBB in two compartments: intravascular space (IVS) and extravascular space (EVS), which are separated by permeable BBB (Fig. 1). It is further assumed (consistent with the literature) that there is rapid mixing in the EVS, implying that this concentration is a function of time only, and that it is the exchange across the capillary membrane, the EVS-IVS boundary, that dominates the exchange calculation [2]. From conversation of the mass of tracer in intravascular and extravascular spaces, the adiabatic equations (1) is derived [4].

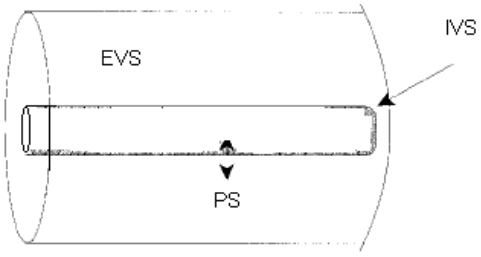

Fig. 1. Tissue homogeneity model, IVS (Intravascular), EVS (Extravascular), PS (permeable surface).

$$\begin{aligned} a_{iv}\frac{\partial C_{iv}(x,t)}{\partial t} &= -F\frac{\partial C_{iv}(x,t)}{\partial x} - \frac{PS}{L}[C_{iv}(x,t) - \frac{C_{ev}(t)}{\lambda}] \\ a_{ev}L\frac{\partial C_{ev}(t)}{\partial t} &= \frac{PS}{L}\int_0^L [C_{iv}(x,t) - \frac{C_{ev}(t)}{\lambda}]dx \end{aligned} \quad (1)$$

Where x and t are position and time, $C_{iv}(x,t)$ and $C_{ev}(t)$ are the concentrations in mMole of tracer in the intravascular space, and the extravascular space, L is the length of the capillary in cm, F is the flow in ml/min/g, a_{iv} represents the cross-sectional area of each compartment in cm^2/g, and PS is the permeability surface area products in ml/min/g.
The quantity of contrast agent or indicator inside and outside of capillary depends on permeability of BBB. We suppose that the capillary bed is composed of identical tube, length, L, total surface area, S, and constant flow rate. There are both uniform and non-uniform permeability, P, in the tube. The flow of the contrast agent through the capillary and BBB are considered as statistical phenomenon. Therefore, they are simulated by Monte Carlo method. In the model, capillary is divided to different sections similar to Patlak model and contrast agent moves from one section to other ones.

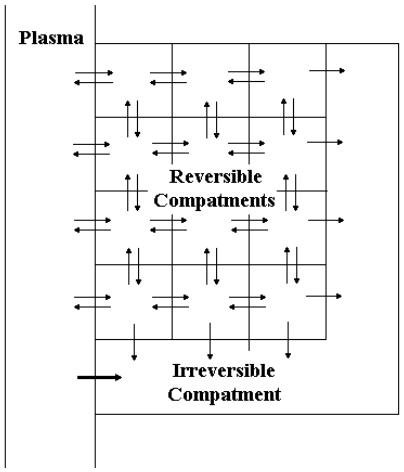

Fig. 2. Patlak Model

The probabilities of particle motion are calculated by the values of permeability, flow of blood, and equilibrium partition coefficient according to adiabatic equations (1):

$$Prc = \frac{\frac{F}{a_{iv}}}{\frac{PS}{La_{iv}} + \frac{PS}{L\lambda a_{iv}} + \frac{F}{a_{iv}}} \quad (2a)$$

$$Poc = \frac{\frac{PS}{La_{iv}}}{\frac{PS}{La_{iv}} + \frac{PS}{L\lambda a_{iv}} + \frac{F}{a_{iv}}} \quad (2b)$$

$$Pic = \frac{\frac{PS}{L\lambda a_{iv}}}{\frac{PS}{La_{iv}} + \frac{PS}{L\lambda a_{iv}} + \frac{F}{a_{iv}}} \quad (2c)$$

where *Prc, Poc, Pic* are probabilities of tracer motion a) in the intravascular space, b) outside of the intravascular space, and c) into the intravascular space, respectively.

L is the length of the capillary in cm, *F* is the flow in ml/min/g, a_{iv} represents the cross-sectional area of each compartment in cm^2/g, and *PS* is the permeability surface area products in ml/min/g.

In other researches, AIF is modeled in a form of gamma, exponential or impulse function. In our model, the input function is generated by Monte Carlo method according to real data (Fig. 3) [5]. AIF was made by two gamma and a uniform functions. AIF function is introduced as time dependent input of the capillary.

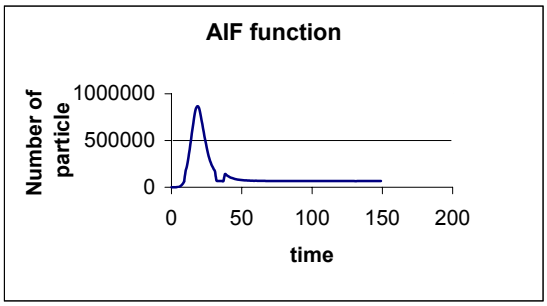

Fig. 3. AIF function results from simulation.

For reconstructing AIF function by Monte Carlo Method [6], we generated random variables from three distributions:

$$AIF(t) = \Gamma(t,20) + \Gamma(t,22) + uniform$$

In general, for $\alpha>1$, $\Gamma(t,\alpha)$ is expressed as:

$$\Gamma(t,\alpha) = \begin{cases} \frac{\lambda\mu x^{\lambda-1}}{(\mu+x^{\lambda})^2} & t>0 \\ 0 & Otherwise \end{cases} \quad (3)$$

where $\lambda = (2\alpha-1)^{1/2}, \mu = \alpha^{\lambda}$

The distribution function is:

$$P(t) = \begin{cases} \frac{t^{\lambda}}{(\mu+t^{\lambda})} & t>0 \\ 0 & Otherwise \end{cases} \quad (4)$$

Inverted function is obtained as:

$$P^{-1}(r) = \left(\frac{\mu r}{1-r}\right)^{1/\lambda} \qquad 0<r<1 \quad (5)$$

If random variables or *r* are generated between (0-1), $P^{-1}(r)$ has Gamma distribution.

Uniform function is expressed as:

$$F(t) = \begin{cases} 1 & a<x<b \\ 0 & Otherwise \end{cases} \quad (6)$$

And inverted function is obtained as:

$$P^{-1}(r) = a + (b-a)r \qquad 0<r<1 \quad (7)$$

Similar to pervious section, we have a uniform distribution for random variable, r.

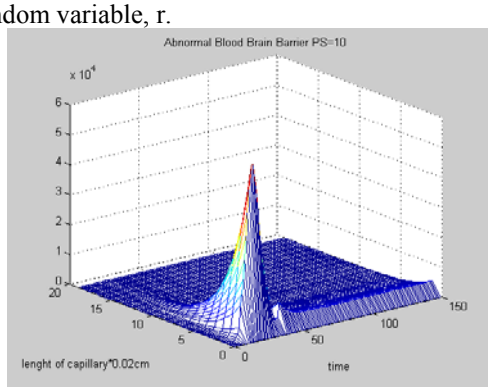

Fig.4. Abnormal BBB results from simulation

III. RESULTS

In this research, the concentration of contrast agent is derived as a function of time and distance in capillary for normal (not permeable due to BBB) and abnormal capillary for both uniform (Fig. 4) and non-uniform permeability. Simulated contrast agent in intravascular space for abnormal BBB is shown as a function of time and position along the capillary in Fig. 4. Note that AIF is reproduced at x=0 and is changed in the distance of the capillary, the concentration at time t=0 is zero, the concentration increases to a maximum value then decreases more slowly as fresh blood enters into the capillary and washes out the contrast agent from the extravascular space.

REFERENCES

[1] St. Lawrence, "An adiabatic approximation to the tissue homogeneity model for water exchange in the brain: I. Theoretical derivation." J Cereb Blood Flow Metab, 18: 1365–1377(1998)

[2] G.R. Moran, "Modeling Tissue Contrast Agent Concentration: A Solution to the Tissue Homogeneity Model Using a Simulated Arterial Input Function," Magnetic Resonance in Medicine, 45:42-45(2001)

[3] John A. Johnson," A model for capillary exchange", Am j. Physiology, 210:1299-1303(1966)

[4] Keith S. St. Lawrence, "An Adiabatic Approximation to the Tissue Homogeneity Model for Water in the Brain: Theoretical Derivation," Journal of Cerebral Blood flow & Metabolism, 18:1365-1377(1998)

[5] Christian Schwarzbauer, "Quantitative Magnetic Resonance Imaging of Capillary Water Permeability & Regional Blood Volume With an Intravascular MR Contrast Agent," Magnetic Resonance in Medicine, 37:236-242(1997)

[6] Averill M. Law, "Simulation Modeling & Analysis," McGraw-Hill, 1991