# Simultaneous Quantification of Cerebral Blood Flow and in-vivo T2 and T2* of Cerebral Blood using Continuous Arterial Spin Labeling

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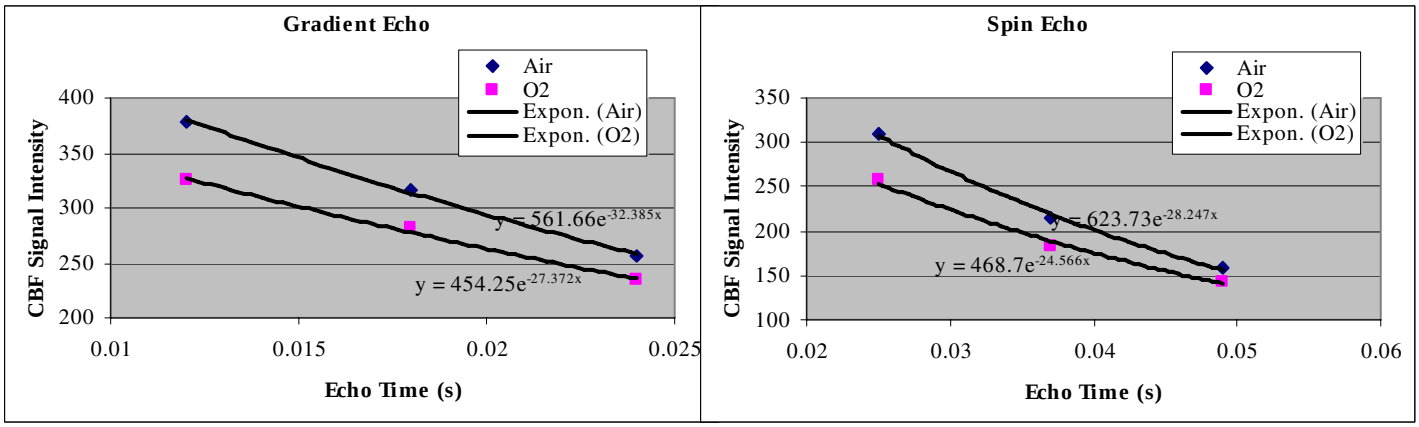
## Abstract

A new pulse sequence has been developed for quantifying in vivo intravascular blood oxygenation level dependence (BOLD) signal using continuous arterial spin labeling (CASL). Specifically, we have measured in-vivo $T_2$ or $T_2$* values of rat cerebral blood using the TE dependence of cerebral blood flow (CBF) signals obtained by CASL. Arterial spin labeling has been a powerful method for studying brain function and cerebral perfusion. On the other hand, the contribution of intravascular BOLD signal to total tissue BOLD signal is important for understanding overall neurovascular BOLD mechanisms including cerebral metabolism. However, to the best of our knowledge, no study has, thus far, directly quantified the intravascular BOLD signal by measuring the in vivo cerebral blood $T_2$ or $T_2$* using ASL. With the transition of inhaled gas from air and 100% oxygen, we have demonstrated that our measurement scheme can be used for reliably quantifying the CBF and in vivo $T_2$ and $T_2$* changes of cerebral blood.

## Materials and Methods

Healthy Sprague-Dawley rats (n=2: ~300g) were anesthetized with 1.5% isoflurane during the MRI experiments. To demonstrate that $T_2$ or $T_2$* of the cerebral blood respond to different oxygenation levels, we used a gas paradigm of inhaling either air or 100% oxygen. A heating pad was used to keep the animal warm throughout the experiment. The MRI was carried out on the Bruker Biospec 9.4T (Magnex magnet) spectrometer with a 12 cm diameter gradient (Magnex gradient). A detuneable 3 x 4 cm oval surface coil was used for imaging while a detuneable 3 x 4.5 cm rectangular surface coil was placed under the rat neck for labeling. During the MRI session, mechanically ventilated (~5 ml x ~35 strokes / min) rats were anaesthetized with 1.3 % isoflurane. For calculating intravascular BOLD signal changes due to hyperoxia (inhaled gas transition from air to 100 % oxygen), we propose to use continuous ASL (CASL) for quantifying $T_2$ or $T_2$* of CBF with various TE values. Gradient and spin echo - echo planar imaging (GE- and SE-EPI) pulse sequences with three different TE's [12, 18, 24 ms for gradient echo (GE): 25, 37, 49 ms for spin echo (SE)] were used while alternating between on/off labeling pulses (labeling duration =3.0 s, post labeling delay=0.5 s). In particular, per each GE- or SE-EPI run (TR = 3.7 s, matrix = 64 x 64, FOV = 2.35 x 2.35 $cm^2$ and slice = 1 (1 mm)), we sequentially alternated (i.e., interleaved) three TE values during CASL (on/off) in order to minimize the effect of time-dependent physiological variation on the average intravascular BOLD signal. The CBF map was calculated from the subtraction of CASL-on images from CASL-off images. The number of average for calculating CBF for each TE was 27 (i.e., total number of repetition / number of TE's / 2 (for CASL on/off) = 162 / 3 / 2) per each inhaled gas (air or 100% oxygen) session (~10 min each).




## Results and Discussion

Upon the transition of the inhaled gas from air to 100% oxygen, the CBF decreased for both Gradient and Spin-Echo experiments (See figures). Commonly, the percent CBF change is calculated without considering intravascular $T_2$* (or $T_2$) relaxation, by measuring the signal intensity difference between ASL on and off images obtained using the lowest possible TE. When we used TE = 12 ms (the lowest possible), the percent CBF (oxygen) following the air to oxygen transition was 85.8 % and 82.8 % of the initial CBF (air) for GE and SE acquisitions, respectively. However, due to the apparent intravascular $T_2$* and $T_2$ relaxation, using the shortest TE did not warrant the measurement accuracy. When asymptotic values (acquired from the exponential fit) were considered for the CBF calculation, the percent CBF (oxygen) was 80.9 % and 75 % of the initial CBF (air) for GE and SE, respectively. Specifically, intravascular $T_2$* increased from 30.9 ms to 36.5 ms while $T_2$ increased from 35.4 ms to 40.7 ms. The finding confirms that increases in blood oxygenation induce the augmentation of intravascular $T_2$* and $T_2$ values, the direct measurement of which can be used for accurately quantifying CBF.

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