Does DSC-derived CA extravasation correlate with DCE K^{trans}?

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Purpose: A 'byproduct' of the contrast agent (CA) DSC leakage correction method proposed by Weisskoff and colleagues[1] is the 'K_2' term reflecting estimated CA extravasation into the interstitial space. If the K_2 parameter really reflects tumor permeability, DSC imaging could potentially provide estimates similar to that of DCE K^{trans}, thereby providing a powerful and time-efficient tool for monitoring of treatment response to anti-VEGF therapy[2]. In our study, we explore the relationship between CA extravasation from DSC and DCE both in simulations and patient data.

Methods and Materials: First, a simulation was performed by modeling an arterial input function (AIF) as a gamma variate function with an additional exponential term to model steady state effects. From this, a K_2-like leakage constant (denoted 'K_a') was determined by incorporating a CA leakage term in the tissue residue function[3]. A corresponding K^{trans} parameter was derived using a standard two compartment model. K_a was compared to K^{trans} over a relevant range of K^{trans} values by including the T1-term in the equation for signal intensity change due to CA induced increase in relaxation rates:

$$\frac{1}{TE}\left[\ln\left(\frac{SI(0)}{SI(C)}\right)\right] = \Delta R2^*(C) - \frac{1}{TE}\ln\left(\frac{E1(C)}{E1(0)}\right) = \Delta R2^*_{app}(C)$$

where $\Delta R2^*$ is change in T2* relaxation rate, C is CA concentration, $\Delta R2^*_{app}$ is the measured apparent change in $\Delta R2^*$ including T1-effects and $E1(C) \geq E1(0)$. The following parameters were fixed for all simulations: TR/TE=1500ms/45ms, CBF=100mL/100g/min and MTT=5s. Second, K_a values from DSC (TE=34ms) and K^{trans} values from DCE were derived from baseline scans part of a retrospective study of 30 patients with recurrent glioblastomas[2] and tumor pixel-by-pixel K_a and K^{trans} values were compared by deriving median K_a values for increasing K^{trans} cohorts similar to the simulations.

Results: Figure 1 shows the results of the comparisons between K_a and K^{trans}. By including a pre-dose in the simulation similar to the patient data (0.1mmol/kg), a T2*-dominant leakage effect and a positive relationship between K_a and K^{trans} was observed for high flip angles (90°; as used in the patient data) and varying extravascular transverse relaxivity ($r2_{ev}$). For the patient data, linear mixed model analysis showed a significant increase in median K_a values for increasing K^{trans} cohorts (P<.001) and a higher goodness of fit was observed when fitting a quadratic function to the data compared to using a linear fit (adjusted R^2=.68, vs. adjusted R^2=.65, respectively).

Conclusion: Although good correlation between permeability markers from DCE and DSC have been previously shown in gliomas[5], the exact relationship between the two parameters has not received much attention. Results from both simulations and patient data clearly suggest that the CA leakage constant estimated from DSC is non-linearly correlated to the underlying permeability surface area product, even when extravasation is permeability limited. The lack of a simple linear correlation is due to the complex relationship between CA concentration in tissue and the measured change signal intensity and corresponding transformation to apparent transverse relaxation rates. Nevertheless, for the ranges of K^{trans} values usually found in enchaning tumor tissue, for high $r2_{ev}$ values (>20$mM^{-1}s^{-1}$), or by assuming a quadratic relationship between K_a and K^{trans} over a larger range of K^{trans} values, a DSC-derived permeability marker could form the basis for a pseudo-leakage parameter in tumor monitoring by MR.

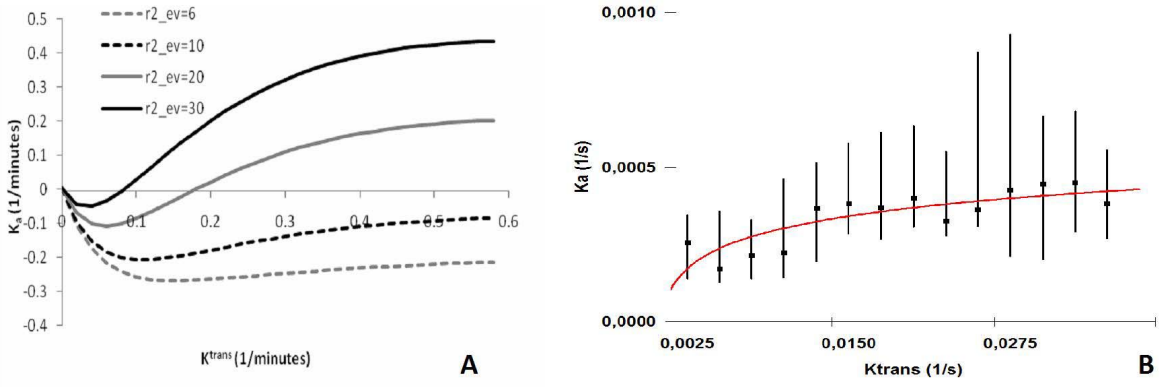

Figure 1: A: Simulations showing the K_a and Ktrans relationship for varying extravascular transverse relaxivity ($r2_{ev}$). **B:** Box plot with 75% confidence intervals of median K_a values as a function of K^{trans} cohorts across all patients. Although the median values across patients have large confidence intervals, results of the linear mixed model analysis showed that K_a increased significantly for increasing K^{trans}.

[1] Weisskoff, et.al. ISMRM 1994;p279 [2] Sorensen AG, et al. Cancer Res 2009:69(13):5296-300,
[3] Bjornerud A, et al. ISMRM 2009;p3623, [4] Tofts et al, JMRI 1999;10:223-232 [5] Cha S et al, AJNR 2006;27(2):409-17