Investigating the temporal characteristics of the BOLD response with field strength

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Introduction: The BOLD response to neuronal activation depends on the properties of the local cerebrovasculature and vessels of different sizes contribute to the BOLD signal with different weightings[1], which depend on both field strength and echo time. Intravascular (IV) and extravascular (EV) contributions to the BOLD signal also have different field strength dependencies[2,3], with reduced IV signal at high field. Therefore studying the variation in BOLD temporal dynamics with field strength should provide information about vascular temporal dynamics, with the expectation that signal from veins is delayed compared to the microvasculature close to the activated neurons[4]. It is therefore hypothesized that the time-to-peak (TTP) in the BOLD response should be shorter at high field. In this study, a short visual stimulus was used to measure the BOLD haemodynamic response functions (hrf) at 1.5, 3 and 7T; these were measured with and without diffusion gradients which were employed to separate the EV and IV BOLD signal contributions.

Method: Six healthy volunteers (4 female, 2 male) participated in the study. A visual stimulus was presented using 8Hz red LED goggles. The visual task comprised an initial 60s baseline, followed by repeats of 5s ON and 55s OFF. The stimulus was presented in short blocks to maintain attention (4 minutes at 1.5T, 6 minutes at 3T & 7T). Scanning was performed on 1.5, 3 and 7 T Philips Achieva systems, equipped with body transmit and 8-ch SENSE receive coil (1.5/3 T), or volume transmit and 16-ch SENSE receive coil (7T). Axial EPI images with a reduced FOV (128x192 mm) were acquired centred on the occipital lobe. Scan parameters: TE = 55/45/32 ms (1.5T/3T/7T), 2 mm isotropic voxels with 8/10/10 slices (1.5T/3T/7T) with no slice gap, in a TR of 1 s, SENSE factor 2/2/3 (1.5T/3T/7T). To suppress the intravascular BOLD component flow suppression (FS) was performed using bipolar diffusion gradients (b=100smm^{-2}). Scans were collected with (FS) and without flow suppression (NoFS), with 3 (1.5T) and 2 (3/7T) repeats of the visual task for each. The order of FS/NoFS scans was randomised across subjects. A whole head EPI and 1 mm isotropic MPRAGE data set was acquired at each field strength to aid cross-field registration. T_2*-maps with and without flow suppression were also acquired (TE=55/65/75/85ms at 1.5T, 45/55/65/75ms at 3T and 32/42/52/57ms at 7T), and a T_2*-weighted image (0.5x0.5x1mm^3) collected at 7T to identify veins.

Data Analysis: All functional images were realigned to a common data space (7T) using FLIRT (FSL, Oxford, UK). Spatial and temporal filtering was applied (3mm FWHM, 120s cut-off period). Using FEAT (FSL, Oxford, UK) Z-statistical maps were generated for each subject at each field strength, for FS and NoFS data sets by combining data across repeats. From these maps, clusters of significant activation (P<0.05 corrected) were determined. ROIs were formed from the overlapping region of the active voxels in V1 at all three field strengths from (i) data with no flow suppression (No FS ROI) and (ii) with flow suppression (FS ROI). BOLD time courses were calculated by averaging across all trials and all voxels in each ROI. The average BOLD time series were then baseline corrected to the final 15s OFF period and normalised to unity to allow variations in the shape of the function to be studied. Intersubject averaged timecourses were fitted to a double gamma variate curve[5], convolved with a 5s boxcar from this fitted curve the following haemodynamic response function parameters were estimated: time-to-peak (TTP), peak width and post-stimulus amplitude relative to peak amplitude. In addition data sets were fitted on a voxel-by-voxel basis to a single gamma variate to form a spatial map of the time-to-peak of the hrf.

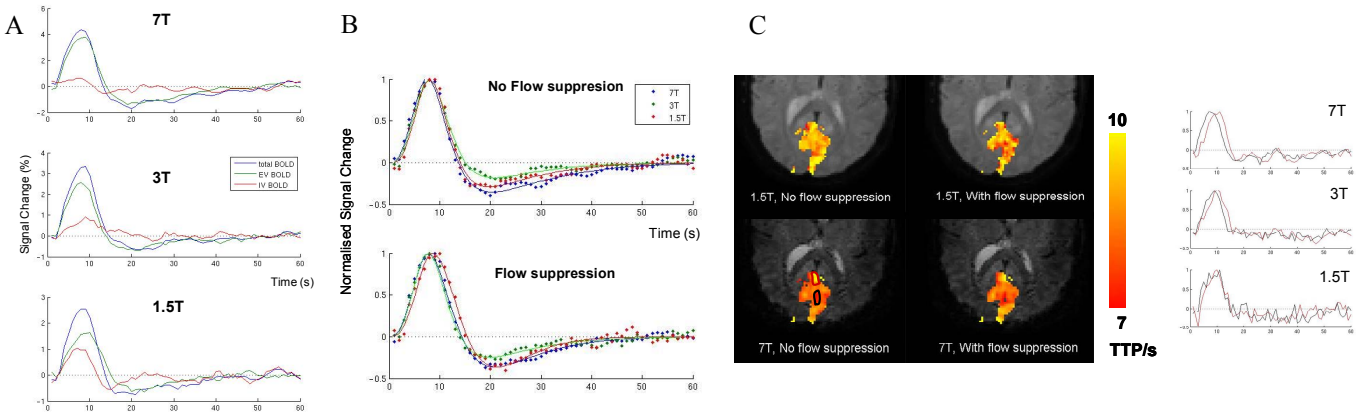

Figure 1: *(A) Percentage BOLD timecourse at 1.5, 3 and 7 T for NoFS ROI (total) and EV and IV contributions (B) corresponding normalised BOLD timecourse for data with and without FS (C) Time-to-peak maps for 1.5 and 7T data for one subject with normalised BOLD timecourses for circled regions.*

Results: *Fig. 1A* shows the average percentage BOLD timecourse, from the NoFS ROI. The curves show the total signal change, the signal change in the FS data (extravascular) and the difference (intravascular). The areas under the positive BOLD region of these curves was assessed and the relative IV/EV fraction of BOLD contrast found to be 0.40 /0.30/0.15 at 1.5/3/7 T respectively. The magnitude of the positive peak was reduced by flow suppression, whilst post-stimulus undershoot was not significantly altered. *Fig. 1B* shows the normalised timecourse and corresponding fits to a double gamma variate[5], no significant difference in shape can be seen across field strength, with mean fitted parameters ($a_2/n_1/n_2/t_1/t_2$ =0.33/3.66/2.18/1.68/5.82 ±0.06/0.17/0.29/0.15/0.58). However the 1.5 T NoFS data did show a trend for a slightly later TTP, (7.39 vs. 7.87 s 1.5T/7 T). *Fig. 1C* compares the time-to-peak maps for 1.5 and 7T data, the active region in primary visual cortex (V1) is seen to display relatively homogenous TTP values with large deviances only occurring in the large vessels, as shown by the corresponding timecourse plots.

Discussion: This cross field study investigated the temporal characteristics of the visual BOLD response. Previous cross-field studies have reported BOLD spatial characteristics[6] and magnitude[3,7-10], but the paradigms have generally employed block designs which have not been optimum for studying the time course of the response. Here we used an event-related paradigm with 1 minute ISI to ensure full recovery. This study used a single TE optimised for tissue but whose value was limited at 7T by the length of the bipolar diffusion gradient; this may have resulted in varying weighting of the intravascular signal, particularly at 7T where the T2 of blood is short. The main result of this study is that the shape of the HRF is very stable across field strengths. The shape and TTP of positive response is also shown to be unaffected by the flow suppression despite being significantly reduced in amplitude, suggesting that the TTP of the vascular signal in small vessels is very similar to tissue. The only exception is that the TTP is delayed in very large vessels (Figure 1C).

References: [1]Boxerman, MRM 34:355,1995; [2]Duong, MRM 49:1019,2003; [3]Gati, MRM 38:296,1997; [4]Hulvershorn, NeuroImage 24:216,2005; [5]Glover, NeuroImage 9:416,1999; [6]Krasnow, NeuroImage 18:813,2003; [7]Turner, MRM 29:277,1993; [8]Yacoub, MRM 45:588,2001; [9]van der Zwaag, NeuroImage 47:1425,2009; [10]Donahue, Proc. ISMRM 220,2009; [11]Triantafyllou, NeuroImage 26:243,2005. **Acknowledgement:** This work was funded by the MRC