Breast BOLD Correlates to Optical Breast Imaging During Respiratory Stimulus

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Background

Blood Oxygen Level Dependent (BOLD) MR imaging offers research utility because of its ability to measure brain activation-induced changes in deoxyhemoglobin and blood flow. The physiological differences of blood oxygenation in normal vs diseased tissue suggests that BOLD images could also have significant clinical benefit in other organs. This study examined the BOLD response in the breast in 11 healthy volunteers during inspired gas changes. To better interpret the data, measurements were acquired concurrently with MR-guided diffuse optical tomography (MRg-DOT), a modality which has been shown to accurately quantify breast tissue blood oxygenation and hemoglobin content [1]. The advantage of combined imaging is that the optical acquisitions can be used to identify the independent effects of oxy- and deoxyhemoglobin. A key factor in this BOLD/optics study is characterization of the background physiological noise variations in individual subjects, which when controlled, allows the data to be interpreted via a correlation analysis.

Methods

Simultaneous BOLD/optical measurements were performed by retrofitting optical fibers to an MR breast coil (USA Instruments, GE Healthcare, Waukasha, WI). The interface, shown in Figure 1, allowed for 2 degrees of freedom (anterior/posterior, and medial/lateral) in positioning 8 optical fiber bundles on each side of one breast. MR images were acquired every 4 seconds with a single-shot fast spin echo sequence to reduce the sensitivity of the BOLD MR to B1 inhomogeneity. MR images were acquired in the coronal geometry to coincide with the plane of the optical probes. Optical intensity and phase measurements for 3 wavelengths were acquired every 30 seconds to form time varying images of oxyhemoglobin and deoxyhemoglobin.

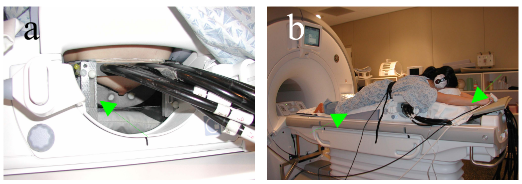
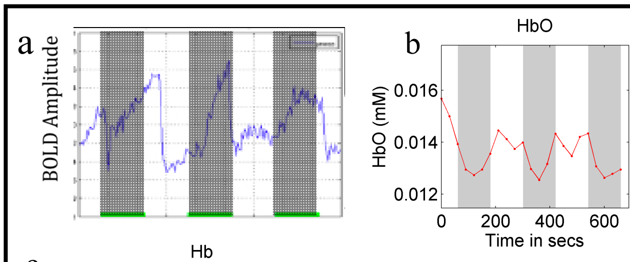


Figure 1: (a) The optical fiber holder attached to the manufacturer's breast immobilization plates. Optical fibers could be moved anterior/posterior along custom built rails, indicated by the green arrow. (b) Subject prepared on the MRI system bed. Green arrows indicate the pulse oximeter and respiratory belt, used to de-noise the BOLD MR signal.

To induce oxygenation changes, carbogen (95% oxygen, 5% carbon dioxide) and oxygen gases were introduced through a respiratory circuit and alternated every 2 minutes. BOLD and optical images were cross-correlated to the respiratory stimulus to produce images of correlation strength and phase lag between the gas stimulus and the measured signals. A protocol consisting of 4 breathing cycles (2 min carbogen, 2 min oxygen per cycle) was used to obtain data from 11 healthy volunteers. The first cycle was dropped to account for transient changes from previous breathing states. An oxycapnograph (Datex Capnomac Ultima, Helsinki, Finland) was used to ensure subject compliance.

Results

Example BOLD and optical time courses are shown in Figure 2. Gray vertical bars indicate the carbogen stimulus, while white bars indicate the oxygen stimulus. These results show good temporal agreement between BOLD MR and deoxyhemoglobin (Hb) optical imaging. Oxyhemoglobin (HbO), on the other hand, is shifted out of phase from the deoxyhemoglobin. A comparison of the phase (related to time) lag of BOLD compared to deoxyhemoglobin (Hb) is shown for the 11 healthy subjects in Figure 3a. Figure 3b utilized a metric, the Gas to Air ratio, which compared the correlation of the deoxyhemoglobin response during the gas stimulus to the correlation between the stimulus and air breathing. The air breathing time course data was acquired prior to the gas stimulus. Figure 3b does not include all subjects (N=4) who had a Gas to Air ratio less than 1, which indicated that the gas stimulus did not induce a significant response.



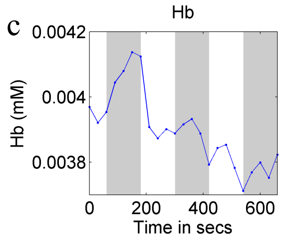


Figure 2: (a) BOLD signal time course, (b,c) HbO and Hb signal time courses determined by MRg-DOT. White bars indicate oxygen stimulus, gray bars indicate carbogen.

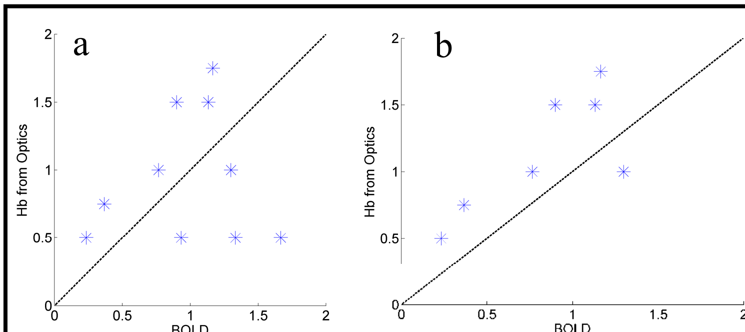


Figure 3: Temporal cycle delay (in units of pi) for BOLD response relative to the optical deoxyhemoglobin response for (a) all subjects, and (b) all subjects who had a greater response from the gas breathing than during air breathing. When controlling for non-responders, BOLD and optical responses correlate significantly r = 0.76, p = 0.048.

Discussion and Conclusions

The results from this work indicate that BOLD and optically-determined deoxyhemoglobin signals correlate significantly in the breast with an oxygen/carbogen respiratory stimulus, as long as only subjects that exhibit a significant response are included. This use of control measurement as a baseline is needed to account for subjects who do not exhibit sufficient hemodynamic change in response to the inspired gas stimulus due to larger variations in their natural physiological processes.

Acknowledgements

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References

[1]B. W. Pogue, S. P. Poplack, T. O. McBride, W. A. Wells, S. K. Osterman, U. L. Osterberg, and K. D. Paulsen, "Quantitative Hemoglobin Tomography with Diffuse Near-Infrared Spectroscopy: Pilot Results in the Breast," Radiology **218** (1), pp. 261-6 (2001).