The accuracy and limitation of two-component model for correcting T1 influence in dynamic susceptibility-contrast MRI in the presence of BBB Breakdown

Y-J. Liu[1], W-C. Wu[2], H-W. Chung[3,4], C-Y. Chen[4], C-J. Juan[4]

[1]Department of Radiological Technology, Yuan-Pei University of Science and Technology, Hsin-Chu, Taiwan, [2]UCSD Center for Functional MRI, La Jolla, CA, United States, [3]Department of Electrical Engineering, National Taiwan University, Taipei, Taiwan, [4]Department of Radiology, Tri-Service General Hospital, Taipei, Taiwan

Introduction

On the premise of intact blood-brain-barrier (BBB), first pass dynamic contrast-enhanced MR imaging can be used to semi-quantitatively measure cerebral blood volume (rCBV) based on the proportionality between perfusion and the change of transverse relaxivity (ΔR2*). However, neurological diseases such as brain tumor and stroke may bring about alterations in BBB permeability to a number of compounds. Once the contrast agent leaks into the interstitial space, it causes T1 shortening effect leading to underestimation of rCBV (1). The amount of leaked contrast agent can be determined on the basis of its extraction fraction (or permeability of the vessels) multiplied by perfusion. In other words, contrast-enhanced MR images reflect both permeability and perfusion of the tissue. To separate intravascular ΔR2* signal and leakage T1 effect, a two-component model was proposed (2) which was recently modified to achieve self-correction (3). However, the accuracy and limitation of these techniques have not been addressed yet. In this study, we use computer simulation to reinvestigate the feasibility of the two-component model and the self-correction strategy.

Materials and Methods

a. ΔR2 generation Concentration-time curves of cerebral tissue were mathematically created by convolution of an arterial input function with tissue residue functions (4). A gamma-variate function was used for the arterial input function ($kt^{\alpha}\exp(-t/\beta)$, where k=0.0173,α=0.3,β=1.5) and the tissue residue function was modeled as an exponential decaying function scaled by cerebral blood flow (CBF) with time constant MTT (CBF×exp(-t/MTT)). 1000 combinations of CBF and MTT were used to randomly generate tissue signal-time curves covering a wide range (CBF: 0.5~2.5, MTT: 1~10 sec) of pathophysiologic and normal hemodynamic situations. Inter-frame noise was subsequently added to the 1000 tissue signal-time curves with baseline signal 500 and signal-to-noise ratio 50.

b. ΔR2 generation with T1 influence The ΔR2 with extravascular T1 effect ($\Delta R2_{T1}$) can be approximated by (2):

$$\Delta R2_{T1} = \Delta R2 - (TR/TE)\cdot(e^{-TR/T1}/(1-e^{-TR/T1}))\cdot R1\cdot Ct(t) \quad \text{.....[1]}$$

where Ct is concentration of Gd leaking into tissue. Ct can be modeled by a triple exponential function with empirically determined constants (5). Among them, the permeability surface area product per unit volume of tissue, k, was chosen to be 0.001, 0.01, 0.03 min^{-1} for different degrees of BBB breakdown. 1000 $\Delta R2_{T1}$ curves were thereby generated for each k value.

c. correct T1 effect Assuming small T1-based enhancement and no back diffusion of contrast agent from the tissue space, [1] can be further simplified to $\Delta\tilde{R}_2^*(t) \approx K_1\overline{\Delta R_2^*}(t) - K_2\int\overline{\Delta R_2^*}(t)dt$ .....[2]

where $\Delta\tilde{R}_2^*(t)$ is the contaminated estimate of ΔR_2^*. Compared with [1], the first term on the right corresponds to original ΔR2 while the second one represents T1 effect. Instead of applying the definition Weisskoff proposed for the $\overline{\Delta R_2^*}$ (averaging $\Delta\tilde{R}_2^*(t)$ for all pixels within a whole-brain mask), we acquired $\overline{\Delta R_2^*}$ using three methods to inspect the influence of references chosen for $\overline{\Delta R_2^*}$. (a) Fit data within the time point of 80% maximum after the peak to a gamma-variate function on the assumption of little T1 influence. (b) Adopt ΔR2 that resembles dynamic signals in gray matter (CBF=2, MTT=2.5). (c) Choose ΔR2 with resemblance to the dynamic signals in white matter (CBF=0.5, MTT=12). Applying $\Delta R2_{T1}$ and $\overline{\Delta R_2^*}$ to the left term and right 2nd term in [2] respectively, "corrected" ΔR2 was obtained by least-squared linear fit.

d. error evaluation Original and corrected CBV were calculated by integrating ΔR2 and corrected ΔR2, respectively. The accuracy of correction was evaluated by error=(CBV_correct – CBV_original) / CBV_original.

Results and Discussion

Fig 1 demonstrates an example of corrected ΔR2 by approximating $\overline{\Delta R_2^*}$ using different methods. Fig 2 shows the mean error and standard deviation under different k values and $\overline{\Delta R_2^*}$ references. According to our study, it is no necessary to do correction in very small BBB breakdown condition (k=0.001 min^{-1}), the mean errors in corrected and uncorrected condition are not substantially different. The capacity of correction methods can reduce the error in large leakage condition (k=0.01, 0.03 min^{-1}), and thus are effective in reducing the underestimation of CBV. In general, correction using white matter performs better in recovering T2*-weighted signals from extravascular T1 effect, with mean error about 10% in three leakage conditions. ΔR2 in normal white matter serves as a satisfactory reference for $\overline{\Delta R_2^*}$.

References

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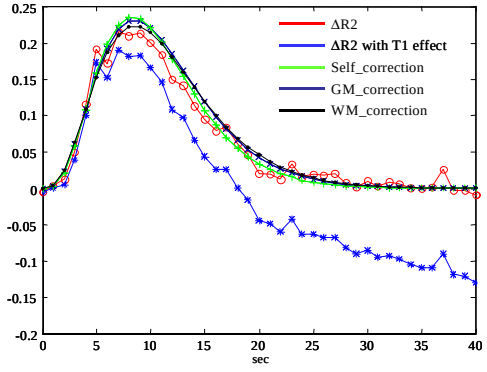

Fig1. a example of corrected ΔR2 by different $\overline{\Delta R_2^*}$ references.

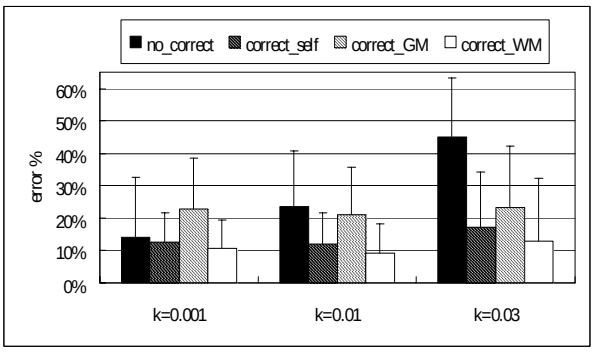

Fig2. The mean error and standard deviation within different permeability and $\overline{\Delta R_2^*}$ references.