Validation of a Dual Echo DSC-MRI Approach that Enables the Simultaneous Measurement of Blood Flow, Blood Volume and K^{trans}

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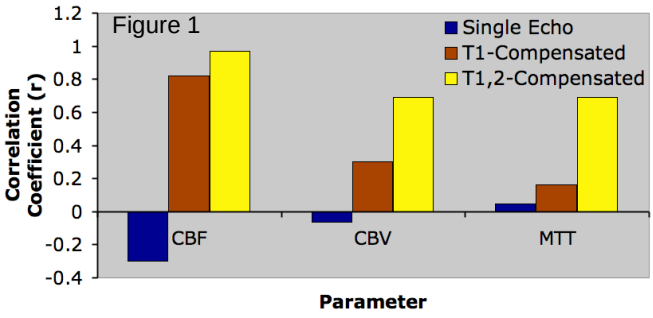
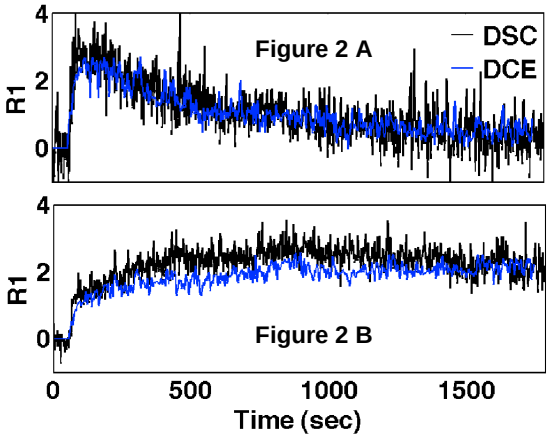
Introduction: Dynamic susceptibility contrast (DSC) MRI methods for assessing brain tumors are confounded by the extravasation of Gadolinium (Gd) agents into the extravascular extracellular space (EES) resulting in unreliable cerebral blood volume (CBV) and blood flow (CBF) measurements (1). The leakage of contrast agent results in simultaneous changes in the EES T_1 and T_2^*, which compete with susceptibility-induced signal decreases. Several methods have been developed to minimize the T_1 changes but as we have recently shown these attempts typically result in enhanced EES T_2 effects (2). In the same study we also proposed a theoretical approach to eliminate these T_1 and T_2^* effects using a dual-echo DSC-MRI while also providing a measure of R_1 time curves typically used to compute K^{trans}. The purpose of this study is to: 1) compare the new dual-echo computed BF and BV measurements to those derived from a DSC study using an intravascular contrast agent in the same animals and 2) compare the dual echo DSC derived R_1 time curves to those measured using a standard DCE-MRI sequence *in the same animal during the same study session*.

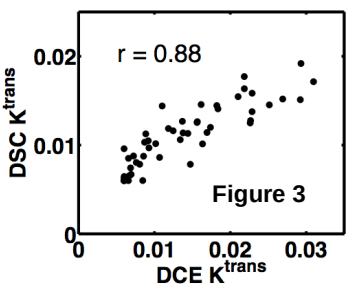
Methods: To evaluate the new dual GE method rat C6 brain tumor (n = 6) images (TR/TE1/TE2/α = 15.625 ms/3 ms/6 ms/25°, FOV = 32 mm x 32 mm, matrix = 64 x 64, 2 mm ST) were collected for 5 minutes using a Varian 7T. At 1 minute into the scan a bolus of 0.3 mmol/kg Gd-DTPA was injected through the jugular vein. A variable flip angle GE approach was employed to produce pre-contrast T_1 maps over the same FOV. In three of the animals we also collected an additional set of first pass images while injecting the intravascular contrast agent Molday-ION (Biophysics Assay Laboratory, Worcester, MA). These images were collected prior to the Gd-DTPA injection and utilized a separate jugular catheter. In the remaining 3 animals typical DCE-MRI images were collected following a second injection of Gd-DTPA. For these animals the time between the Gd-DTPA injections was 4 hours. Using the new analysis we generated $R_1(t)$ curves and tumor CBF, CBV and MTT using one of the echos (labeled Single Echo), corrected for only T1 effects (labeled T1-Compensated), corrected for T_1 and T_2^* effects (labeled T1,2-Compensated). For the first part of the validation we compared these tumor CBF, CBV and MTT measurements to those derived from the Molday-ION datasets. For the second part of the validation we compared the DSC and DCE derived R1(t)-R_0 (1/pre-contrast T_1) curves and the resulting K^{trans} values which were derived using the reference region approach (3).





Results: Figure 1 shows the voxel-wise correlation between the Gd-DTPA and the Molday-ION derived CBF CBV and MTT parameters. The single echo approach, which provides no correction, produced unreliable parameters that were essentially uncorrelated to those derived from the Molday-ION data. The T_1-compensated and T_1, T_2^*-compensated dual-echo tumor CBF measurements were highly correlated with the CBF derived from the intravascular contrast agent. However, the T_1-compensated dual-echo CBV and MTT measurements had a much lower correlation than the T_1,T_2^*-compensated parameters. As compared to the T_1-compensated tumor MTTs, the T_1,T_2-compensated values were, on average, 48% closer to those derived from the Molday-ION signals. Unlike the parameters computed from the single echo and T_1-compensated signals, the correlations for the T_1,T_2^*-compensated tumor CBF, CBV and MTT were comparable to those found in normal brain tissue where leakage effects do not occur. The DSC and DCE derived R1(t)-R_0 time curves were very similar for both muscle (Fig 2A) and tumor (Fig 2B) tissue. A power injector wasn't used for these studies so there may have been some minor differences in the absolute volume and rate of injection. There was a strong correlation between the DSC and DCE derived K^{trans} values but the absolute DSC values were slightly lower than those computed using the DCE data (Figure 3).

Discussion: This study has experimentally shown that EES T_1 and T_2^* contrast agent extravasation effects can be minimized if not removed using DSC-MRI signals acquired at two echo times and a pre-contrast T_1-map. This study also emphasizes the necessity to correct for EES T_2^* leakage effects. To our knowledge this is the first study to demonstrate a correlation between Gd-DTPA based DSC-MRI tumor hemodynamic parameters corrected for contrast extravasation and those derived from an intravascular contrast agent. The preliminary DCE/DSC comparison also suggests that the dual echo approach can be used to compute reliable R1(t) curves and the derived kinetic parameters. For clinical use this could be advantageous since it shortens scan durations and enables a more comprehensive assessment of the tumor. We are currently in the process of increasing the number of animals utilized in this study and performing a more thorough statistical analysis of the comparison datasets.



References: 1. Donahue, MRM 43:845-853; 2004. 2. Quarles, ISMRM Miami: 2100, 2004. 3. Yankeelov, MRI, 23 (2005) 519–52. *Grant support provided by NIH SAIRP U24 CA 126588.*