Can Contrast Extravasation be Separated from Intravascular Recirculation in DSC MRI of The Brain?

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Introduction

In dynamic susceptibility contrast (DSC) MRI, the concentration time curves commonly do not return to baseline after the first pass. In normal brain tissues with intact blood-brain barrier (BBB), the elevated concentration during the recirculation phase could be caused by the intravascular contrast agents. However, when the BBB is disrupted, as the case with brain tumor, both the intravascular component and the contrast extravasations contribute to the measured concentration time curves during recirculation. The recirculation behavior was studied in brain tumors and interpreted as the degree of vascular tortuosity and disturbances in blood flow within brain tumors (1, 2). However, contrast leakages in brain tumors were also investigated as T1 and T2 effects in the recirculation phase of the DSC curves, which were linked to vessel permeability (3, 4). The contrast leaked to the extravascular extracellular space (EES) can appear as additive (if T2) or subtractive (if T1) effects to the intravascular recirculation. The aim of this study is to investigate whether the contrast extravasation can be separated from intravascular recirculation in DSC MRI of the brain.

Methods

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

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:

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

$\Delta\tilde{R}2^*(t)$ is a measurement of contaminate $\Delta R2^*(t)$, and is obtained by computing the ratio of S(t)/S_0. Then we assume the concentration of tumor without leakage could be written as:

$$C_{nonleakage}^{tumor}(t) = K_1 \cdot C_{1st}^n(t) + K_4 \cdot C_{rec}^n(t) \quad [3]$$

Where K_1 and K_4 are proportional factors between normal and tumor contrast agent concentration time course. $C_{nonleakage}^{tumor}(t)$ is contrast agent concentration time course of tumor that without leakage. $C_{1st}^n(t)$ is concentration time course of first pass in normal tissue that was fitted to a gamma variant function. And $C_{rec}^n(t)$ is concentration time course of recirculation part in normal tissue and was approximated by the average of $\Delta R2^*(t)$ over normal parts of the brain ($\overline{\Delta R2_m^*}$):

$$C_{rec}^n = \frac{1}{r_2} \cdot \overline{\Delta R2_{rec}^*}(t) = \frac{1}{r_2} \cdot \left(\overline{\Delta R2_m^*} - \overline{\Delta R2_{1st}^*}\right) \quad [4]$$

Over this time scale (≦1 minute), we neglect back diffusion of tracer from the extravascular to the intravascular space and can therefore represent the accumulation of agent in the tissue, $C_{leakage}$, as:

$$C_{leakage} \approx ps \cdot \int_0^t C_{nonleakage}(t')dt' = \frac{ps}{BV} \cdot \frac{1}{r_2} \cdot \int_o^t \left[K_1 \cdot \overline{\Delta R2_{1st}^*}(t') + K_4\left(\overline{\Delta R2_m^*}(t') - \overline{\Delta R2_{1st}^*}(t')\right)\right]dt' \quad [5]$$

Where ps is permeability surface area product per unit mass of tissue. The BV is average blood volume in brain. By replacing Eq. [2] with Eqs. [3]-[5], one can show:

$$\Delta\tilde{R}2^*(t) \equiv K_1 \cdot \overline{\Delta R2_{1st}^*}(t) + K_4\left(\overline{\Delta R2_m^*}(t) - \overline{\Delta R2_{1st}^*}(t)\right) + K_2 \cdot \int_o^t \left[K_1 \cdot \overline{\Delta R2_{1st}^*}(t') + K_4\left(\overline{\Delta R2_m^*}(t') - \overline{\Delta R2_{1st}^*}(t')\right)\right]dt' - \frac{1}{TE} \cdot \ln\left(\frac{1 - K_3 \cdot e^{-TR \cdot \frac{r_1}{r_2} \cdot K_2 \cdot \int_o^t \left[K_1 \cdot \overline{\Delta R2_{1st}^*}(t') + K_4\left(\overline{\Delta R2_m^*}(t') - \overline{\Delta R2_{1st}^*}(t')\right)\right]dt'}}{1 - K3}\right) \quad [6]$$

Where true $\Delta R2^* = K_1 \cdot \overline{\Delta R2_{1st}^*}(t)$, $K_2 = ps/BV$, $K_3 = e^{-\frac{TR}{T1}}$, and K_4 is represent an index for intravascular recirculation. In our computer simulation, $\overline{\Delta R2_m^*}(t)$ and $\overline{\Delta R2_{1st}^*}(t)$ was obtained from a DSC dataset of a patient with brain tumor, and K_2 and K_4 were used to generate DSC time curves with different leakage and recirculation conditions.

Results

The $C_{rec}^n(t)$ obtained from the patient data is demonstrated in Fig. 1, which shows a clear 2nd-pass peak followed by recirculation. By observing in fig. 2, a negative $\Delta R2^*$ must be resulted from contrast leakage (K_2). However, a positive $\Delta R2^*$ during recirculation phase can be caused by either contrast leakage (K_2) or intravascular recirculation (K_4) or both. Figure 3 illustrates a special condition when the K_2 and K_4 effects cancel out each other and thus appear zero concentration during the recirculation phase. In such condition, however, differences exist during the first pass of the curve..

Conclusion

This study showed that contrast leakage (K_2) and intravascular component (K_4) during the recirculation phase could be subtractive effects or additive effects, and difficult to separate from each other. This makes it challenging to extract vessel permeability information from DSC time curves. In principle, the first-pass data may be useful but its sensitivity requires further studies.

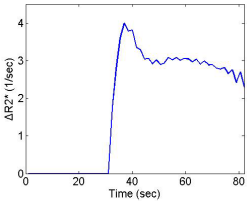

Figure 1 Intravascular component of the recirculation phased, $\overline{\Delta R2_{rec}^*}(t)$, obtained from normal tissues.

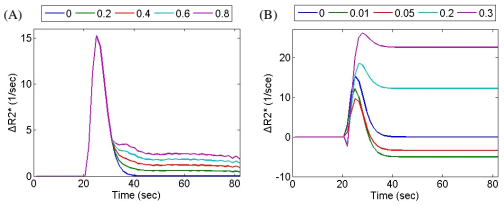

Figure 2. Effects of pure intravascular recirculation (K_2=0, K_4 =0~0.8) (A), and pure contrast leakage (K_4=0, K_2 = 0~0.3) (B).

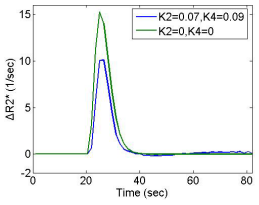

Figure 3. Two different combinations of K2 and K4 (leakage and intravascular recirculation, respectively) can resulted in the same $\Delta R2^*$ level at the recirculation phase, but different during the first-pass.

References

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