Target Audience: This study is targeted toward researchers interested in the development of advanced perfusion imaging methods.

Purpose: Previous studies have shown that DSC-MRI based CBV values corrected for gadolinium contrast agent (CA) leakage are correlated with glioma tumor grade. Depending on the leakage mechanism – \( T_1 \) and/or \( T_2^* \) – the uncorrected CBV may be either underestimated (\( T_1 \) leakage) or overestimated (\( T_2^* \) leakage). Various leakage correction strategies have been proposed, although few have been validated against a reference standard with the exception of CBV estimates using the Weisskoff correction for \( T_1 \) based leakage effects. Here, we propose a new strategy to correct for \( T_2^* \) leakage effects on \( T_1 \)-insensitive dual echo \( T_2^* \) derived time series. As we have previously shown, \( \Delta R_2^* \) can be modeled as the sum of the intra- and extravascular \( \Delta R_2^* \) components, scaled by their respective CA relaxivity values. If we assume that the dual-echo derived \( T_1 \) changes are equal to \( \nu \cdot C_r (t) \), we can estimate the extravascular CA relaxivity using the transverse relaxivity at tracer equilibrium \( r_{ve} (\text{TRATE}) \) and then subtract \( T_0 \).

Methods: 9L gliosarcoma cells were implanted in Fischer rats (n=3), and MRI was performed at 4.7T (Agilent) at 22 days. Intravenous catheters were inserted for contrast administration with Gd-DTPA and MION. Pre-contrast \( T_1 \) maps were acquired using an inversion recovery technique (TR=8s, TE=2.9ms, 8 TI from 0.25s to 6s, FA=15\(^\circ\)). A dual echo DSC sequence (TR = 1s, TE1 = 8.6ms, TE2 = 35.0ms, 1000 repetitions) was used. After 80s of baseline images, 0.4 mmol/kg Gd-DTPA was injected. At 30 minutes after Gd-DTPA injection, 3 mg Fe/kg MION was injected. The MION injection was diluted to provide an equal volume as the Gd-DTPA injection. The dual echo tissue \( \Delta R_2^* \) was calculated from TE1 and TE2. The Weisskoff (applied to TE2) and TRATE corrections, and MION reference.

Results: Figure 1 shows the \( \Delta R_2^* \) curves for tumor tissue using dual echo and the Weisskoff and TRATE corrections. The calculated CBF and CBV maps are shown in Figure 2, with the MION reference values in the far right column. Figure 3 shows bar plots for tumor CBF and CBV using each \( \Delta R_2^* \) curve against the MION values.

Discussion: The dual echo \( \Delta R_2^* \) signal is insensitive to \( T_1 \) leakage but shows clear \( T_2^* \) leakage effects, leading to inflated \( \Delta R_2^* \) values and overestimated CBV. Interestingly, the dual echo CBF values were not substantially different than those derived from MION. The Weisskoff and TRATE corrections led to reduced \( \Delta R_2^* \) values and CBV values that were closer to the MION reference values, but both underestimated CBF. It should be noted that the Weisskoff model assumes an identical MTT between the reference and corrected tissue, which may lead to inaccurate hemodynamic estimates. In 9L tumors, the Weisskoff model likely performs reasonably well due to the similarity between tumor and normal tissue MTTs (5.2 vs. 4.6 sec, respectively). Conversely, because the TRATE correction is based on voxel-wise measures of \( \nu_e \cdot C_r (t) \), it is insensitive to MTT differences and should be more accurate in more heterogeneous human tumors.

Conclusions: The DSC \( \Delta R_2^* \) signals in leaky tissues, e.g. tumors, must be corrected for leakage to produce accurate CBF and CBV maps. Future work in this study is ongoing and will aim to apply these and other corrections in more animals.

References: