Quantification of Vessel Contribution to BOLD Nonlinearity

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Introduction We have demonstrated that the source of BOLD nonlinearity can completely originate from vascular origin, presumably caused by viscoelastic properties of blood vessel, under the condition in the absence of neuronal refractoriness. It is of great interest to see which component(s) inside the vascular tree (capillary or venous vessel) has dominant contributions. To answer this question, we divided all activated pixels in the fMRI map into two groups: in the first group, the pixels primarily contain microvasculature; in the second group, the pixels are biased by large vessels. An index υ defined by the ratio between the standard deviation and mean of signal intensity obtained from a time series of fMRI images at resting condition. Since fMRI signal intensity at large vessel is relatively low and variation is high, a pixel containing large vessels tends to have a large υ value while a pixel only containing microvasculature tends have a small υ value. It has been demonstrated that large vessel contamination can be successfully eliminated using this υ value[1]. Hence, in the present study we used υ index to segregate pixels biased by large vessels and pixels primarily containing capillaries. We set several different thresholds on υ value and examined whether BOLD nonlinearity demonstrated different characteristics between these two pixel groups.

Method Visual stimulation presented as brief flashing red light was generated by a pair of LED goggles (Grass Instruments, Quincy, MA). Visual stimuli were displayed in the full visual field either singly or in pair separated by an ISI. Successive trials of single or paired stimuli were separated by a long inter-trial interval (ITI) of 25 seconds to allow the hemodynamic response to return to the baseline. During the baseline condition, subjects were in uniform darkness. The fMRI experiment was conducted using an ER design. All experiments were performed on a 4T/90 cm bore magnet (Oxford, UK) system interfaced with the Varian INOVA console (Varian Inc., Palo Alto, CA). Six coronal images covering most of the calcarine fissure were selected for acquiring fMRI data using the gradient-echo planar images (GE EPIs) with the parameters of FOV = 18×18 cm^2, 64×64 in plane matrix size,TR/TE = 415/31 ms, slice thickness= 5 mm.

Results Figure 1 demonstrates the dependency of BOLD integral ratio on ISI at two thresholds. Clearly, BOLD nonlinearity is less significant (i.e. BOLD integral ratio is less dependent on ISI, and approaching to 1) when excluding the pixels containing large vessels (υ < 0.005). Further increasing the threshold to υ < 0.003 continues to reduce BOLD nonlinearity. Averaged BOLD time courses from activated ROI pixels at the threshold of υ < 0.003 are shown in Figure 2. Comparing to the BOLD time courses without the vessel removal procedure, BOLD amplitudes in response to the second visual stimulus considerably decrease at short ISIs but remain almost unaltered at long ISIs. This figure also suggests that BOLD nonlinearity is less significant after excluding pixels containing large vessels. Fitting the BOLD time course averaged from all pixels at υ < 0.003 with two Gamma functions enables us to calculate onset latency of the BOLD response after vessel removal. The onset latency is no longer correlated with ISI (R^2 = 0.02) after vessel removal (Figure 3), indicating weaker dependency of BOLD activity on ISI and thus less significant BOLD nonlinearity in the microvasculatures.

Conclusion The data conclude that excluding pixels containing large vessels significantly increases the BOLD amplitude and shortens the BOLD onset latency when vascular response is in the refractory period, whereas the procedure of vessel removal has little effect on BOLD activity when vascular refractoriness disappears. These results collectively suggest that a very large component, if not all, of BOLD refractoriness is attributed to the large vessels.

Acknowledgements NIH grants: NS41262, EB00329, EB00513, P41 RR08079 and P30NS057091; the Keck foundation and the MIND institute.

References: 1. *Chen, W. et al PNAS 1999.*

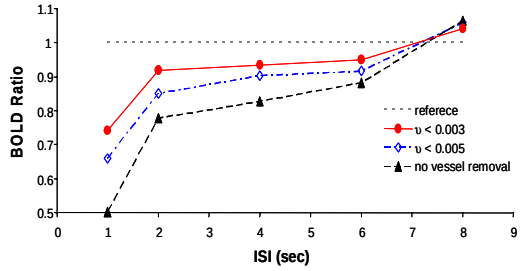

Figure 1. Dependency of BOLD integral ratio on ISI at two threshold on υ values.

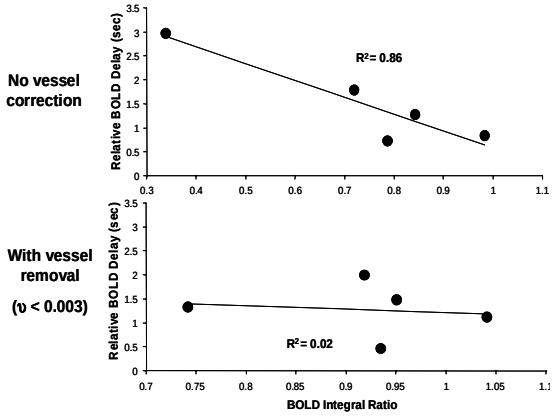

Figure 3. Correlation of BOLD refractoriness with BOLD onset latency with and without the vessel removal procedure.

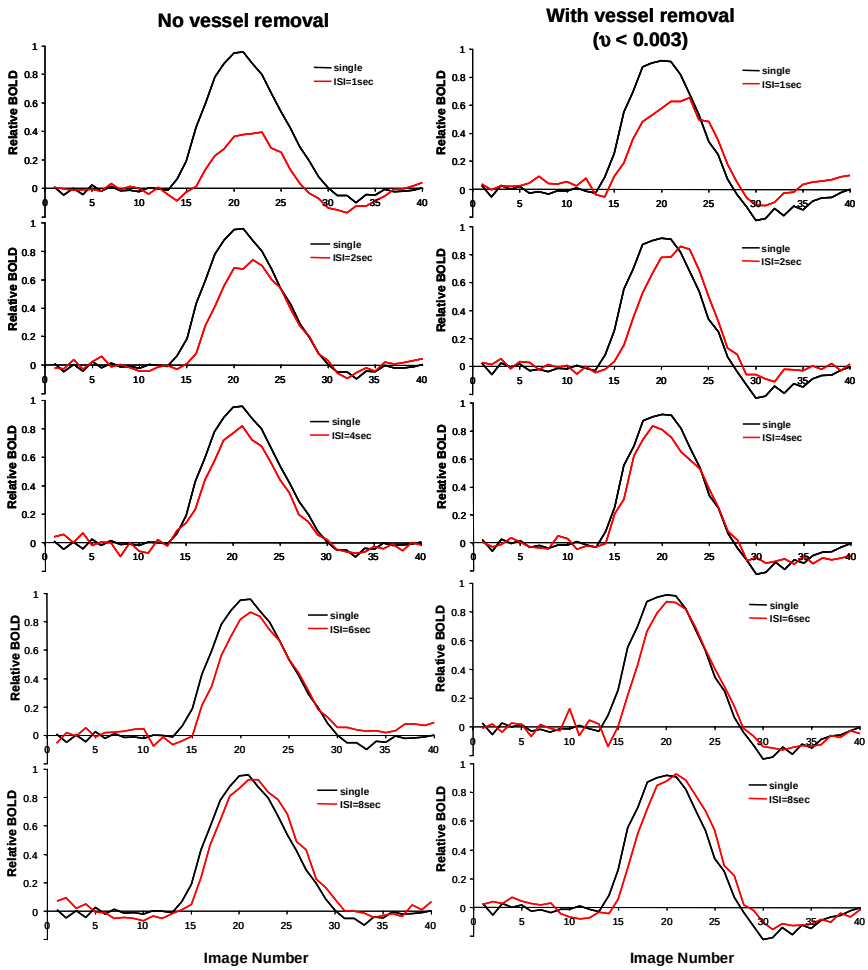

Figure 2. BOLD time courses with and without the vessel removal procedure.