T_1 and T_2* weighted dynamic contrast-enhanced MRI predicts clinico-pathological response to neoadjuvant chemotherapy in primary breast cancer

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Introduction: For women being treated with neoadjuvant chemotherapy for primary breast cancer, the ability to identify early during treatment those who will fail to respond can enable the use of alternative therapies that may be more beneficial[1]. Here, we assess the ability of multi-functional dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) to identify non-responders after 2 cycles of treatment.

Materials and Methods: 24 patients with primary breast cancer (median age 45.5 years old, range 29 - 59) were imaged prior to and following two cycles of 5-fluorouracil, epirubicin and cyclophosphamide (FEC) neo-adjuvant chemotherapy (NAC) using a dedicated breast coil in a Siemens 1.5T Symphony scanner. Spoiled gradient-echo [FLASH] sequences (8 different TE [5-75ms], TR=100ms, α=40°, 1 slice) were used for R_2* measurement using an IDL® least-squares fitting routine. T_1W DCE-MRI images were acquired using another FLASH sequence (TE=4.7ms, TR=11ms, α=35°, 4 slices). 40 images were acquired every 12 seconds for 8 min 5s. An injection of 0.1mmol/kg Gd-DTPA was given using a power injector at 4ml/s during the 5th data acquisition point. The data were fitted to the Tofts and Kermode model[2] using methods previously described[3] with semi-quantitative (mean gradient [MeanGrad], maximum signal amplitude [MaxAmp] and washout gradient [Wt]) and quantitative (transfer constant [K^{trans}], leakage space [v_e], rate constant [k_{ep}], and maximum Gd-DTPA concentration [MaxGd]) kinetic parameters calculated. Following this, a T_2*-weighted DCE-MRI sequence was used to acquire data every 2 seconds over 2 minutes (TE=20ms, TR=30ms, α=40°, 1 slice) with 0.2mmol/kg Gd-DTPA injected at 4ml/s after 20s. These data were used to calculate relative blood volume (rBV), relative blood flow (rBF) and mean transit time (MTT) using the central volume theorem by applying a gamma variate fit function[4]. All calculations were performed pixel-by-pixel using in-house software (Magnetic Resonance Imaging Workbench – Institute of Cancer Research, London). Median and 5th-95th centile values for each parameter were derived from whole tumour regions of interest and treatment changes calculated. Pre-treatment parameter values and treatment changes were correlated with clinical and pathological response following 6 cycles of chemotherapy using the Mann-Whitney U-test and the statistical significance was the 2-tailed p-value for rejecting the hypothesis of zero correlation.

Results: Of the 24 patients assessed, 17 were clinical responders and 7 were clinical non-responders; 9 patients were pathological responders and 15 were pathological non-responders. Pre-treatment parameter values and MRI-defined tumour size changes following 2 cycles of NAC did not predict for final clinico-pathological response. Changes in median MeanGrad, MaxAmp, K^{trans}, K_{ep}, rBV and rBF significantly correlated with both final clinical and pathological response (Figure 1) as did changes in the 5th-95th centile range for MeanGrad, K^{trans}, MaxGd, rBV and rBV ($p<0.05$ for all groups). The change in median MaxGd and 5th-95th centile range for MaxAmp was also significant for clinical response alone and the change in 5th-95th centile range for K_{ep} was significant for pathological response alone ($p<0.05$ for all groups). Changes in Wt, v_e, MTT and R_2* did not predict for final response however judged.

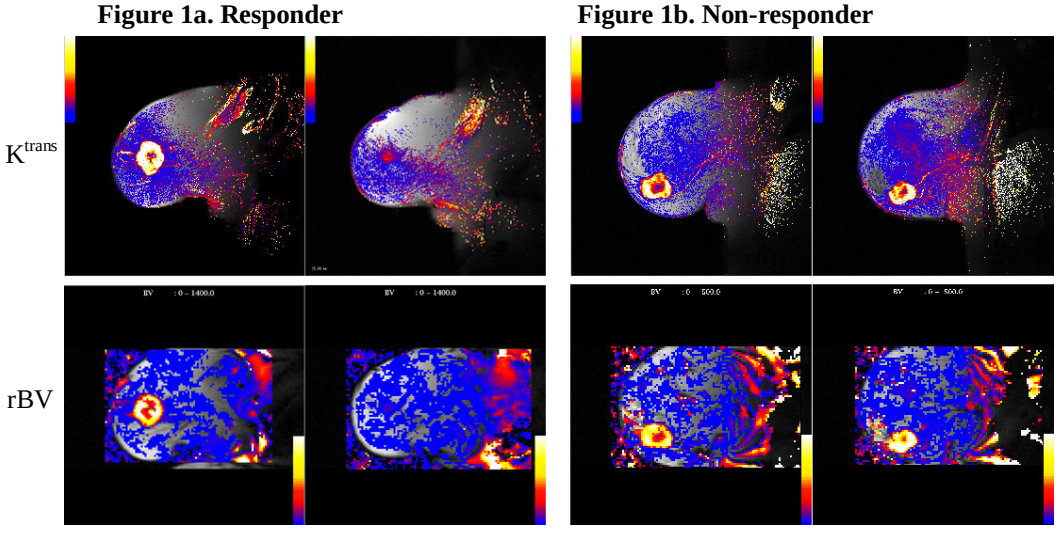

Figure 1: Parametric images of transfer constant K^{trans} and relative blood volume rBV, pre- and post 2 cycles FEC chemotherapy for a) pathological responder and b) pathological non-responder. Both patients had grade III invasive ductal carcinoma.

Conclusion: Changes in DCE-MRI-derived semi-quantitative and quantitative vascular parameters following 2 cycles of neoadjuvant FEC chemotherapy can identify patient groups who would gain no clinical or pathological benefit from further cycles of FEC chemotherapy. We are currently determining the measurement error of DCE-MRI in another cohort of breast cancer patients in order to determine the level of change in kinetic parameters needed to alter patient treatment.

References:

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