Optimizing and Understanding BOLD Contrast Imaging in the Breast

R. Rakow-Penner[1], B. Daniel[1], and G. Glover[1]

[1]Radiology, Stanford University, Stanford, CA, United States

Introduction: Blood oxygen level dependent (BOLD) contrast imaging has the potential to evaluate tumor metabolism and angiogenesis [1-3]. Variations in oxygenation may give insight on tumor types [1], predict susceptibility to antiangiogenic therapeutics [2], and monitor chemotherapeutics [4]. Specifically, BOLD contrast MRI may be increasingly useful for breast cancer detection and management. Our group is developing a robust method for detecting BOLD contrast MRI and understanding its meaning in healthy volunteers in preparation for scanning breast cancer patients. Previous results [5,6] on healthy volunteers indicated the complexity of BOLD contrast imaging in the breast, motivating further evaluation of the stimulus and optimization of the overall approach.

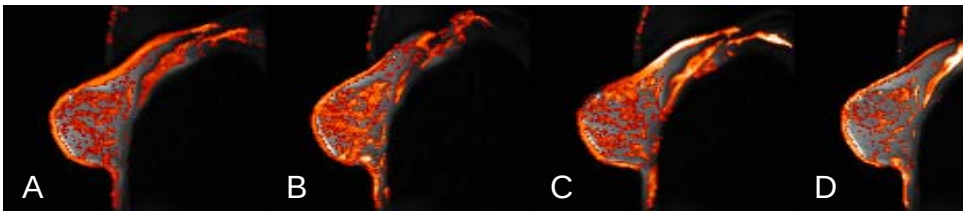
Methods: Functional data were collected on 5 healthy female volunteers (ages 24 – 29) with a single shot fast spin echo (HASTE) sequence with the following imaging parameters: 3T (GE Healthcare, Waukesha, WI), 8 channel breast coil (GE, Waukesha, WI), TE = 60ms, TR = 4 s, bandwidth = 83 MHz, matrix size = 128 x 128, FOV = 20 cm, slice thickness/spacing = 5mm/5 mm, 240 time frames/slice, 1 sagittal slice. A respiratory belt and pulse oximeter were placed on the volunteers to record respiratory motion and cardiac rate. Tidal O2 and CO2 were also monitored. We evaluated 4 variations of hyperoxic stimuli (not all volunteers received all stimuli). Each of the 4 paradigms were delivered to the volunteer with 4 block cycles totaling 16 minutes. The block stimuli consisted of: (1)pure oxygen delivered first, interleaved with carbogen (95% O2, 5% CO2) for 4 cycles, (2) carbogen delivered first, interleaved with oxygen, (3) room air interleaved with oxygen, and (4) room air interleaved with carbogen.

Retroicor was used to reduce image noise from respiratory motion and cardiac pulsation in time [7]. Next, the BOLD signal time series for each voxel was cross correlated with a sinusoid model of the periodic stimulus. Thirdly, a sigma filter was applied which averages nearby voxels with less than one standard deviation from the center voxel, thus eliminating noisy single voxels. The first cycle of data was not used in the analysis to avoid error introduced from air inhaled previous to the start of the scan.

Results: In previous years' results, we evaluated BOLD contrast in the breast using room air vs. oxygen as our stimulus and found that several volunteers' signals positively correlated to the stimulus while others' signals negatively correlated. Thus, we wanted to investigate carbogen as a potentially more robust stimulus. In Volunteer 1 (Table 1), we evaluated air vs. oxygen and air vs. carbogen. She presented with a positive correlation to O2 and a negative correlation to CO2. We found similar results in our other volunteers with the caveat that Volunteer 2 presented with the reverse condition, yielding positive correlation to CO2 and negative correlation to O2. This motivated further investigation of using CO2 and O2 as alternating gases in the block stimulus without room air to maximize BOLD contrast. In 2 out of the 3 volunteers where we evaluated this condition, we found opposing contrast when delivering the stimulus O2 vs. CO2 in comparison to CO2 vs. O2. In Figure 1, the correlation coefficient maps are superimposed on average images for each of the 4 paradigms for Volunteer 5. The CO2 vs. O2 condition maximized BOLD contrast for this volunteer (and for 3 out of the 4 volunteers overall). The time series plot demonstrates the complementary contrast of the O2 vs. CO2 study in comparison to the CO2 vs. O2 study.

Subject	O2 vs. CO2		CO2 vs. O2		Air vs. O2		Air vs. CO2	
	ϕ	cc	ϕ	cc	ϕ	cc	ϕ	cc
1	NA	NA	NA	NA	$\pi/3$	0.002*	$7\pi/6$	0.132
2	π	0.082	$11\pi/6$	0.129	$7\pi/6$	0.064	$\pi/6$	0.044
3	NA	NA	$\pi/2$	0.062	$\pi/6$	0.029*	$7\pi/6$	0.187
4	2π	0.002*	2π	0.086	$11\pi/6$	0.012*	NA	NA
5	$\pi/2$	0.039	π	0.093	$5\pi/3$	0.022*	π	0.023

Table 1. Phase (ϕ) and correlation coefficient (cc) measurements from an ROI of the image with maximum positive correlation per sequence. The phase is relative to the peak delivery of the second gas listed on the top of each column. *= insignificant correlation.



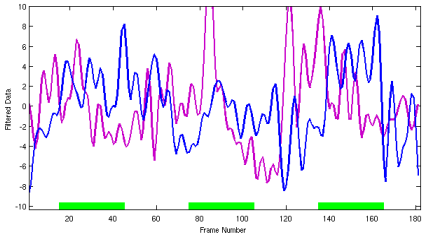


Figure 1. (*Images*)Correlation coefficient maps superimposed on the average images for Volunteer 5. (A) O2 vs. CO2, (B) CO2 vs. O2, (C) Air vs O2, (D) Air vs. CO2. *(Graph)* Filtered time series corresponding to a large ROI in the glandular tissue of volunteer 5. Blue: O2 vs. CO2; Purple: CO2 vs. O2, Green: corresponds to CO2 on for the blue signal and to O2 on for the purple signal (the alternate gas is on between the green bars).

Discussion: BOLD contrast imaging in the breast is a challenging but promising technique. In this study, we demonstrated that BOLD contrast MRI can consistently detect the opposing vasodilatory effects of carbogen and oxygen in the breast. Volunteers who positively correlate with carbogen, correlate negatively with oxygen and vice versa. Preliminary results indicate that a stimulus using CO2 modulated with either air or O2 produces improved BOLD contrast results in the breast in comparison to an air vs. O2 stimulus. Also, breast tissue response to the stimuli are individualized as each person demonstrated a different response time (measured by the phase offset) to the presented stimulus. We hypothesize that the variation in correlation and response time may correspond to the phase in the menstrual cycle (estrogen acting as a endogenous vasodilator), and possibly the varying admixture of fat between volunteers. In order to test these hypotheses, we are currently evaluating a group of volunteers with our protocol, once a week over 4 weeks with simultaneous near infrared breast optical imaging. The optical imaging component provides a quantitative measurement of oxy and deoxyhemoglobin in the fat and glandular tissue of the breast and will complement our BOLD results. Further studies will also focus on optimizing the pulse sequence parameters for detecting BOLD contrast in the breast. In this study, we used an SSFSE HASTE sequence to collect data rather than a GRE spiral sequence used in our previous studies. The SSFSE sequence has provided us with more consistent results and we plan to do a more thorough comparison of the two pulse sequences as applied to breast BOLD contrast imaging.

REFERENCES: [1] Taylor et al, JMRI, 2001. [2] Gilad et al, Int J Cancer, 2005. [3] Al-Hallaq et al, NMR in Biomedicine, 2002. [4] Zhou et al, J of Biomedical Optics, 2007. [5] Rakow-Penner et al, ISMRM Proceedings #3476, 2006. [6] Rakow-Penner et al, ISMRM Proceedings #586, 2008. [7] Glover et al, MRM, 2000. Funding provided by NIH P41-RR09784, DOD W81XWH-06-1-0358, and the California Breast Cancer Research Program.