Oxygenation-dependent 9.4-T BOLD 3D Microscopy

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Introduction

High-resolution vascular imaging has been performed based on blood oxygenation level dependent (BOLD) contrast at high fields [1]. Hypointense pixels in these T_2^*-weighted images can be of not only venous origin, but also magnetic susceptibility effects from sources other than venous deoxyhemoglobin (e.g., arterial dHb, iron deposits, air/tissue/bone interfaces). To confirm the venous origin of dark vascular patterns, oxygenation-dependent 9.4-T BOLD 3D microscopy was performed and the results were examined based on previous vascular histology and our computer simulations in this study.

Materials and Methods

Male Sprague-Dawley rats weighing 260–450 g were used ($N = 6$). The rats were mechanically ventilated under ~1.5% isoflurane anesthesia in an air:O_2 mixture with $FiO_2 = 30\%$. The femoral artery and femoral vein were catheterized for blood gas sampling and for fluid administration, respectively. Rectal temperature was maintained at 37 ± 0.5 °C with a water-heating pad, controlled by a thermocouple and feedback unit. The head of the animal was carefully secured to a home-built cradle by means of ear pieces and a bite bar. Reduced FiO_2 values of 21% and 15% were attained by changing the gas mixture to air and air:N_2 mixtures, respectively. Images were not acquired until at least 10 minutes after each target O_2 level was achieved.

The experiments were carried out on a Varian 9.4 T / 31-cm MRI system with a 12-cm I.D. Magnex gradient coil. A home-built quadrature RF surface coil (I.D. of each of 2 lobes = 1.6 cm) was provided RF excitation and reception. Voxel-localized shimming was performed. BOLD microscopy was performed with a 3D flow-compensated gradient-echo pulse sequence. The RF power level was adjusted to maximize subcortical signal. Imaging parameters were: TR = 50 ms, TE = 20 ms, FOV = $3.0 \times 1.5 \times 1.5$ cm^3, matrix = $384 \times 192 \times 192$, and total scan time = 34 min 38 s. A total of three 3D datasets were acquired for each animal; one each at $FiO_2 = 30$, 21, and 15%.

To obtain further insight into vessel detectability at 9.4 T, computer simulations were performed based on a cylinder model of a blood vessel perpendicular to the main magnetic field [2,3]. The condition with the lowest partial blood volume fraction (i.e., when the center of the venous vessel is located at a corner of a voxel) was chosen for our simulation of minimum detectability. Parameters for the simulation were T_1 of tissue and venous blood = 1.9 and 2.2 s, respectively; tissue $T_2^* = 35$ ms; venous $T_2^* = 4.9$, 6.4, 9.0, and 15.2 ms for oxygen saturation levels of 60, 70, 80, and 90%, respectively [4] (based on venous T_2 values, which is conservative in terms of detectability); relative spin density of tissue and venous blood = 0.89 and 0.86 [5]; hematocrit level = 0.4; and susceptibility difference between fully oxygenated and deoxygenated blood = 0.2×10^{-6} in cgs units [2]. Venous pixel with intensity below 85% of tissue signal intensity was considered to be detectable.

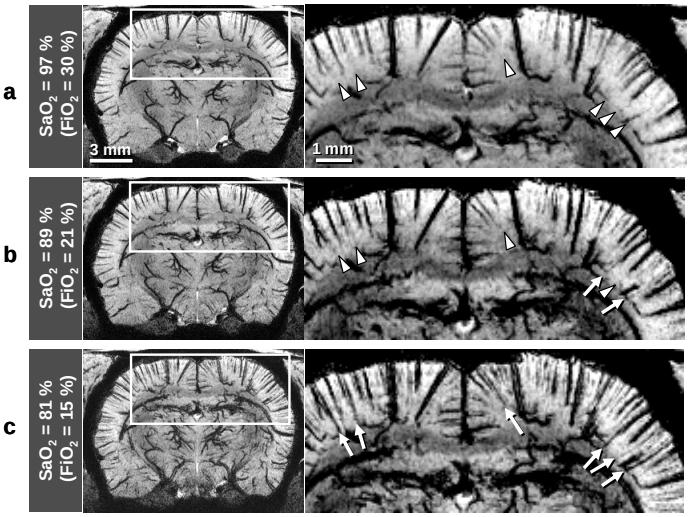

Figure. 1. Oxygenation-dependent 9.4-T BOLD 3D microscopy study. Data were acquired with TE = 20 ms ($N = 6$ total). Displays are minimum-intensity projections of 1-mm thick coronal slabs. SaO_2 and FiO_2 in **a–c** represent values for the oxygen saturation level of systemic arterial blood and the fraction of inspired oxygen, respectively. Regions within the boxes (left) are expanded (right), with intensity and contrast levels adjusted to emphasize the SaO_2 dependence of vessels presumed to be arteries. Arterial candidates are marked when they are visible (arrows) and not yet visible (arrowheads).

Results and Discussion

When the FiO_2 level was 30, 21, and 15%, the systemic arterial oxygen saturation level (SaO_2) ranges were 97–100, 89–98, and 80–90% in six animals (99 ± 1, 95 ± 3 and 85 ± 5%), respectively. Data from one oxygenation-dependent study are shown in Fig. 1. The dark lines observed at the highest O_2 level (Fig. 1a) thicken but do not lengthen as the O_2 levels are reduced (Fig. 1b and c), confirming that the dark patterns in data with $FiO_2 = 30\%$ are indeed of vascular origin. Notably, some new lines appear at the reduced O_2 levels (arrows in Fig. 1b and c), which are thin and appear with low contrast relative to other vascular patterns existing within comparable or shallower cortical depths. Even though it is not obvious from the 2D displays, careful evaluation of 3D data shows that these new vascular patterns appearing at reduced O_2 levels usually have increased contrast at deeper cortical regions, and some disappear near the cortical surface. There was no continuation of these patterns in adjacent volumes, indicating that this aspect of their appearance is not due to a partial volume effect. When $FiO_2 = 15\%$, these new vascular patterns were evident in all animals ($N = 6$, systemic $SaO_2 = 85 \pm 5\%$). When $FiO_2 = 21\%$, some of these new vascular patterns were observed in half of the animals ($N = 3$, systemic $SaO_2 = 93 \pm 3\%$), while there was no evidence in the remainder ($N = 3$, systemic $SaO_2 = 97 \pm 1\%$). Based on these characteristics, the new vascular patterns are likely of arterial origin [6,7].

According to the computer simulations, minimum-detectable vessel diameters for our conditions (e.g. TE = 20 ms, scan resolution = 78 μm, etc.) are ~22, ~25, ~30, and ~48 μm for local oxygen saturation levels of 60, 70, 80, and 90%, respectively. Since local (intracortical) arterial oxygen saturation levels are lower than systemic SaO_2 [7], these simulation results suggest that 30–48 μm diameter intracortical arteries should be detectable when systemic $SaO_2 = 80$–90%, in agreement with both our oxygenation-dependent studies (Fig. 1c) and with the actual diameter of large intracortical arteries (30–50 μm) known from rat brain histology [6,8].

References

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