

A Comparison of Blood Agent Level Dependent (BALD) and Blood Oxygenation Level Dependent (BOLD)  $\Delta R2^*$  and  $\Delta R2$  Magnitudes and Ratios Using Synchronous Gradient-Echo and Spin-Echo (SGS) EPI

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Introduction:

Models of susceptibility contrast (1-3) suggest that, with susceptibility modulation – either by administration of a paramagnetic contrast agent or by changing blood oxygenation – information about blood volume and predominant compartment size may be obtained. The magnitudes of  $\Delta R2^*$  and  $\Delta R2$  give approximate information of blood volume from all sized and small compartments respectively. The ratio of the rates gives a measure of compartment size. Assuming similar proton dynamics, a larger ratio corresponds to a larger compartment size.

Because of subject motion and non-repeatability of agent dose, activation task, or hemodynamic stress, it is difficult to make more than an approximate comparison of  $\Delta R2^*$  and  $\Delta R2$  across separate time series. In this study,  $\Delta R2^*$  and  $\Delta R2$  are simultaneously measured using Synchronous Gradient-echo and Spin-echo (SGS) - EPI, in which two readouts are obtained in one excitation: one during the FID and one during the spin-echo.

Questions that are addressed include: How do  $\Delta R2^*$  and  $\Delta R2$  compare between blood agent level dependent (BALD) contrast and blood oxygenation level dependent (BOLD) contrast in voxels that show activation - induced BOLD signal changes? What are the BALD  $\Delta R2^*/\Delta R2$  ratios in gray matter voxels? How do  $\Delta R2^*$  and  $\Delta R2$  correlate with  $\Delta R2^*/\Delta R2$  on a voxel-wise basis? One issue is intravascular susceptibility effects - small compartments (red blood cells) having a  $\Delta R2^*/\Delta R2$  ratio of approximately 1.5 - on BOLD and BALD contrast.

Methods:

SGS-EPI was performed using a local three axis gradient coil at 3T (Bruker). GE TE = 30 ms, and SE TE = 110 ms. Five axial planes (3.75 x 3.75 x 10 mm) were obtained. Two types of time series were collected. For the BOLD series (repeated twice), TR = 2 sec., Repetitions = 165. Subjects viewed LED goggles (GRASS<sup>TM</sup>), and performed bilateral finger tapping when the stimulus was on. Timing was cyclic 30 sec on / 30 sec off. For the BALD time series, subjects remained in a resting state. The same imaging parameters were used except: TR = 1 sec. Repetitions = 180. Three repeats of this time series were carried out. For each of these time series, an intravenous bolus of 0.05 mmol / kg of Gado-Teridol (ProHance) was given after 1 min. of acquisition. The time series were registered and averaged. Functional BOLD contrast maps were obtained using correlation analysis. Three voxel groups were compared: 1) only the voxels showing common GE and SE BOLD changes, 2) all voxels showing either GE or SE BOLD changes, and 3) all gray matter.

Results and Conclusions:

Figures 1 and 2 were obtained from the voxels that showed common activation - induced SE and GE BOLD changes. Simultaneously obtained SE and GE signal during bolus injection of contrast agent and during brain activation are shown. In Figure 2, it is shown that BALD and BOLD relaxation rate ratios ranged between 1 and 5. An approximately monotonic correlation is shown between BOLD and BALD  $\Delta R2^*$ . Figure 3 shows scatter plots of  $\Delta R2^*/\Delta R2$  vs.  $\Delta R2$  and  $\Delta R2^*$  from all gray matter voxels.  $\Delta R2^*$  shows a linear correlation with  $\Delta R2^*/\Delta R2$  while  $\Delta R2$  does not. The maximum ratio almost never exceeds 20, which according to most models, corresponds to a vessel radius of about 50  $\mu$ m. Because larger vessels than this are common, it is hypothesized that an intravascular effects - susceptibility gradients between Gado-Teridol in plasma and 5  $\mu$ m diameter red blood cells (ratio = 1.5) - cause a reduction in the overall ratio.

Table 1 shows average values measured across the three voxel groups. No significant differences between BOLD and BALD  $\Delta R2^*/\Delta R2$  ratios are observed - suggesting similar relative intravascular and extravascular contributions for both effects.

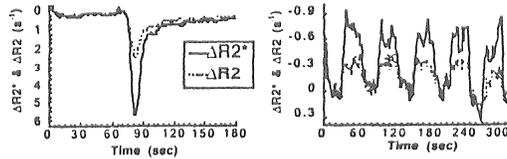


Figure 1:  $\Delta R2^*$  and  $\Delta R2$  from identical regions during a. bolus injection of a susceptibility contrast agent, and b) brain activation.

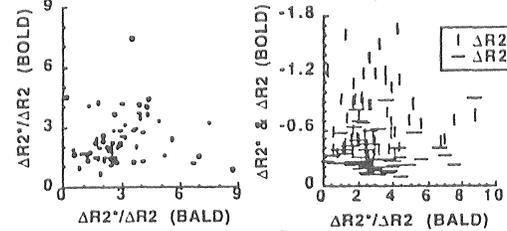


Figure 2: Plots from voxels showing BOLD activation. a. BALD vs BOLD  $\Delta R2^*/\Delta R2$ . b. BALD vs. BOLD  $\Delta R2^*$  and  $\Delta R2$  values.

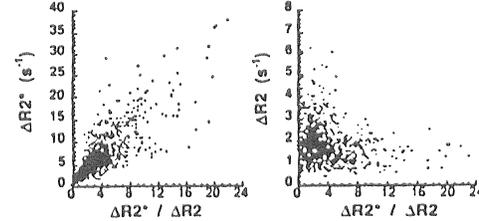


Figure 3: Plots from gray matter of BALD  $\Delta R2^*/\Delta R2$  vs. a.  $\Delta R2^*$  and b.  $\Delta R2$ . Significantly different correlations are apparent.

n	$\Delta R2^*$	$\Delta R2$	$\Delta R2^* / \Delta R2$
(66) BOLD (com)	-0.68 ± 0.13	-0.32 ± 0.02	2.34 ± 0.36
(165) BOLD (all)	-0.68 ± 0.02	-0.20 ± 0.01	5.09 ± 0.58
(66) BALD (com)	5.30 ± 0.42	1.89 ± 0.10	3.31 ± 0.34
(165) BALD (all)	5.50 ± 0.31	1.71 ± 0.62	4.29 ± 0.36
(2461) BALD (gray)	5.56 ± 0.12	1.83 ± 0.02	3.38 ± 0.06

Table 1: Rate changes and ratios from commonly activated (GE and SE), all activated (GE or SE), and gray matter (gray) voxels.

Conclusions:

The similarity of  $\Delta R2^* / \Delta R2$  ratios between BOLD and BALD suggests similar average compartment size contributions. Given the significant (50 to 76%) intravascular BOLD effect (4), a similar effect may contribute to BALD contrast, making it necessary, when using  $\Delta R2^*/\Delta R2$  to extrapolate vessel radius (5), to take into consideration intravascular BALD effects.

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