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 leakage 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:

\[ S(t) = M_0 \left[ 1 - e^{-\left( R_1^c + C_{tumor}(t) \right) T} \right] + \frac{\alpha}{T} \left( 1 - e^{-\left( R_2^c + C_{tumor}(t) \right) T} \right) \]

Where \( R_1^c \) and \( R_2^c \) are the baseline longitudinal and transverse relaxation rates, \( t_1 \) and \( t_2 \) are longitudinal and transverse relativity of contrast agents and the flip angle =90°. In this model, we assumed the contrast concentration in the plasma only reduces T2, but in EES both T1 and T2.

\[
\Delta R_2^c(t) = -\frac{\ln(S(t)/S_0)}{T_E} = -\frac{1}{T_E} \ln \left( \frac{1 - e^{-\frac{t_2}{T_2}}}{1 - e^{-\frac{t_1}{T_1}}} \right)
\]

\(\Delta R_2^c(t)\) is a measurement of contaminant \(\Delta R_2^c\), 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:

\[ C_{tumor}(t) = K_1 C_{tumor}^0(t) + K_2 C_{tumor}(t) \]

Where \( K_1 \) and \( K_2 \) are proportional factors between normal and tumor contrast agent concentration time course. \( C_{tumor}^0(t) \) is contrast agent concentration time course of tumor that without leakage. \( C_{tumor}^0(t) \) is concentration time course of first pass in normal tissue that was fitted to a gamma variant function. And \( C_{tumor}(t) \) is concentration time course of recirculation part in normal tissue and was approximated by the average of \(\Delta R_2^c(t)\) over normal parts of the brain \(\Delta R_2^c(t)\):

\[ C_{tumor}^0(t) = \frac{1}{T E} \left[ \Delta R_2^c(t) \right] \]

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:

\[ C_{leakage} = ps \cdot BV \cdot \frac{1}{T E} \int K_1 \left[ \Delta R_2^c(t) \right] dt \]

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

\[
\Delta R_2^c(t) = K_1 \left[ \Delta R_2^c(t) \right] + K_2 \left[ \Delta R_2^c(t) - \Delta R_2^c(t) \right] + K_3 \left[ \Delta R_2^c(t) - \Delta R_2^c(t) \right] dt
\]

Where \( ps = K_1 \), \( BV = K_2 \), and \( K_3 \) is represent an index for intravascular recirculation. In our computer simulation, \(\Delta R_2^c(t)\) and \(\Delta R_2^c(t)\) was obtained from a DSC dataset of a patient with brain tumor, and \( K_1 \) and \( K_2 \) were used to generate DSC time curves with different leakage and recirculation conditions.

Results
The \( C_{tumor}^0(t) \) obtained from the patient data is demonstrated in Fig. 1, which shows a clear 2\(^{nd}\)-pass peak followed by recirculation. By observing in fig. 2, a negative \(\Delta R_2^c\) must be resulted from contrast leakage (\( K_2 \)). However, a positive \(\Delta R_2^c\) 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, \(\Delta R_2^c(t)\), obtained from normal tissues.

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

Figure 3. Two different combinations of \( K_2 \) and \( K_4 \) (leakage and intravascular recirculation, respectively) can resulted in the same \(\Delta R_2^c\) level at the recirculation phase, but different during the first-pass.

References

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