Permeability Fitting of DSC Perfusion Data through Constrained Optimization

T. Tasciyan[1]

[1]Medical Numerics Inc, Sterling, VA, United States

INTRODUCTION

Blood-brain-barrier (BBB) leakage can be estimated by fitting the concentration curves derived from the T2* weighted MR signal, recorded during the passage of the contrast agent. The fitting method described below, simultaneously determines the CBV and the permeability transfer and rate constants, using 5 parameters and an algorithm based on the Marquardt-Levenberg method with constraints introduced to regularize the leak contribution to the bolus term. Prior to implementation for routine use, the method was assessed on curves randomly selected from a pool of clinical perfusion studies[1] based on dynamic susceptibility contrast (DSC) imaging.

METHODS

The tissue concentration of the contrast agent is[2]: $C_t\,(t\,) = v_p C_p\,(t) + K_{trans}\,C_p\,(t) \otimes e^{-kept}$ where p refers to the plasma and K_{trans} and k_{ep} are the permeability and rate constants, respectively. Assuming the form of a gamma variate $K\,t^a e^{-bt}$ for the bolus,

$$C_t\,(t) = K_p\,t^a e^{-bt} + K_{trans}\,e^{-k_{ep}\,t} \int_0^t \tau^a e^{-(b-k_{ep})\tau} d\tau \qquad \text{where} \quad K_p = v_p\,K$$

and the fitted parameters are $K_p,\ a,\ b,\ K_{trans}$, *and* k_{ep} The starting point of the fit, i.e. the arrival time is determined prior to the fitting process. The ratio of the integral of the first term (CBV) to the integral of the arterial input function[1] (AIF) provides an estimate for v_p. The primary constraints are to regularize the values of K_p and K_{trans} such that after each iteration of the Marquardt-Levenberg (ML) *mrqmin* algorithm[3], negative K_p and K_{trans} values are incremented in the positive direction; K_p is further forced to be greater than $2{*}K_{trans}$ to ensure that the bolus term is the main contributor to the overall fit. The quality of the fit at each iteration is monitored by the chisq values generated by *mrqmin* and through the more sensitive root-mean-square (rms) error. The iteration process is terminated when the percent change in chisq<0.05 and the percent change in rms < 0.01 or is negative, in the latter case signifying a deterioration in the quality of the fit.

RESULTS AND DISCUSSION

The Figures illustrate the contribution of the main bolus and leakage terms to the overall fit. Figure 1 demonstrates that the fitting is robust enough not to interpret recirculation as leakage when there is no leakage. Figures 2 and 3 illustrate cases of slight and moderate leakage, with the orange and blue lines representing the bolus and leakage terms, respectively. The constraints have been crucial in ensuring that neither of these terms goes negative and that the primary contribution to the overall fit is from the main bolus term, and not from the leakage.

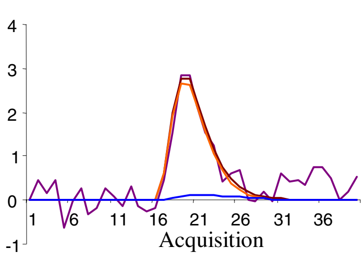

Fig.1. K_p= 0.43; a=2.90; b=0.57; K_{trans}.= 0.007; k_{ep}= 0.196

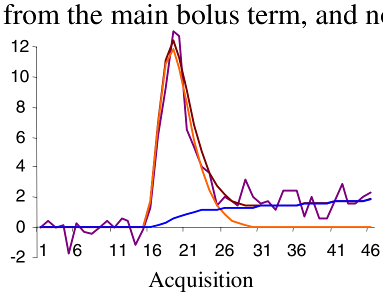

Fig.2. K_p= 1.08; a=3.19; b=0.55; K_{trans}.= 0.012; k_{ep}= -0.012

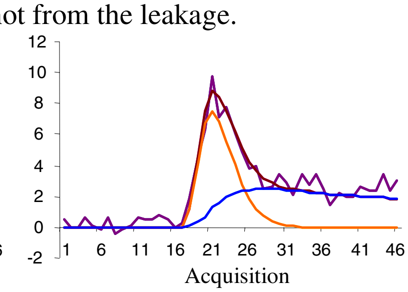

Fig.3. K_p= 0.70; a=3.05; b=0.52; K_{trans}.= 0.030; k_{ep}= 0.012

REFERENCES

1. Butman JA, Tasciyan T. *ISMRM* 2004; 13:1126. 2. Johnson G et al *Magn Reson Med* 2004; 51:961-8.
3. Press et al. Numerical Recipes in C++. Cambridge, University Press 2002.