Blood Oxygenation Level Dependent (BOLD) and Gd-DTPA contrast MRI for early evaluation of breast cancer chemotherapy

L. Jiang[1], R. McColl[1], P. Weatherall[1], D. Tripathy[2], R. P. Mason[1]

[1]Radiology, UT Southwestern Medical Center, Dallas, TX, United States, [2]Internal Medicine, UT Southwestern Medical Center, Dallas, TX, United States

Introduction: Tumor microcirculation and oxygenation play critical roles in tumor growth and responsiveness to cytotoxic treatment. These characteristics may provide prognostic indicators for cancer therapy and /or early evaluation of tumor therapeutic efficacy. Dynamic Contrast-Enhanced (DCE) MRI of small extrinsic paramagnetic contrast agents, such as Gd-DTPA provides an indication of vascular perfusion, and permeability. Deoxyhemoglobin ($dHbO_2$) is also paramagnetic and can serve as an endogenous contrast agent causing signal loss in echo planar MR images. Interventions improving tumor vascular oxygenation, which convert $dHbO_2$ to HbO_2 are expected to produce signal gain. The BOLD effect is also sensitive to changes in blood flow and vascular volume. The aim of this study was to characterize the effect of the intrinsic susceptibility contrast mechanism in breast tumors, in order to explore the potential application of BOLD for evaluating breast tumor therapy in the clinic.

Methods: Ten female patients (average age, 49.8 years old) with locally advanced breast cancer were treated with preoperative chemotherapy. Each patient received a standard course of doxorubicin and cyclophosphamide for four cycles every two or 3 weeks and MRI exams (1.5 T Philips Intera) scheduled three times (before, after 1 cycle and after all chemotherapy). For the BOLD study, patients breathed room air for 45 s, to establish a baseline value, then oxygen (8 liters/min.) for 6 min and finally room air again. The parameters for BOLD were TR/TE (500/41.4 ms) and reconstruction matrix size= 256×256. In the DCE study, the patient breathed room air with imaging performed prior to and every 2 mins after an IV bolus injection of Gd-DTPA (Omniscan™, 0.1 mmol/kg). The parameters for DCE MRI were TR/TE (32.9/6.5 ms) with 18-20 cm FOV and reconstruction matrix size= 256×256. The data were analyzed on a voxel-by-voxel basis. A separate method of data assessment was also performed to refine our technique. This used only the BOLD data from the third through the sixth minute of oxygen breathing (after equilibrium is reached) and confined the region of interest (ROI) to the area in each tumor that had the highest vascularity (based on DCE images).

Results: ^{1}H MRI showed there was a region of BOLD contrast enhancement (relative signal intensity gain of 2 to 20% (Fig.1a)) in all patients. The DCE MRI showed a greater contrast enhancement in the same region (Fig.1b). The relative signal intensity of DCE decreased with treatment. Three patients showed a particularly high BOLD response (>10% (Fig.2)) before or during therapy, and they were all found to have complete or near complete pathological response upon subsequent resection. Additional analysis (with smaller ROIs) of the tumor zones known to have high vascularity revealed major differences between tumors that had good (vs. poor) response to chemotherapy. The good responders had an average BOLD effect of 15.4% vs. only 3.4% for poor chemotherapy responders (Fig. 3).

Discussion: Previously, we have found similar results in five patients. We believe that the consistent data for the larger group of 10 patients with 3 complete responders is very significant. The correlation between high BOLD response (greater than 2-fold difference in high vascularity areas of tumors) and better treatment outcome suggests a prognostic capability for BOLD MRI and we believe this approach is worthy of more extensive investigation.

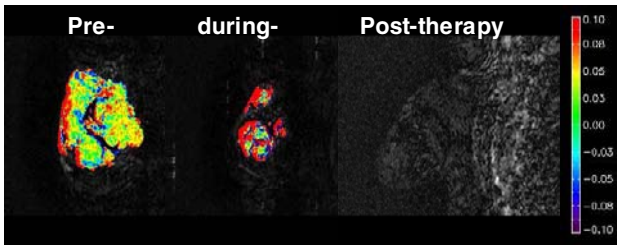

Fig. 1a **BOLD**

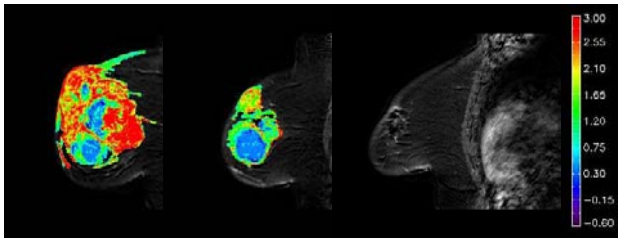

Fig. 1b **DCE**

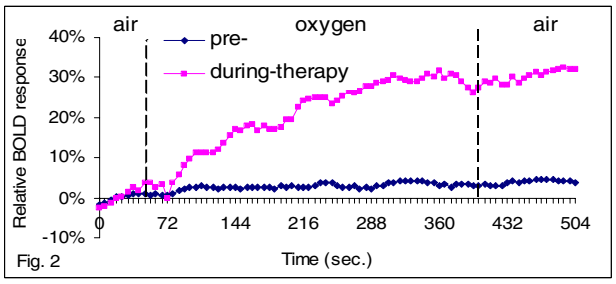

Fig. 2

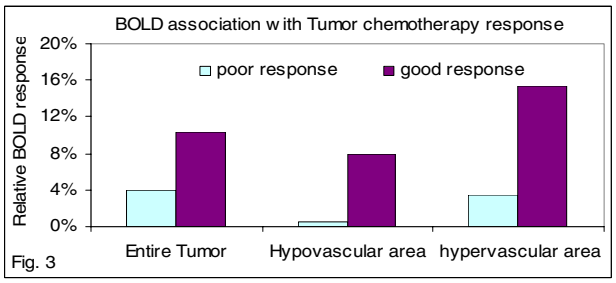

Fig. 3

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