# Breath-Hold Regulated Blood Oxygenation-Level Dependent MRI and Vascular Space Occupancy MRI of Brain Tumors

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## Introduction

Blood oxygenation-level dependent (BOLD) MRI at 1.5-Tesla showed that there were breath-hold regulated signal increases in normal brain tissues, and not in brain tumors (1). Tumor neovasculature does not have normal microanatomy and lacks smooth muscles, vasodilatation and increased cerebral blood flow mediated by the effects of reduced extracellular pH on the arterial side of normal capillary bed are therefore absent (2). Recently, vascular space occupancy (VASO) MRI was developed for cerebral blood volume quantification in a manner that is independent of blood oxygenation and flow (3). In this study, BOLD and VASO techniques were integrated on a clinical 3-Tesla scanner to evaluate the cerebrovascular responses of normal adults and patients with cerebral tumors under repeated breath holding challenges.

## Method

Six normal adults (2 women, 4 men, 19 – 26 year-old) were recruited as the normal group. The breath-hold paradigm comprised of one preparation stage (30-second natural breathing) and three one-minute periodic breath-hold cycles (5, 10, 15, 20, or 30-second breath-hold periods). A total of 70 dynamic measurements were obtained. Fourteen patients (8 women, 6 men, 30 – 70 year-old) with brain tumors (7 meningiomas, 2 astrocytomas, 2 oligodendrogliomas, 3 metastatic adenocarcinomas) were recruited. The 15-second breath-hold paradigm was applied in patient group. A single-shot T2*-weighted gradient-echo EPI sequence was applied for BOLD MRI: TR/TE = 3000/35 msec, flip angle = 90°, slice thickness = 5 mm, matrix size = 64 x 64, and in-plane resolution = 3 x 3 $mm^2$. An inversion-recovery gradient-echo EPI sequence was applied for single-slice VASO MRI: TR/TI/TD = 3000/888/1712 msec, slice thickness = 8 mm, matrix size = 64 x 64, and in-plane resolution = 3 x 3 $mm^2$. An averaged signal-time course of subcortical gray matters was used as the reference function. Pixels with significant changes in BOLD and VASO signal were then determined using a correlation analysis at a level of $P<10^{-8}$ and $P<0.001$, respectively.

## Results

In the normal group, significant BOLD signal increases and VASO signal decreases could be detected in the gray matter for a breath-hold duration as short as 5 seconds (Fig. 1). The fractional activation volume of BOLD response was higher than that of VASO at every different breath-hold duration.

In the patient group, the breath-hold regulated BOLD and VASO signal changes in normal appearing gray matters were generally the same as those in normal group (Fig. 2). Contrarily, there was no breath-hold regulated BOLD signal increase, nor VASO signal decrease, in the tumors (Fig. 2). Two of the patients with meningiomas had breath-hold regulated BOLD signal decreases or VASO signal increases inside the tumor (Fig. 3).

**Fig. 1.** BOLD signal increases (red) and VASO signal decreases (blue) in gray matters of normal subjects during different breath-hold periods.

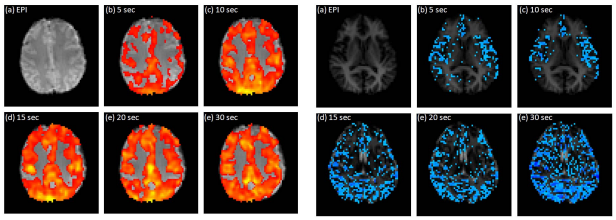



**Fig 2.** Breath- hold regulated signal changes in gray matters (blue lines), not in the tumors (red lines).

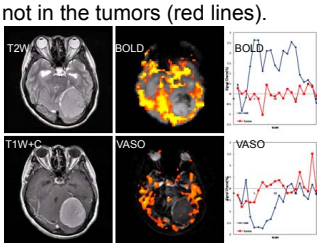
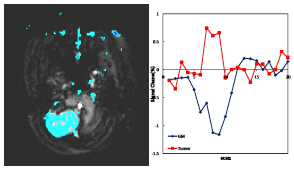



**Fig 3.** VASO signal decreases in gray matters (blue line), but increases in the meningioma (red line).



## Discussion

This study showed that there were breath-hold regulated BOLD signal increases and VASO signal decreases in the normal appearing gray matter of normal subjects and patients, with a higher sensitivity of signal detection by using BOLD technique. Absence of signal changes in a hypoperfused tumor is most likely due to reduced local hematocrit or absence of normal vasculature. Absence of signal changes in a hyperperfused tumor is more complicated, which may be due to unresponsiveness of the neovasculature and the overwhelming hypo-oxygenation status of the tumor (4). Under hypercapnia stress, blood from a region where the vessels do not dilate is redistributed to a responsive region and surrounding normal tissue, causing a focal worsening of tumor perfusion (5). This so-called steal phenomenon may be exaggerated in a meningioma where cellularity is high and neovascularity is dense and result into the reverse BOLD or VASO signal changes. Further evaluation in a large cohort study is necessary to solidify the preliminary findings.

## References

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