

Repeatable First Pass DSC-MRI Measurements Using Saline as a Reverse-Effect Contrast Agent

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Introduction: Dynamic Susceptibility Contrast (DSC) MRI provides measures of cerebral blood flow (CBF), cerebral blood volume (CBV) and mean transit time (MTT) but is typically limited to one measurement per imaging session because multiple measures require repeated injections of the contrast agent. Multiple measurements of these metrics could be useful for functional and pharmacological brain imaging. The goal of the present study is to assess the potential of using saline as a reverse-effect contrast agent for multiple DSC-MRI measurements. This method relies on first reducing the MRI-signal intensity using an intravascular iron oxide contrast agent prior to the bolus injection of saline.

Methods: MRI studies have been performed using a 4.7T Varian Scanner, a 63 mm volume transmit/receive coil and a MRI-compatible stereotactic head holder. Anesthesia was induced in the rat using 1.1% isoflurane in air and core temperature was maintained at $37.5 \pm 0.5^\circ\text{C}$. A GE-EPI pulse sequence (TR/TE = 1000 ms / 15 ms, 3 slices, slice thickness = 2 mm, FOV = 40 x 40 mm, matrix = 64 x 64) was used for DSC-MRI data acquisition. DSC-MRI signals were first acquired during a 4-second bolus injection of an intravascular iron-oxide contrast agent (CA), (Molday-ION, BioPal, Inc) at a dose of 8 mg/kg. DSC-MRI signals were then acquired during multiple 4-second bolus injections of 500 - 750 μL of saline. A power injector was used for all injections.

Results: Figure 1 shows example cortical gray matter DSC-MRI signals (normalized to the pre-injection baseline intensity) following the injection of the CA (green) and saline (black). While the iron-oxide produced the expected signal decrease, the saline bolus injection increased the signal intensity by approximately 25% (at peak value). With the exception of the substantial and prolonged recirculation effects observed for the CA-derived signal, the shape of the saline signal was consistent with that of the CA. Saline injections alone did not change the baseline MRI signal intensity (data not shown). Larger peak signals for saline injections were acquired as the loading dose of the CA increased (from 4 mg/kg to 8 mg/kg) likely due to a larger dynamic range for potential signal recovery. Figure 2 shows the DSC-MRI signals following two bolus injections of saline that were separated by two minutes. The peak signal change for the second injection was slightly higher than the first. This effect was observed several times and is likely due to the slight hemodilution caused by the prior saline injection.

Discussion: This preliminary study shows the potential of using saline as a dilution-based DSC-MRI contrast agent for multiple measurements of tissue hemodynamics. Several aspects of this study warrant further investigation. Quantification of blood flow and blood volume from the dynamic time series requires the derivation of an appropriate theory relating signal change (or R_2^* change) to saline volume (or to the diluted CA concentration). The saline-derived hemodynamic parameters would then need to be spatially correlated to those derived from the initial CA DSC-MRI study. While multiple measurements are clearly possible the absolute number of such measurements will be limited by the total injected volume of saline and CA, which could substantially alter the total blood volume. Thus, more studies are needed to optimize the signal reduction and the contrast to noise ratio of the saline induced signal change while minimizing total injected fluid volume. Once validated, this approach could potentially be a new tool for assessing normal and pathological tissue's temporal hemodynamic response to pharmacological agents and functional stimuli.

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