Quantification of Vessel Permeability by Modeling Contrast Agent Extravasation in Dynamic Susceptibility Contrast MRI of Brain Tumors

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Introduction

In dynamic susceptibility contrast (DSC) MRI, 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. Previous studies focused on modeling the T1 (1,2) or the combined T1 and T2 effects (3) and introduced a parameter that related to vessel permeability. This study aimed to provide absolute quantification of the permeability surface area product (ps) at the same time when correcting the relaxation effects at 3T.

Methods

In DSC studies, the signal intensity time curve, S(t) can be approximated as: $S(t) = M_0 \cdot \left[1 - e^{-\left(R1_0 + r_1 \cdot C_{leakage}(t)\right)TR}\right] \cdot e^{-\left[R2_0^* + r_2 \cdot \left(C_{nonleakage}(t) + C_{leakage}(t)\right)\right]TE}$

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. Define:

$$\Delta\tilde{R}2^*(t) \equiv -\frac{\ln\left(S(t)/S_0\right)}{TE} = r_2 \cdot C_{nonleakage}(t) + r_2 \cdot C_{leakage}(t) - \frac{1}{TE} \cdot \ln\left(\frac{1 - e^{-\frac{TR}{T1}} \cdot e^{-TR \cdot r_1 \cdot C_{leakage}(t)}}{1 - e^{-\frac{TR}{T1}}}\right)$$

$\Delta\tilde{R}2^*(t)$ is a measurement of contaminate $\Delta R2^*(t)$, and is obtained by computing the ratio of $S(t)/S_0$. Over this time scale (≦1 minute), we neglect back diffusion of agent from the extravascular to the intravascular space and can therefore represent the accumulation of agent in the tissue, $C_{leakage}$, as(1,2):

$$C_{leakage} \approx ps \cdot \int_0^t C_{nonleakage}(t')dt' = \mathrm{ps} \cdot \frac{1}{BV} \cdot \frac{1}{\mathrm{r}_2} \cdot \int_o^t \overline{\Delta R2^*}(t')dt'$$

Where ps is permeability surface area of product per unit mass of tissue. We assume that the average of $\Delta R2^*(t)$ over parts of the brain without extravasation is proportional to $C_{nonleakage}$ (t). The BV is average blood volume in brain. Then we assume the true $\Delta R2^*$ for each pixel is a scaled version of the $\overline{\Delta R2^*}(t)$:

$$\Delta\tilde{R}2^*(t) \equiv \mathrm{K1} \cdot \overline{\Delta R2^*}(t) + K2 \cdot \int_0^{\kappa} \overline{\Delta R2^*}(\kappa)\, d\kappa - \frac{1}{TE} \cdot \ln\left(\frac{1 - K3 \cdot e^{-TR \cdot \frac{r_1}{r_2} \cdot K2 \cdot \int_0^{\kappa} \overline{\Delta R2^*}(\kappa)\, d\kappa}}{1 - K3}\right)$$

Where true $\Delta R2^*$=K1 . $\overline{\Delta R2^*}$, K2= ps/BV, and K3=$e^{-\frac{TR}{T1}}$. K1, K2, and K3 can be determined by linear least-squares fitting. Note the ps can be quantified from K2 with a known BV. In this study, the BV (averaged blood volume of normal brain tissue) was assumed 0.06. A corrected $\Delta R2^*$ can be computed:

$$\Delta R2^*_{corr}(t) = \Delta\tilde{R}2^*(t) - K2 \cdot \int_0^{\kappa} \overline{\Delta R2^*}(\kappa)\, d\kappa + \frac{1}{TE} \cdot \ln\left(\frac{1 - K3 \cdot e^{-TR \cdot \frac{r_1}{r_2} \cdot K2 \cdot \int_0^{\kappa} \overline{\Delta R2^*}(\kappa)\, d\kappa}}{1 - K3}\right)$$

Then $\Delta R2^*_{corr}(t)$ could be use to calculate the corrected rCBV, that will as:

$$rCBV_{corr} = \int_0^T \Delta R2^*_{corr}(t)dt$$

Three patients with brain tumors participated in the study with informed consent. A $T2^*$-weighted gradient-echo EPI sequence (TR/TE/FA=1500 ms/ 35 ms/90) was applied for the DSC imaging at a 3T clinical scanner. A dose of 0.1 mmol/kg of Gd-DTPA was injected at a rate of 5 ml/s through the antecubital vein for the DSC imaging. Contrast enhanced T1-weighted images was then obtained using a conventional SE sequence (TR/TE = 700/19 ms).

Results

Tumor blood volume were over-estimated in all cases due to predominate T2* effect from the leakage. The percentage difference of the blood volume ratio resulted from the correction was significantly larger for the tumor/white matter than the gray/white matter, exhibiting contrast extravasations (Table 1). The derived ps parameters from the same ROIs were be list in table 2. In the tumor, the ps were all larger than normal tissue and with values comparable to those in literatures. The ps parameter maps are compared with the post-contrast T1-weighted image in Fig1.

Conclusion

The proposed model was able to fit DSC signal time curves measured at 3T for correcting perfusion measurements and obtain quantitative permeability estimates in patients with brain tumors.

Table 1. Gray/White matter and Tumor/White matter ratio calculated form corrected and uncorrected rCBV maps of three patients.

Case no.	Gray matter/White matter ratio		
	Uncorrected	Corrected	Difference (%)
1	1.96	1.93	1.8
2	1.72	1.53	12.9
3	1.51	1.31	15.4

Case no.	Tumor/White matter ratio		
	Uncorrected	Corrected	Difference (%)
1	7.39	4.41	67.4
2	3.89	1.55	151.3
3	3.49	2.21	58.3

Case no.	GM	WM	Tumor
1	0.138	0.129	0.738
2	0.075	0.082	0.283
3	0.116	0.142	0.289

Table 2. Permeability surface area products (min^{-1}) obtained from three ROIs of three patients.

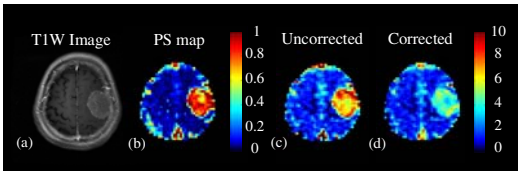

Figure 3.Post-contrast T1w image (a), ps parameter map (b), uncorrected (c) and corrected (d) rCBV maps from one of the patients.

References

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3. Wu et al. ISMRM 16th Annual Meeting 2008; p1912