Impact of tube hematocrit on calibrated fMRI  

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INTRODUCTION
Cerebral oxygen consumption (CMRO2) – using multi-modal measurement of BOLD signal (S), blood flow (CBF), and volume (CBV) – have been thoroughly investigated and shown to be coupled to neural activity by calibrated fMRI [1], and is based on the biophysical basis of the BOLD signal, where the transverse relaxation rate term (R2) depends on [2,3]

\[ R_2 \propto (1 - Y) \cdot b \cdot Hct \]

where (1 - Y) is the blood deoxygenation term, b is the total blood volume fraction, and Hct is the blood hematocrit. While the systemic hematocrit (discharge or macrovessel Hct) does not change during functional activity, studies have not yet assessed the impact of tissue (or microvessel) hematocrit on BOLD signal. Tube hematocrit, defined as the instantaneous volume fraction of red blood cells (RBCs) in microvessels (Hct_micro), depends on not only the volume ratio of RBC and plasma but also on their velocities, which may change dynamically as velocities of RBC and plasma components, especially in microvessels, are not equivalent [4]. Here we combined laser-Doppler flowmetry (LDF) and fMRI measurements of RBC (\(\nu_{rbc}\)) and plasma (\(\nu_{plasma}\)) velocities because they directly impact Hct_micro [4].

RESULTS
The \(\nu_{rbc}\) was estimated from the ratio of the LDF flux and RBC concentration, where the latter was calculated from backscattered signal. Fig. 1 shows results of our recent multi-modal studies in rats. The \(\nu_{rbc}\) transient arises from temporal mismatch between transients of RBC flux and concentration (Fig. 1A). The \(\nu_{plasma}\) was estimated from the first derivative of \(\nu_{plasma}\). The stimulation-induced fluctuations in \(\nu_{plasma}\) (Fig. 1A), which arise primarily due to slow \(\nu_{plasma}\) dynamics, are significantly smaller (p<0.001) than changes in \(\nu_{rbc}\). The dissimilar velocity patterns of RBC and plasma correspond to Hct_micro decrease immediately after stimulus onset which was sustained throughout the stimulus (Fig. 1B). CMRO2 variations were calculated with and without the Hct_micro effect (Fig. 1C).

DISCUSSION
Dynamic changes in \(\nu_{plasma}\) and \(\nu_{rbc}\) corresponded to a sustained drop in Hct_micro, based on the observations of Gaehgens [4]. A key component for Hct_micro variation is \(\Delta\nu_{rbc}\) since \(\Delta\nu_{plasma}\) seems quite passive. In fact, even if \(\Delta\nu_{plasma}\) is allowed to vary by ±50% of \(\Delta\nu_{rbc}\), simulations show negligible effects on \(\Delta\text{Hct}_{\text{micro}}\). Recently we showed that discharge hematocrit, equivalent with volume percentage of RBCs in blood, is not appreciably affected during functional activation [5]. The hyperemia-induced decrease in Hct_micro is consistent with a drop in blood viscosity, which in turn would improve efficiency of RBC movement through capillaries during function. These results suggest that Hct_micro needs to be included in the functional hyperemic response of the BOLD signal. Given that our measured changes in Hct_micro are almost as large as CBV_plasma changes measured by fMRI, we estimate that current calibrated fMRI studies could potentially be underestimating the \(\Delta\text{CMRO2}\) (Fig. 1C).

REFERENCES

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