Comparison of cerebral blood volume and contrast leakage correction efficiency with dynamic susceptibility contrast enhanced perfusion imaging

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[Introduction]
MR perfusion weighted imaging (PWI) using dynamic susceptibility contrast (DSC) technique has been used to evaluate brain tumor characterization. Quantitative or semi-quantitative evaluation of cerebral blood volume (CBV) is potentially useful for tumor staging and treatment decision-making. It has been shown that maximum CBV in tumor could be a maker of tumor grade. However, CBV quantitative measurement suffers from contrast leakage effect when the blood brain barrier (BBB) is disrupted. Post-processing correction methods have been proposed to correct this contrast leakage effect and to obtain accurate CBV estimation from DSC data[1]. With these methods, a reference time course is used to estimate contrast leakage. The estimated leakage effect from DSC can vary with the reference time course used in the post-processing. To overcome these issue, we evaluated the impact of reference time course to estimate the leakage effect using numerical simulation and clinical data. Then the results were compared between the different reference time courses.

[Materials and Methods]
Assuming that contrast in the extra-vascular extra-cellular space (EES) shortens T1 and T2, but contrast in plasma only shortens T2, then MR signal can be written as the following equation (1). For given contrast concentration in the plasma $C_p(t)$, total tissue contrast concentration $C_t(t)$ and the concentration in EES $C_e(t)$ can be described as following equation (2) using first-pass pharmacokinetic modeling (FPPM)[2]. MR signal change with contrast leakage out of extra-vascular space can be calculated using equation (1) and (2) when $C_p(t)$ is known.

$$S(t) = S_0(1-\exp(-TR\times r_1\times v_e C_e(t))\exp(-TR/T_1))\exp(-TE\times r_2\times(v_p C_p(t)+v_e C_e(t))\exp(-TE/T_2^*) \quad (1)$$

$$C_t(t) = v_p C_p(t) + v_e C_e(t) \qquad C_e(t) = K_{trans}/v_e \times \int C_p(\tau)\exp(-K_{trans}\times(t-\tau)/v_e)d\tau \quad (2)$$

The concentration change is assumed as gamma variate function, and for given parameters, we simulated the MR signal change in tumor. Then estimated delta R2* change from this MR signal change was calculated. This delta R2* change was converted to tracer concentration. Three different width of reference time course, including narrow, wide and the exactly same as $C_p(t)$ were used for leakage estimation. These are corresponds to global arterial input function (AIF), whole brain average (WBA) signal, and local input function for actual data, respectively. Leakage effect was estimated and the leakage corrected CBV (cCBV) can be calculated using the following equation (3) for given reference time course $C_{ref}(t)$. Two coefficients k_1 for un-leaked compartment and k_2 for leakage effect were estimated using the least square fit[1].

$$C_t(t) = k_1 C_{ref}(t) - k_2\int_0^t C_{ref}(t-\tau)d\tau \qquad cCBV = CBV + K_2\int_0^T dt\int_0^t C_{ref}(\tau)d\tau \quad (3)$$

DSC image data of three brain tumor patients were analyzed using the proposed algorithm to evaluate its accuracy and robustness. The processed images were visually assessed qualitatively and the maximum CBV value in tumor are measured and compared for each reference time course. Image processing algorithm was implemented in C++ using DICOM Toolkit ver.3.5.2. The platform used to implement and test the algorithms was DELL LATITUDE D430, Intel Core2 Duo processor 1.33 GHz, 1.99GB RAM running Windows XP operating system.

[Results and Discussion]
Leakage effect could be detected with both wide or narrow reference time course in simulated tumor MR signal change. The result was shown in table.1. The corrected CBV values are –22.9% of true CBV for narrow and 23.7% for wide and 0.35% for the exact same reference as $C_p(t)$. When the leakage estimation was applied to the simulated normal tissue MR signal, positive leakage signal was obtained with the wide reference time course and negative leakage signal with the narrow reference. This positive leakage estimation with wide reference could be pseudo leakage effect in the normal tissue. Overestimation of the corrected CBV value (63.5% from true CBV) was observed when the reference time course with wide width was used.
The measured maximum CBV values in tumor are shown in table 2. The values are increase when the leakage effect was corrected. Calculated corrected CBV maps and K2 maps were presented in Figure.1. Large difference was not seen in map appearance of the corrected CBV map between the reference time courses used in the analysis. The K2 map appearance was dramatically changed with the reference used in the analysis. When the AIF signal was used as the reference time course, only tumor area has high K2 value in the map. When the whole brain averaged delta R2* time course was used as the reference time course, normal gray matter was also visualized as high signal area. This pseudo leakage effect in the gray matter is what is observed in the simulation study and this pseudo leakage may cause false positive in leakage map.

[Conclusion]
This study showed that appropriate selection of reference time course is an important factor to obtain reasonable contrast leakage index using DSC MRI. Reference time course with wider width may introduce false positive signal in leakage map.

[Reference]
[1] AJNR Am J Neuroradiol 27: 859-67 [2] JMRI 1999; 10: 223-232 [3] Nishimura et al. The vast expanse of diffusion and perfusion MRI for diagnostic imaging (2006)

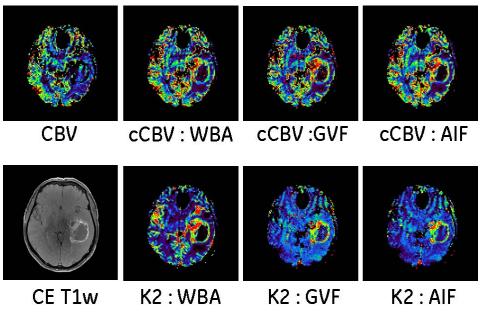

Figure 1: corrected CBV map and K2 map
CBV : uncorrected CBV. cCBV corrected CBV.

Table 1: Numerical simulation result

cCBV%	no leakage	with leakage	K2 [A.U.]	no leakage	with leakage
WBA (wide)	63.54545932	23.69861757	WBA (wide)	2.48986E-08	5.28257E-08
Cp	-0.001970899	0.3542977	Cp	-1.40294E-09	7.93515E-05
AIF (narrow)	-24.63185484	-22.89357837	AIF (narrow)	-1.80182E-05	6.45389E-05

cCBV % = (cCBV – CBVtrue)/CBVtruex100 [%]
Ktrans = 0.034 [ml/ml/min]
ve=0.25% vp=0.0351%
r1=4.5[sec-1mM-1]
r2=5.5[sec-1mM-1]

Table 2: maximum CBV measurement result for tumor cases

Max CBV [ml/100g]	case1	case2	case3
CBV	0.161	1.029	3.233
cCBV WBA	19.32	5.578	13.387
cCBV GVF	7.867	2.513	5.02
cCBV AIF	6.49	2.561	5.728