Increased Specifity in Functional Magnetic Resonance Imaging from Vessel-Size Estimates

T. H. Jochimsen[1], and H. E. Moeller[1]
[1]Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

Introduction Functional magnetic resonance imaging (fMRI) based on the blood oxygenation level dependent (BOLD) effect employs deoxygenated hemoglobin (deoxyHb) as an endogenous contrast agent to detect changes in regional hemodynamics due to cortical activation. However, a general problem with the BOLD contrast is its inability to properly localize the region of activity. Rather, the contrast reflects changes in blood oxygenation which can be distant from the activated site, e.g. in the presence of large veins [1]. In this work, the approach of vessel-size imaging (VSI) [2-4] was employed using deoxyHb as the contrast agent to increase the specifity of the BOLD contrast. This was achieved by classifying activated voxels according to their microstructure, i.e. the average vessel radius, in order to filter out voxels which contain predominantly large vessels.

Materials and Methods Using VSI, the ratio $q=\Delta R2^*/\Delta R2$ of BOLD-induced changes in $R2^*$ and $R2$ yields an estimation of the average venous vessel radius, r, of each activated voxel. In order to be applicable to routine fMRI studies, we have developed an ultra-fast gradient-echo sampling of FID and echo (GESFIDE) sequence [5], exploiting parallel imaging to implement short single-shot readouts. With this method dubbed multi-gradient-echo single-shot-sampling of spin-echo refocusing (MESSER), absolute $R2^*$ and $R2$ can be measured simultaneously. Thus, the hemodynamic response can be tracked with sufficient temporal resolution in order to extract the change in relaxation rates, and hence q, from the fMRI data which is then used to estimate r of activated voxels in order to exclude voxels with large vessels.

Signal acquisition of the MESSER sequence can be divided into three intervals: free-induction decay (FID), spin-echo rephasing (SER) and spin-echo dephasing (SED). Each interval contained three consecutive echo-planar imaging (EPI) modules (no sampling during ramps) with separation of 15 ms. The following sequence parameters were used: A reduction factor of 3; SE echo time, TE = 111 ms; repetition time, TR = 2100 ms; 64 × 51 matrix; 125-kHz receiver bandwidth; 200 × 159-mm field of view; phase encoding direction from left to right; 5 slices (4-mm thickness, 4-mm gap).

Seven healthy volunteers were measured on a Siemens 3T Trio during visual stimulation. Stimulation consisted of six blocks of successive periods of stimulation and rest, each 36 s long. From the FID and SED part, $R2^*$ was then calculated by linear regression of the logarithm of the signal magnitude. The relaxation rate during the SER part, $RSER$, yielded $R2=(R2^*+RSER)/2$. fMRI analysis was performed by a linear correlation with the $T2^*=1/R2^*$ time course. All voxels with a Bonferroni-corrected error probability of less than 0.1 were regarded as activated. Using the activated voxels as a mask, mean $R2^*$ and $R2$ during stimulation and rest were calculated for each voxel. Differences of both yielded q. Finally, using the results of an appropriate Monte-Carlo simulation [6], an associated r was assigned to each activated voxel.

Results A histogram of r of all subjects and trials is shown in Fig. 1. The maximum count occurs at $r \approx 5$ µm which is of the same order as the radii of capillary vessels. A relatively sharp cut-off in the range from 2 to 4 µm corresponds well with the lower boundary of vessel radii encountered in tissue. A considerable amount (≈ 54%) of activated voxels has an r above 10 µm which is larger than the size of capillaries and can be attributed to venules and veins. The mean r in activated was 17.4 µm. This result is in excellent agreement with a previously reported value of 18 µm in gray matter obtained by a double-echo GESFIDE sequence using the bolus passage of an exogenous contrast agent [7]. Fig. 2 shows the effect of applying a threshold where all voxels with r>30 µm are removed. With this thresholding, activated voxels in the vicinity of the sagittal sinus are successfully eliminated.

Discussion and Conclusions Despite the relative complexity of deriving r from q, the technique increases the specifity of BOLD-based fMRI. In addition, it has the potential to provide additional insight into the origin of the BOLD contrast, such as the impact of the significance threshold on the macrovascular contribution to the fMRI signal [6].

References [1] Turner R. *NeuroImage*, 16(2002):1062. [2] Prinster A, et al. *NeuroImage*, 6(1997):191. [3] Dennie J, et al. *Magn Reson Med*, 40(1998):793. [4] Troprès I, et al. *Magn Reson Med*, 45(2001):397. [5] Ma J, et al. *J Magn Reson B*, 111(1996):61. [6] Jochimsen TH, et al. *NeuroImage*, (2007):accepted. [7] Kiselev VG, et al. *Magn Reson Med*, 53(2005):553.

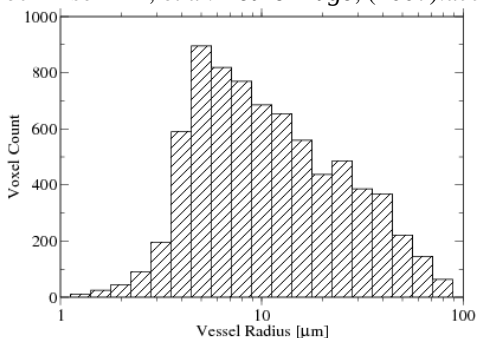

Fig.1: Histogram of the venous vessel radius of activated voxels. Please note the logarithmic scale of the abscissa.

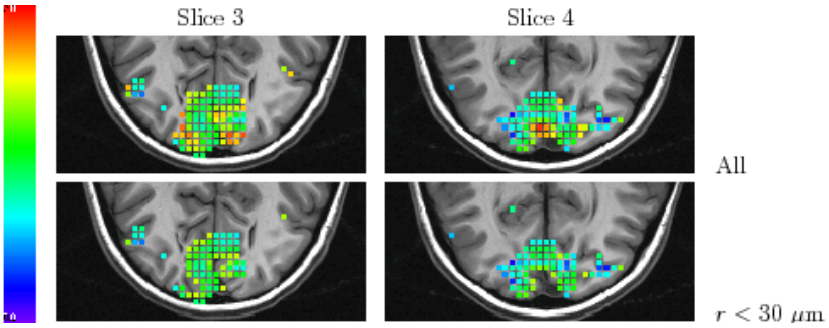

Fig. 2: Maps of the average vessel radius of activated voxels of one subject overlayed on T1-weighted images. Values are color-coded by the decadic logarithm of the average vessel size in µm, e.g. ranging from 1 to 100 µm. The top row shows the activation pattern with all voxels included. In the bottom row, all activated voxels with r above a threshold of 30 µm are removed from the pattern.