

## Effects of Spinal Cord vascular geometry on the BOLD-fMRI contrast

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With the introduction of the fMRI, different BOLD models have been developed to characterize fMRI signal in the brain grey matter [1,2]. Nonetheless, there is still poor literature about the characterization of the BOLD in the spinal cord (SC). All these models are strongly influenced by the vessel geometry (i.e. orientation and size), which in SC substantially differs from brain. The vascular network of the brain is randomly distributed with respect to the external magnetic static field [3,4]. On the contrary, within the SC the macro- and the micro- vasculature is preferentially oriented parallel or perpendicularly to the external magnetic field, respectively [3,4]. The study was performed by means of numerical simulations of the static magnetic field on the SC vascular network. In particular, we studied the effect of the vessel orientation on the BOLD signal of simplified vessel models and subsequently using more complex vasculature systems extracted from tomographic images in a mouse SC.

Numerical simulations on a simplified model of SC vasculature have been performed in order to quantify the effect of the vessel micro and macro distribution in the BOLD contrast. The induced local magnetic field was determined in terms of angular frequency, through several numerical simulations representing the vessels as the so-called Infinite Cylinder Model. After that, the diffusion random walk of the water molecule was computed by means of a Montecarlo simulation implemented in Matlab. The induced magnetic field was then integrated over these Brownian paths in order to calculate the accumulated phase for a particular echo time. Thanks to the knowledge of the phase, it was possible to determine the effective transverse relaxation rate constant  $R2^*$  and consequently the BOLD signal [1,2,5,6].

We improved the model using the COMSOL Multiphysics software simulator and the SC vascular network extracted from the segmented tomographic images [7] (Figure 1). The  $R2^*$  was then computed in the same way as described for the simplified model. Our results shows that small vessels contribute the most in the variation of the transverse relaxation rate  $R2^*$  and therefore of the BOLD signal. On the contrary, a smaller contribution arises from large vessels, whose distribution is parallel to the direction of the external magnetic field. In Figure 2, the relaxation rate constant value as a function of the vessel radius is reported for different vessel radius (small, large and aggregate). We observed that  $R2^*$  value is greater for the small transverse compared to the large longitudinal vessels. These results indicate that SC microvascular system contributes to the BOLD more than the macrovascular one. Moreover, our results suggest that SC BOLD contrast function is greater with respect to the brain [8] (0.7-0.9 a.u.) being in the range of 0.8-1 a.u. as function of the echo time (range of 0-100 ms).

We have obtained computational evidence that the BOLD contrast in SC is larger than in brain due to the more anisotropic distribution of the vascular network. The SC distribution of large vessels, only on the surface of the SC, should enhance the specificity of fMRI BOLD signal, even with  $R2^*$  weighting, because of the inherent elimination of the confounding, unspecific effect of larger vessels from the grey matter signal. Similarly, the disposition of small vessels, all radial and thus orthogonal to magnetic field should

emphasize the dephasing effect of deoxyhemoglobin. Therefore, the vascular anatomy of SC is optimally organized for the generation of strong and spatially specific BOLD effect. This can help in overcoming the numerous other difficulties that involves the SC fMRI. Overall, our study provide a theoretical framework for the experimental validation of the predicted BOLD signal, which will be useful for improving the design and analysis of SC fMRI data.

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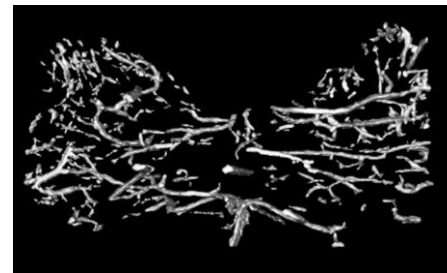


Figure 1. Segmented X ray Tomography image from a mouse SC.

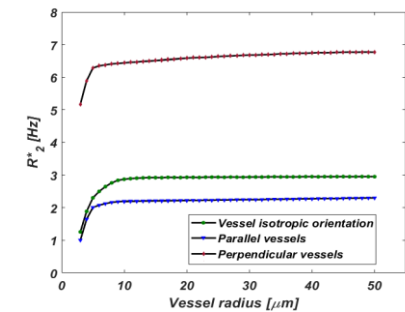


Figure 2. Relaxation rate constant  $R2^*$  as a function of the vessel radius. The small-vessels are represented with red line, the large-vessels with green line and the aggregate (all vessels) distribution, which characterize the brain, is represented with blue line.

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