BOLD Contrast in the Breast at 3T

R. Rakow-Penner[1], L. Pisani[1], B. Daniel[1], S. Oberfoell[1], C. Law[1], and G. H. Glover[1]
[1]Radiology, Stanford University, Stanford, CA, United States

Introduction: Blood oxygen level dependent (BOLD) contrast imaging applied to breast tumors may provide useful clinical information on tumor oxygenation. This information has the potential to help guide therapy and diagnosis. A previous study of BOLD contrast in a mouse tumor model [1] indicates that BOLD contrast measures the tumor's vascular maturity. Rapidly growing vasculature in certain tumors often does not develop the musculature for a vasoactive response; thus, malignant vessels will not dilate or constrict in response to a stimulus. Besides mouse tumor models, there are few studies evaluating BOLD contrast in human breasts, healthy or unhealthy [2,3]. Before approaching the study of tumors, our group is interested in better understanding BOLD contrast in healthy breast tissue. In order to evaluate this topic, we are developing a robust technique for measuring BOLD contrast in the breast. Previously, we reported [4] that heart saturation allows us to measure BOLD signal in the breast verses not being able to detect it. We have further improved our technique by increasing the field strength to 3T and altering parameters for optimal imaging. The purpose of this abstract is to report on what we have observed to date with BOLD breast imaging.

Methods: A 2D gradient echo spiral pulse sequence, with fat saturation and heart saturation was designed for this study. Heart saturation works by applying a cylindrical saturation in the left – right direction. Pure oxygen interleaved with room air delivered through a nasal cannula provided the BOLD stimulus with a block paradigm of 3 periods over 12 minutes. We have chosen oxygen as our stimulus because of its comfort in comparison to less tolerable gases such as carbogen. At 3T we developed our protocol with several volunteers and tested our most robust version on the left breasts of two healthy volunteers with the following imaging parameters: 3T(GE Healthcare, Waukesha, W)I, 8 channel breast coil (GE, Waukesha, WI), TE = 30 ms, TR = 1.1 ms, flip angle = 60, bandwidth = 125 kHz, matrix size = 80 x 80, FOV = 20 cm, slice thickness/spacing = 5 mm/5 mm, 2 interleaves, 327 time frames/slice, 12 slices. A respiratory belt and pulse oximeter were placed on the volunteers to record respiratory motion and cardiac rate.

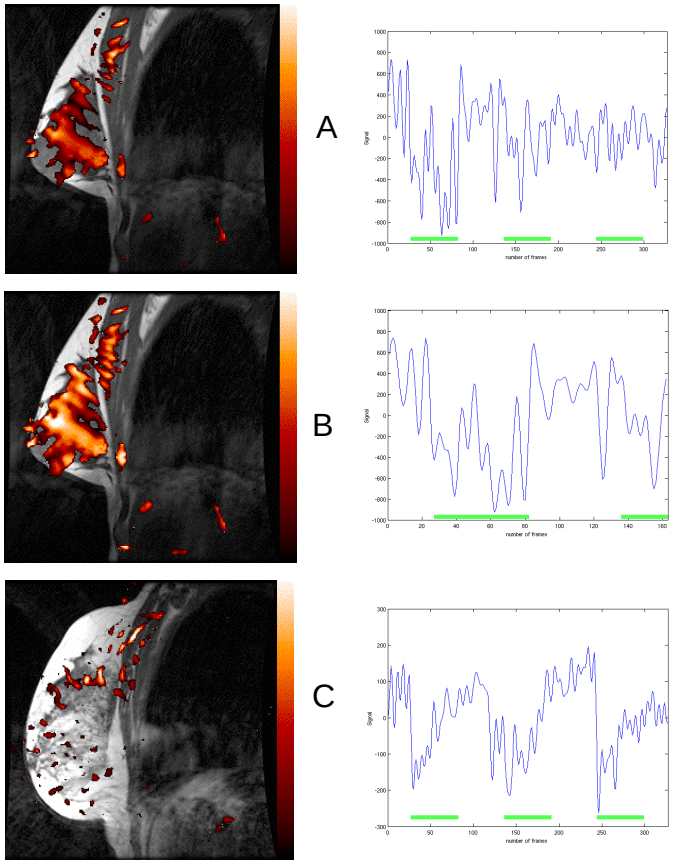

Figure 1. Left column: BOLD contrast activation maps superimposed on anatomic images. Right column: (blue) filtered time series corresponding to an activated ROI on the image to the left, (green) time when oxygen stimulus was turned on. Notice the inverse correlation between the stimulus and the BOLD contrast time series.

Retroicor was used to reduce image noise from respiratory motion and cardiac pulsation in time [5]. Next, the BOLD signal time series for each voxel was cross correlated with 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. Finally, a Fourier filter was applied with an upper limit of 0.07 Hz. Coregistration parameters were evaluated to discount motion as causing periodic correlation with the stimulus. The threshold for activation was set at p = 0.003.

Results: Figure 1 displays the correlation between the stimulus and the breast tissue. The plots are filtered versions of the time series by frame number in relation to signal intensity of a designated ROI (selected based on activation). The activation maps are superimposed on T1 anatomical images. Although the BOLD sequence was conducted with heart saturation, the T1 anatomical sequence was not (heart motion is seen in Figure 1, though it did not affect BOLD contrast measurements). In all studies, we found an inverse correlation between the stimulus and activation, meaning that by increasing oxygen intake, healthy breast tissue increases its deoxyhemoglobin content (becoming less oxygenated). These results agree with what we found in our previous study at 1.5T [4]. A and B are of the same 20 year-old volunteer. In A, we found that activation more closely correlated between the first half of the time series but attenuated over the second half. B shows the increased correlation activation map for the first half of the time series. We have noticed this effect before in previous preliminary studies. In C, we had minimal global activation in our 42 year-old volunteer. The areas of activation corresponded to glandular tissue, while areas without activation corresponded to more fatty tissue. In focal areas of activation, the entire time series strongly correlated with the stimulus.

Discussion: Results at 3T and previous results at 1.5T indicate that there is an inverse correlation between BOLD contrast and oxygen as a stimulus. Our hypothesis is that with an increase in oxygenation, specifically in healthy breast tissue, that there is a decrease in carbon dioxide. Without carbon dioxide to act as a local vasodilator, the vessels constrict, decreasing oxygen delivery to the tissue. We expect the BOLD contrast in the breast to act uniquely compared to other tissues in the body due to its admixture of fat and water, and its lower level of importance in sympathetic response. Also we are aware that menstrual cycle may affect tissue properties (our two volunteers' cycles, by chance, matched exactly). Eliminating cardiac motion and accounting for respiratory motion and cardiac pulsation, while rapidly collecting data at 3T have greatly improved the robustness of measuring BOLD contrast in breast tissue. In future studies, we intend to further enhance the robustness of our technique by spectrally separating out fat and water. Understanding healthy BOLD contrast will allow us to better understand breast patient results.

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