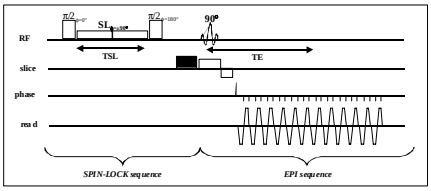
Cerebral Blood Volume Contrast in Spin-Locked fMRI at 3 T

M. A. Elliott[1], A. Borthakur[1], L. Bloy[1], R. Reddy[1], J. S. Leigh[1], J. Hulvershorn[1]

[1]MMRRCC, University of Pennsylvania, Philadelphia, PA, United States

Introduction: Spin-locking is a technique wherein a radio-frequency pulse applied in the transverse plane prevents T2 relaxation in certain spins. $T_{1\rho}$, the spin lattice relaxation time in the rotating frame, is sensitive to physical processes with correlation times (τ_c) close to the reciprocal of the applied spin locking frequency (typically on the order of several milliseconds). Processes with relevant τ_c include dipolar fields created by slowly tumbling molecules [1], the diffusion of spins through susceptibility gradients [2], and chemical exchange processes [3]. Work by Kettunen et. al. has shown that $T_{1\rho}$ contrast is sensitive to blood volume changes [4]. In the present study we model CBV and blood oxygen saturation dependent changes in $T_{1\rho}$ in the brain at 3T using physiologically plausible values, and compare them to experimental results from an fMRI study.

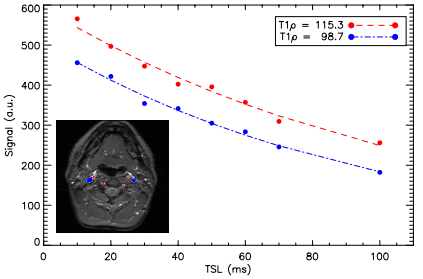


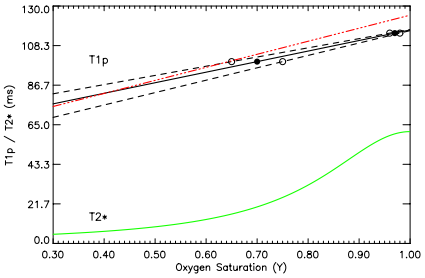
Methods: In the spin-locked EPI (SLEPI) pulse sequence (**Figure 1**, top left), two non-selective $\pi/2$ pulse are separated by a pair of spin-locking pulses (SL) with opposite phase. A conventional gradient-echo EPI sequence acquires the image data. Eight SLEPI fMRI runs were performed at 3T (TR=2s; TE= 30 and 50 ms, TSL=50 ms; SL pulse amplitude = 500 Hz, 3.75x3.75x5 mm voxels), using a 2s duration checkerboard reversing at 8 Hz, and compared to eight gradient echo (GE) EPI functional runs using the same slice parameters and echo times. **Figure 2** (middle right) presents *in vivo* blood $T_{1\rho}$ values obtained using SLEPI images acquired with TSL times of 10, 20, 30, 40, 50, 70, and 100ms. ROIs in the carotid and jugular vessels were used to determine hemoglobin saturation effects on $T_{1\rho}$. The solid line in the bottom panel represents a linear regression of the measured values of $T_{1\rho}$ in arterial and venous blood. The dashed lines account for the uncertainty in the assumed saturation levels of arterial and venous blood. The dash-dotted line (red) reproduces the results from Kettunen et al. [4] at 4.7 T. The bottom line (green) shows an estimate of blood T2* saturation dependence at 3T.

Results: Arterial and venous blood was measured to have values of 115.3 and 98.7 ms, respectively. The mean increase in functional signal contrast due to the spin-locking preparation period was 0.69±0.06%.

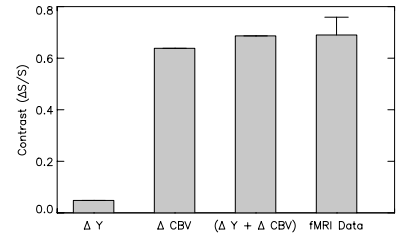
$$S(TSL) \propto x_{tissue} e^{\frac{-TSL}{T_1\rho_{tissue}}} + x_{blood} e^{\frac{-TSL}{T_1\rho_{blood}}} = e^{\frac{-TSL}{T_1\rho_{apparent}}} \qquad [1]$$

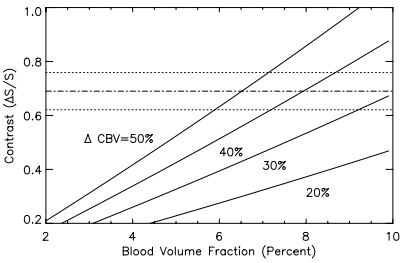
Equation [1] describes the two-compartment model used to describe the signal contrast expected from the $T_{1\rho}$-weighted preparation period, where x_{blood} and x_{tissue} are the blood and tissue volume fractions, respectively. A summary of the model parameters used in the simulation is presented in Table 1. **Figure 3** (bottm left) presents the modeling and experimental results of the $T_{1\rho}$ derived functional contrast. The simulation results indicate that both the blood volume (ΔCBV) and blood oxygenation (ΔY) induced contributions to $T_{1\rho}$ contrast were positive. The majority (93%) of the modeled $T_{1\rho}$ contrast was due to the increase in CBV during activation. The total signal change predicted using the two-compartment model (0.68%) was in excellent agreement with the experimentally determined SLEPI contrast (0.69%).





Discussion: The contrast estimate in the model was highly dependent on the resting blood volume fraction and the percent change in the CBV. To illustrate this dependence, the modeled SLEPI contrast ($\Delta S_{T1\rho}/S$) for a range of physiologically relevant blood volume fractions (1-10%) and activation induced CBV changes (20-50%) is presented in the bottom panel of Figure 3. The isolated $T_{1\rho}$ contrast obtained from the fMRI trials is included for comparison (dash-dotted line), along with its error bounds (dotted lines). In order to agree with our experimental results, any combination of resting blood volume fraction and ΔCBV that intersect with the dash-dotted line can be used in the two-compartment model. However, over the range of these values that are consistent with the data, the relative contribution of saturation and CBV changes to the total contrast is only moderately affected. For example, the CBV-derived component of the SLEPI contrast accounted for 87%, 91%, 93%, and 95% of the total modeled contrast when using ΔCBV values of 20%, 30%, 40%, and 50%, respectively. Similarly, choosing a resting blood fraction anywhere in the range of 4-8% results in an estimate of the ΔCBV based component of the total SLEPI contrast which is always in excess of 90%. Consequently, the two-compartment model suggests that the SLEPI derived functional contrast in the visual cortex is primarily due to increases in CBV with activation, and is large enough to be efficiently detected in functional studies.





Parameters Used for the Two-Compartment $T_{1\rho}$ Simulation

Blood Fraction	ΔCBV	Tissue $T_{1\rho}$	Y_{vein} rest	Y_{vein} active	Y_{artery} rest	Y_{artery} active
8%[1]	40%[2]	76 ms[3]	0.54[4]	0.68[4]	0.97	0.97

[1]This volume fraction is slightly higher than reported range of values of 4-6% [5, 6]

[2]This is in the range of reported values (30-40%) [7-9]

[3]Calculated by subtracting 8% blood contribution from the measured resting T1ρ in brain (79ms)

[4] Values from Hoogenraad et. al. [10]

References

1. Brown, R.D., 3rd and S.H. Koenig, Magn Reson Med, 1992. **28**(1): p. 145-52.
2. Engelhardt, R.T. and G.A. Johnson, Magn Reson Med, 1996. **35**(5): p. 781-6.
3. Duvvuri, U., et al., Proc Natl Acad Sci U S A, 2001. **98**(22): p. 12479-84.
4. Kettunen, M.I., et al., Magn Reson Med, 2002. **48**(3): p. 470-7.
5. Oja, J.M., et al., Magn Reson Med, 1999. **42**(4): p. 617-26.
6. Phelps, M.E., R.L. Grubb, Jr., and M.M. Ter-Pogossian, J Appl Physiol, 1973. **35**(2): p. 274-80.
7. Wu, G., et al., Magn Reson Med, 2002. **48**(6): p. 987-93.
8. Kennan, R.P., et al., Magn Reson Med, 1998. **40**(6): p. 840-6.
9. Stefanovic, B. and B.G. Pike. in *Proc. Intl. Soc. Mag. Reson. Med.* 2002.
10. Hoogenraad, F.G., et al., Magn Reson Med, 2001. **45**(2): p. 233-46.