

# Unexpected BOLD behavior at 11.7 Tesla: A Comparison of Experimental Data with the Integrative BOLD Signal Model

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**Introduction:** It is generally accepted that the contrast of BOLD response increases with higher magnetic field strength [1]. However, in experimental and clinical studies it was shown that the intravascular component (IV) of the BOLD effect disappears for magnetic fields higher 4.0 Tesla, which is due to very short blood T2 at higher fields. Extravascular components (EV) are still expected to increase linearly to super-linearly with field strength [2]. Data up to 7.0 Tesla support this argument, but no data comparing higher field strengths has been published so far. Latest results in our group pointed out that this increase might diminish at higher field strengths [3]. Recently, theoretical predictions by the Integrative BOLD Signal Model [4] support this finding for spin-echo (SE) EPI whereas for gradient-echo (GE) EPI an increase with magnetic field strength is still expected. Here, experimental data are compared to theoretical predictions, an explanation for SE-EPI BOLD behavior is given and GE-EPI data are discussed.

**Methods:** MRI Bruker BioSpec 70/30 (Magnet 7.0 Tesla, Gradient 400 mT/m, 8 cm and 14 cm Helmholtz coil for transmission, 2.8 cm surface coil for reception). Bruker BioSpec 117/16 USR/TT (Magnet 11.7 Tesla, Gradient 750 mT/m, 72 mm quadrature resonator for transmission, 35 mm quadrature surface array coil for reception). SE- and GE-EPI, Matrix (64)<sup>2</sup>, FOV (25.6 mm)<sup>2</sup>, Resolution (400  $\mu\text{m}$ )<sup>2</sup>, 5 slices of 2 mm, TR 3000 ms, TE 25 ms (SE), 16 ms (GE). Animals + Stimulation 16 male Wistar rats, 250 – 450 g. Initial halothane or isoflurane anesthesia, medetomidine (Domitor) sedation [5]. Electrical forepaw stimulation, I = 2 mA, f = 6 Hz with block diagram: 45 sec rest + 15 sec stimulation, 5 repetitions = 5 min 45 sec, plus 5 min rest. Analysis Software program *stimulate* [6], student's t-test, confidence level 99%, PVMZ baseline correction, 115 time points (repetitions). Cluster size (CS), as well as minimum (MIN), average (AVG) and maximum (MAX) BOLD contrast in % of cluster in S1 were analyzed (see Fig. 1).

**Results:** A comparison of SE-EPI BOLD response at two different field strengths, 7.0 and 11.7 Tesla, using a resolution of 0.32 mm<sup>3</sup> (Fig. 1) showed no significant difference for both, amplitude of BOLD contrast (7.0T: MIN = 1.2%, AVG = 1.8%, MAX = 2.7%, 11.7T: MIN = 1.1%, AVG = 1.7%, MAX = 2.8%) and size of activation cluster (7.0T: 13 pixels = 2.1 mm<sup>2</sup>, 11.7T: 13 pixels = 2.1 mm<sup>2</sup>). Also, GE-EPI BOLD response at both field strengths did not show any significant difference for BOLD contrast (MIN = 0.8%, AVG = 1.6%, MAX = 3.8%) and activation size (43 pixels = 6.9 mm<sup>2</sup>). Furthermore, a comparison of GE-EPI to SE-EPI (GE/SE) at both field strengths individually showed the advantage of GE-EPI over SE-EPI (Fig. 2):

- 1.) better detectability of pixels of lowest BOLD contrast, due to lower minimum BOLD contrast.
- 2.) 40% higher maximum BOLD contrast (3.8%/2.7%) in the center of the activation in S1.
- 3.) Three times greater number of activated pixels (43/13).
- 4.) At 11.7 Tesla GE-EPI as well as SE-EPI can reveal microstructure without any contributions from big vessels using high spatial resolution (recent study, unpublished). S2 activation was observed in some cases, thalamus activation was not observed, using this low resolution (SE-EPI study, both field strengths).

**Discussion:** SE-EPI and GE-EPI did not show any increase in BOLD contrast comparing field strengths of 7.0 and 11.7 Tesla (Fig. 1) in contradiction to comparison studies so far, which examined BOLD contrast up to 7.0 Tesla [2]. Here, extravascular static (GE-EPI only) and dynamic (SE- and GE-EPI) effects can be considered separately. Dynamic effects, which are expected to diminish at very high fields are still present and provide additional 40% of the BOLD contrast at both field strengths (Fig. 2). A recent theoretical model [4] predicts an increase in EV signal for SE with increasing field strength for capillaries and veins which is compensated by decreases of venular and arteriolar EV signals and IV signals of all vascular compartments. In contrast to earlier models, thus, SE signal levels off for field strengths >7.0 Tesla in agreement with the experimental findings of this study. For GE, however, it is expected that the BOLD signal is significantly larger for 11.7 Tesla than for 7.0 Tesla [4]. The lack of GE-fMRI signal differences for these field strengths might be due to different ROIs sampled, partial volume effect with CSF and physiological variability. Clearly, more work has to be done clarify the field strength dependence of both SE and GE.

**References:** [1] Norris, 2006. "Principles of magnetic resonance assessment of brain function." *JMRI* **23**: 794–807. [2] Yacoub, *et al.*, 2001. "Imaging brain function in humans at 7 Tesla." *MRM* **45**: 588–94. [3] Seehafer, *et al.*, 2008. "Comparison of BOLD response with SE-EPI between two Magnetic Field Strengths: 7.0 and 11.7 Tesla." ISMRM Toronto, poster 2358. [4] Uludag and Ugurbil, 2008. "An integrative model for neuronal activity-induced signal changes for gradient and spin echo functional imaging", submitted. [5] Weber, *et al.*, 2006. "A fully noninvasive and robust experimental protocol for longitudinal fMRI studies in the rat". *NeuroImage*. **29**: 1303–10. [6] Strupp, 1996. "Stimulate: A GUI based fMRI analysis software package". *NeuroImage*. **3**: S607.

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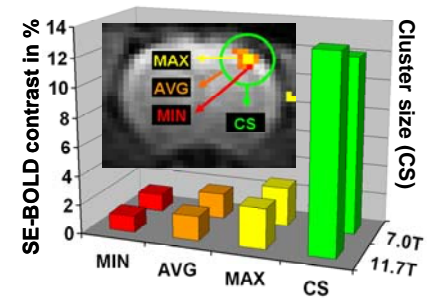


Figure 1: No significant difference for SE-EPI comparison 7.0T vs 11.7T.

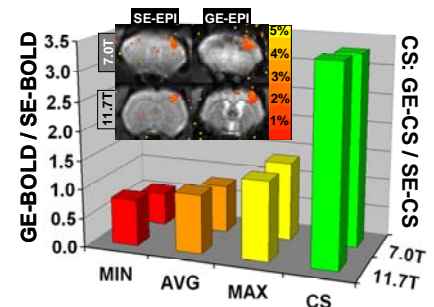


Figure 2: No significant difference for the ratio of GE/SE of 7.0T vs 11.7T.

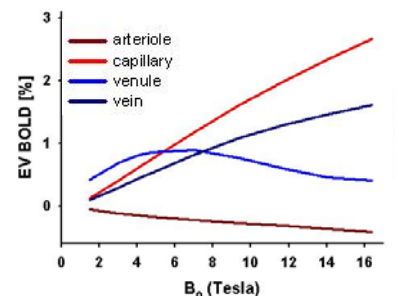


Figure 3: The Integrative BOLD Signal Model [4] predicts EV BOLD components for high field strengths.