Modeling T1 and T2 effects of contrast agent extravasation and pre-loading dose in dynamic susceptibility contrast MRI

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Introduction

In dynamic susceptibility contrast (DSC) MR imaging, when there is a disruption of the BBB, as is frequently the case with brain tumors, contrast agent leaks out of the vasculature into the extravascular extracellular space (EES), resulting in both additional T1 and T2 relaxation effects. In the slightly leaky conditions, previous studies successfully modeled the T1 effect and were able correct it for better CBV and CBF quantifications [1, 2]. However, in the very leaky conditions, the T2 effect can be significant and needs to be taken into account. This study proposed a two-compartmental model that is able to describe the combined T1 and T2 effects in the measured signals. In addition, the commonly applied pre-loading dose for reducing the errors caused by leakage was included in our model.

Methods

The concentration of tracer within the tissue at time t, $C_T(t)$, after the bolus injection is given by:

$$C_T(t) = F \cdot C_A \otimes R(t) \quad [1]$$

where F is tissue blood flow, $C_A(t)$ is the arterial input function and R(t) is the vascular residue function. In our model, R(t) is given as weighted sum of the two compartments of without and with leakage:

$$R_{nonleakage} = w_1 \cdot e^{-(t/MTT)} \quad [2]$$

$$R_{leakage} = w_2 \cdot e^{-(t/\tau)} \quad [3]$$

where w1 and w2 are constants for leakage weighting factor ($w_1+w_2=1$) and τ is the time constant for the contrast agent leaks to the EES (τ >> MTT). Therefore, $C_T(t)$ can be written as :

$$C_T(t) = C_{nonleakage}(t) + C_{leakage}(t) \quad [4]$$

$$C_{nonleakafe}(t) = F \cdot C_A \otimes R_{nonleakage}(t) \quad [5]$$

$$C_{leakage}(t) = F \cdot C_A \otimes R_{leakage}(t) \quad [6]$$

And the signal intensity time curve, S(t) can be approximated as:

$$S(t) = M_0 \cdot \left[1 - e^{-(R1_0 + r_1 \cdot C_{leakage}(t))TR}\right] \cdot e^{-\left[R2_0^* + r_2 \cdot (C_{nonleakage}(t) + C_{leakage}(t))\right]TE} \quad [7]$$

where $R1_0$ and $R2_0$ are the baseline longitudinal and transverse relaxation rates, r_1 and r_2 are longitudinal and transverse relaxivity of contrast agents and the flip angle =90^0. In this model, we assumed the contrast concentration in the plasma only reduces T2, but in EES both T1 and T2. When the pre-loading dose is applied before the DSC scan, we add a steady-state concentration to the $C_{leakage}(t)$ component, the pre-loading dose factor, C_{pre}. In such case, the Eq. [6] is substituted as:

$$C_{leakage}(t) = F \cdot C_A \otimes R_{leakage}(t) + C_{pre} \quad [8]$$

Results

Our model was able to simulate tissue signal time courses and $\Delta R2^*$ curves in a slightly leaky conditions, as demonstrated in Fig. 1, which agreed well with previous models (1, 2). However, in a very leaky tumor, as showed in Figure 2, the previous model failed to describe the strong T2 effect from the contrast agents in the EES (Fig. 2b and 2d) whereas the current model fitted well with the measured time curves (Fig. 2c and 2e). It can be noted that during the dynamic measurements, the initial T1-caused signal increases were followed by strong and sustained signal decreases that is resulted from the T2 effect. Figure 3 illustrates the effect of pre-loading doses as incorporated in our model. As expected, in the slightly leaking conditions, rCBV is under-estimated which can be compensated with proper pre-loading doses. However, in the very leaky conditions, rCBV is over-estimated, due to the T2 effects, even with pre-loading doses.

Conclusion

The present model is able to describe the combined T1 and T2 effects during the contrast passage with disrupted BBB, even in the very leaky condition and when a pre-loading dose is applied. This model could be used to fit DSC signal time curves measured in different leaky conditions for correcting perfusion measurements and obtaining permeability information in tumor patients.

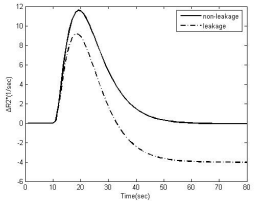

Figure 1 Examples of ΔR2* curves without and with slight leakage, as generated from Eq. [4].

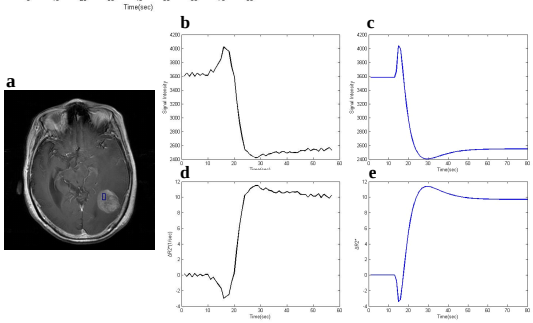

Figure 2 From a very leaky ROI in the tumor (the blue square in (a)) of one of the patients, the measured signal time curves (b) and $\Delta R2^*$ curves (d) were well simulated by our model (c, e).

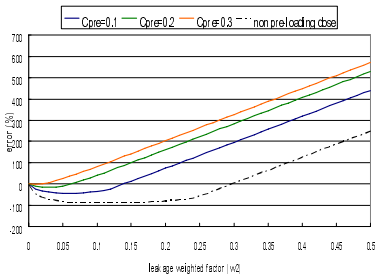

Figure 3 Percent rCBV errors in different leaky conditions, when different pre-loading dose factors are given.

References

1. Quarles et al. MRM 2005; 53: 1307–1316
2. Boxerman et al. AJNR 2006; 27:859–67