Mapping Hepatic Blood Oxygenation based on quantitative BOLD

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Target Audience: Radiologists and MRI scientists engaged in functional liver imaging.

Purpose: Changes in regional hepatic oxygen delivery and oxygen consumption are significant indicators of cellular dysfunction in diseases such as rheumatic heart disease (1), trauma-hemorrhagic shock (3), and hepatocellular carcinoma (HCC).For example, hypoxia in HCC is known as an important biomarker of angiogenesis. As such, tissue oxygenation may predict the outcome of interventions including partial hepatectomy (4) and hepatic chemoembolization (5). Blood oxygen level dependent (BOLD) MRI is sensitive to tissue oxygenation, and has been used in multiple organs including brain, kidney, muscle and liver. Oxygen-enhanced MRI, in which the subject breaths normal air followed by 100% oxygen, has been utilized to detect alterations in hepatic tumor oxygenation status. The changes on R2* or R1 provide a sensitive indicator of tissue oxygenation (6, 7). However, both baseline R2* and its change also depend on the regiona1 hepatic blood volume, hence the BOLD response is relative and not specific. MRI-based quantitative BOLD (qBOLD) technique allows for the separation between blood oxygenation level and the deoxygenated blood volume, thereby providing regional mapping of blood oxygen saturation in the brain, kidney and skeletal muscle. In this study, we will apply MR qBOLD technique to assess regional hepatic blood oxygenation and blood volume in human subjects.

Methods: Liver is a highly vascularized organ with a regional blood volume of ~26 mL/100 g (8). As illustrated in the SEM image of microvascular casts of a rat liver (**Fig 1**), hepatic venule (25-40 μm), portal venule (15-100 μm) and sinusoids (5- 22 μm, mean of 14 μm) are randomly orientated (2, 9). Due to the rapid water exchange between intra- and extra-vascular water (10) and high blood volume, a single water compartment liver MR qBOLD signal model will be adopted in this study (11, 12):

$$S(t) = S_0 \cdot \exp\left(-R2 \cdot t - HBV \cdot f_c\left(\delta\omega \cdot t\right)\right), \text{ and}$$

$$\delta\omega = 4/3 \cdot \gamma \cdot \pi \cdot \Delta\chi_0 \cdot Hct \cdot (1 - Y) \cdot B_0,$$

Where B_0 is the MR scanner field; $\Delta\chi_0 = 0.264$ ppm (cgs unit); Hct is the hematocrit ratio; HBV is hepatic blood volume; Y is hepatic blood oxygen saturation; f_c is a function defining contribution of blood vessel network to the tissue MR signal decay (12).

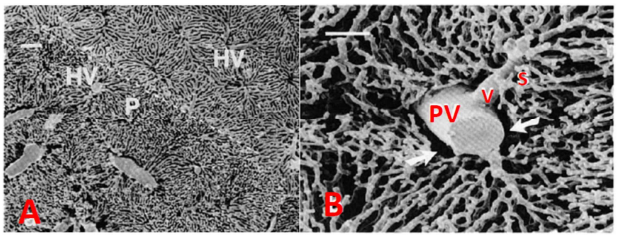
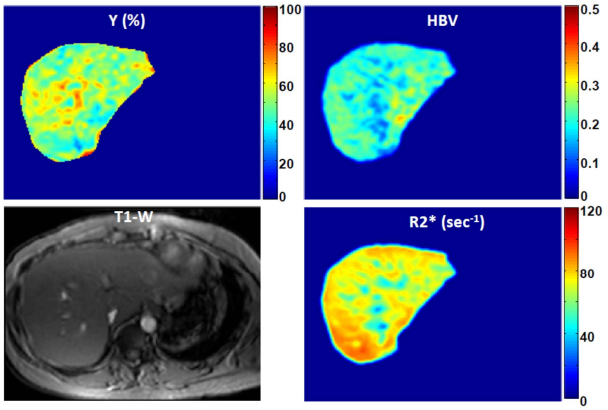


Figure 1. Microvascular casts of normal rat livers reveals the terminal hepatic venules (HV) and portal tract (P) on the surface (A); and the portal vein (PV), smaller venules (v) and sinusoid (s) within acinar structure in cross section of the liver (B). Bar = 100 μm. Adapted from Ref (2).

Five healthy subjects were recruited in this IRB-approved study. All experiments were performed on a 3T Siemens Trio scanner. To reduce the water diffusion effect, a 2D multi gradient-echo sequence as used in kidney qBOLD studies was employed. MRI parameters were: TR of 100 ms; sampling matrix of 208×156; voxel size of 1.5×1.5×6 mm^3; echo spacing of 2.38 ms with echo train length of 25; first gradient echo time of 3.0 ms. Each qBOLD Image set was acquired under a 18s breath-holding. 4 repetitive data sets were acquired. The field map was acquired by a 3D double-echo sequence with voxel size of 1.5×1.5×3 mm^3.



Results: **Fig. 2** illustrates a typical result from a liver qBOLD study. For this subject, mean hepatic blood oxygen saturation (Y) is 52%, and is relatively uniform across the entire liver. The estimated HBV is about 20.6%. At the vicinity of large blood vessels (low R2* area), the estimated tissue blood oxygenation and HBV may not be reliable due to the partial volume effect. Across five subjects, the mean hepatic blood oxygen saturation is 54±11%, consistent with the published mean hepatic venous oxygen saturation of 57% (1) or 67% (13) using catheter sampling in human subjects. The estimated mean HBV is 25±3%.

Conclusion and Discussion: We have demonstrated the feasibility of utilizing the liver qBOLD approach to estimate regional hepatic blood oxygen saturation and blood volume. Thus, liver qBOLD provides an in vivo approach to quantitatively assess regional liver tissue hypoxia in liver diseases. It should be noted that the estimated venous blood oxygenation is not the same as the hepatic oxygen extraction fraction (OEF), since the upstream portal vein blood is partially deoxygenated. Therefore, portal and hepatic venules/veins both contribute to qBOLD-derived hepatic blood oxygenation and HBV(hepatic arterioles is not included due to its high blood oxygenation). A potential confounding factor for the liver qBOLD technique is the hepatic iron concentration, which can modulate the magnetic susceptibility difference between blood and hepatic tissue, influencing the accuracy/bias of the hepatic blood oxygenation estimation.

References: **1.** Bishop, et al, JCI 1995;34:1114; **2.** Lim, et al, DigDisSci 1994;39:1683; **3.** Ba, et al, CCM 2000; 28:2837; **4.** Yoskioka, et al, Hepatology 1998;27:1349; **5.** Choi, et al, AntiCancerRes 2013;33:1887; **6.** O'Connor, et al, IJROBP 2009; 75:1209; **7.** Naik, et al, ProcISMRM 2008;3741; **8.** Blustajn, et al, MRI 1997;15:415; **9.** Oda, et al, CHM 2003;29:162; **10.** Goresky, et al, CanMedAssocJ 1965;92:517; **11.** He, et al, MRM 2007;57:115; **12.** Yablonskiy, et al, MRM 1994;32:749; **13.** Myers, JCI 1947;26:1130;