BOLD and Gd-DTPA Contrast Enhanced MRI for Early Assessment of Breast Cancer Chemotherapy

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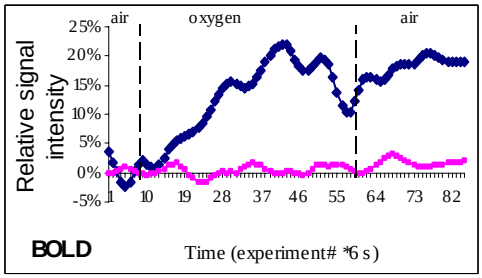
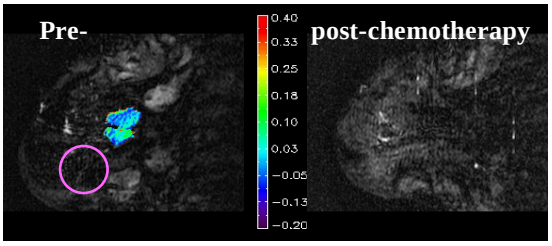
Introduction: Tumor microcirculation and oxygenation play critical roles in tumor growth and responsiveness to cytotoxic treatment. These characteristics may provide prognostic indicators for cancer therapy and /or early evaluation of tumor therapeutic efficacy. Dynamic Contrast-Enhanced (DCE) MRI of 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: Five female patients (average age, 53.2 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. MRI exams performed on a 1.5 T Philips Intera system. For the BOLD study, patients breathed room air for 45 seconds, 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 (172.1/32 ms) or (500/41.4 ms) and acquisition 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 acquisition matrix size= 256×256. The data were analyzed on a voxel-by-voxel basis.

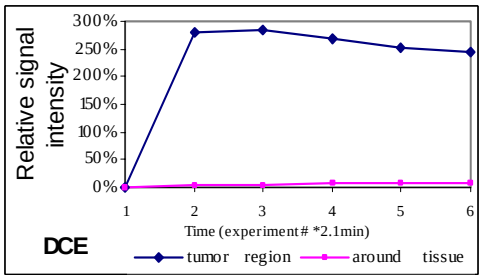
Results: ^{1}H MRI showed there was the BOLD contrast enhancement region (relative signal intensity gain of 3 to 15%) in five patients. The DCE MRI showed a greater contrast enhancement in the same region. Normal surrounding tissue showed minimal response to either oxygen breathing or Gd-DTPA infusion. The relative signal intensity of DCE decreased with treatment. The initial rate response to contrast agent injection in DCE was also diminished during chemotherapy. Following successful chemotherapy, one patient, who showed complete pathological response and has had the biggest BOLD response (15%) before treatment, showed no further BOLD or DCE response after treatment.

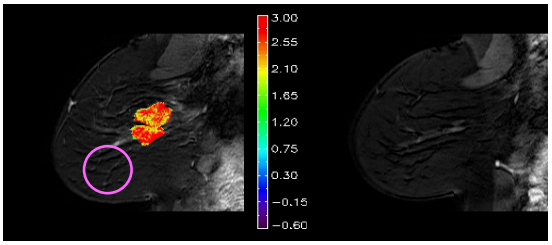
Discussion: These results demonstrate the logistic feasibility of combined BOLD and DCE MRI in patients. Some early studies failed because of patient motion during MRI. Although the contrast to noise ratio of the BOLD response is lower than accompanying Gd-DTPA, we believe it provides a second perspective on tumor physiology and response to therapy. Since it is entirely non-invasive and the study is rapid, we find good patient tolerance. Anecdotally, the patient with the largest BOLD response pre-therapy has the best outcome. As patient numbers increase we will assess rigorous correlations between the BOLD and DCE kinetic response and therapeutic success.





BOLD





DCE

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