Influence of Breast Cancer Receptor Status on Multi-parametric Magnetic Resonance Imaging for Predicting Treatment Response: Preliminary Results

Xia Li[1], Vandana G Abramson[1], Lori R. Arlinghaus[1], Hakmook Kang[1], Jason M Williams[1], Richard G Abramson[1], A. Bapsi Chakravarthy[1], Praveen Pendyala[1], and Thomas E Yankeelov[1]

[1]*Vanderbilt University, Nashville, Tennessee, United States*

TARGET AUDIENCE Basic and clinical scientists studying breast cancer

PURPOSE The purpose of this study is to determine if classifying breast cancer patients by subtype improves the ability of integrated dynamic contrast enhanced MRI (DCE-MRI) and diffusion-weighted MRI (DW-MRI) to predict eventual response after the first cycle of neoadjuvant chemotherapy (NAC).

METHODS *Data Acquisition* Thirty-five patients with Stage II/III breast cancer were enrolled in an IRB-approved clinical trial where DCE- and DW-MRI data were acquired before (t_1), and after one cycle of chemotherapy (t_2). At surgery, 12 patients achieved a pathological complete response (pCR) while 23 patients were non-responders (non-pCR). Imaging was performed on a 3.0T MR scanner (Philips Healthcare, The Netherlands) and employed a 3D spoiled gradient echo sequence with a spatial resolution of 6.6 mm^3 and a temporal resolution of 16 seconds collected at 25 time points before and after the intravenous injection of 0.1 mmol/kg of gadopentetate dimeglumine (Magnevist, Wayne, NJ). DW-MRIs were acquired with a single-shot spin echo (SE) echo planar imaging (EPI) sequence. Details on the acquisition and analysis methods have been presented elsewhere [1].

Data Analysis Estimates of K^{trans} (vessel perfusion and permeability), k_{ep} (delivery and retention of contrast agent), v_e (extravascular extracellular volume fraction), and v_p (plasma volume fraction) were generated from the DCE-MRI data using the Extended Tofts-Kety model [2]. The apparent diffusion coefficient (ADC; related to cellularity) was estimated from the DW-MRI data. The derived parameter k_{ep}/ADC was also assessed. The patients were divided into three groups according to receptor status: 1) ER-/PR-/HER2- (5 pCRs + 5 non-pCRs), 2) HER2+ (5 pCRs + 10 non-pCRs), and 3) HR+/HER2- (2 pCRs + 8 non-pCRs). Receiver operating characteristic (ROC) analysis was applied to the three groups, as well as all patients, and the areas under ROC curve (AUC) were calculated. The bootstrap method was performed with 500 replicates to assess if the AUC was significantly different between groups.

RESULTS Comparing all parameters, the derived parameter k_{ep}/ADC provided the best predictive values achieving AUCs of 1.00, 0.92, and 0.94 for each subgroup, respectively, versus 0.88 for all patients. k_{ep}/ADC yielded a perfect score of one for sensitivity, specificity, positive predictive value, and negative predictive value for the ER-/PR-/HER2- patients, compared with 0.92, 0.78, 0.69, and 0.95, respectively, for all patients. The AUC of k_{ep}/ADC in the triple negative group was improved significantly ($p<0.05$) over the all-patient group. Table 1 shows the AUCs and optimal cutoff points for all parameters.

	ER-/PR-/HER2- (n = 10)	HER2+ (n=15)	HR+/HER2- (n=10)	All patients (n=35)
ADC ($mm^2/s \times 10^3$)	0.64 (1.66)	0.80 (1.25)	0.89 (1.40)	0.82 (1.40)
K^{trans} (1/min)	0.52 (0.10)	0.80 (0.11)	0.69 (0.10)	0.67 (0.10)
k_{ep} (1/min)	0.92 (0.28)	0.78 (0.34)	0.69 (0.28)	0.76 (0.28)
v_e	0.60 (0.65)	0.52 (0.53)	0.50 (0.49)	0.54 (0.41)
v_p	0.80 (0.06)	0.72 (0.03)	0.50 (0.07)	0.61 (0.04)
k_{ep}/ADC ($1/mm^2$)	1.00 (2.83)	0.92 (4.31)	0.94 (2.53)	0.88 (3.32)

Table 1. The AUC values (and optimal cutoff points) for the DCE- and DW-MRI parameters post-1 cycle of treatment by subtypes.

CONCLUSION These preliminary results demonstrate that DCE- and DW-MRI may be able to better predict treatment response for patients with particular subtypes of breast cancer by using a parameter cut-off point unique to each sub-type. Our previous study [2] has shown that k_{ep}/ADC improved the predictive ability, compared with single parameters for all patients. This study demonstrated that this combination outperformed other parameters in each of the major receptor-specific groups. This observation should be confirmed in a large cohort of patients in the future.

REFERENCES 1. Li X et al. Invest Radiol 2014. 2. Yankeelov TE et al. Curr Med Imaging Rev 2009, 3(2):91-107.

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