Quantitative DCE- and DW-MRI to Predict the Response of Primary Breast Cancer to Neoadjuvant Therapy

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TARGET AUDIENCE Basic and clinical scientists studying breast cancer

PURPOSE Dynamic contrast enhanced MRI (DCE-MRI) and diffusion weighted MRI (DW-MRI) report on tissue vascular and cellular characteristics, respectively, and have been used to predict treatment response in breast cancer[1,2]. Quantitative DCE- or DW-MRI parameters are usually investigated separately, and it is unclear whether combining information obtained from each of these methods could improve our ability to predict response of primary breast tumors to neoadjuvant therapy. The goal of this study was to determine if quantitative changes in both DCE- and DW-MRI following a single cycle of chemotherapy can be used to separate patients achieving pathologic complete response (pCR) from non-responders.

METHODS Twenty-eight 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, 11 patients achieved a pCR while 17 patients were non-responders. 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, with two *b*-values (0 and 500 s/mm^2 for 13 patients, 0 and 600 s/mm^2 for 15 patients), TR/TE = 3080 ms/43 ms Δ = 20.7 ms, δ = 11.6 ms and number of signal acquisitions =10 for a total scan time of 4 m and 40 s.

Three pharmacokinetic models were used to estimate K^{trans}, v_e, v_p, k_{ep} ($=K^{trans}/v_e$), and τ_i: the Tofts-Kety (TK), the Extended Tofts-Kety (ETK), and the fast exchange regime (FXR). In this study, we focus on the efflux constant (k_{ep}), as a previous analysis showed that it is the most predictive of the kinetic parameters. The apparent diffusion coefficient (ADC) was calculated from the DW-MRI data. The DW-MRI data of three patients at t_1 were not available, thus, the analysis was performed only on the data from t_2. The mean tumor k_{ep} and ADC at t_2 were calculated. Receiver operating characteristic (ROC) analysis was then performed on both k_{ep} and k_{ep}/ADC to determine if k_{ep}/ADC can improve the diagnostic accuracy. The rationale for using the ratio k_{ep}/ADC is that we hypothesis that k_{ep} will decrease while the ADC will increase if a patient has a positive response to therapy.

RESULTS The table displays the ability of k_{ep}, ADC, and k_{ep}/ADC to predict treatment response after a single cycle of neoadjuvant therapy as summarized by the sensitivity, specificity, positive predictive value (PPV), and area under the curve (AUC). The results show that k_{ep}/ADC yielded higher AUCs for all three models than k_{ep} alone. In particular, using the k_{ep} value returned from the ETK model, the AUC improved from 0.74 (for k_{ep} alone) to 0.82 for k_{ep}/ADC.

Table 1. Diagnostic accuracy of k_{ep}, ADC, and k_{ep}/ADC to predict treatment response after the first cycle of neoadjuvant chemotherapy.

Model	Parameter	Sensitivity	Specificity	PPV	AUC
DW-MRI	ADC	82%	65%	60%	0.80
TK	k_{ep}	91%	59%	59%	0.66
TK	k_{ep}/ADC	82%	76%	69%	0.77
ETK	k_{ep}	82%	65%	60%	0.74
ETK	k_{ep}/ADC	91%	71%	67%	0.82
FXR	k_{ep}	83%	53%	53%	0.63
FXR	k_{ep}/ADC	73%	65%	57%	0.68

DISCUSSION Our results show that the combination of k_{ep} and ADC may improve the ability to predict treatment response following a single cycle of neoadjuvant chemotherapy. To the best of our knowledge, this is the first effort to combine quantitative DCE- and DW-MRI parameters to show that the combination of the two provides a more accurate approach to predict the response of breast tumors to therapy at this very early time point.

CONCLUSION The study indicates that the integration of the DCE- and DW-MRI parameters may have a better ability to predict treatment response than either method alone. Future work includes further investigating a multi-parameter predictive model based on a larger cohort of patients.

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