High spatial resolution DWI for evaluation of breast tumor early treatment response: Association of ADC changes with pCR

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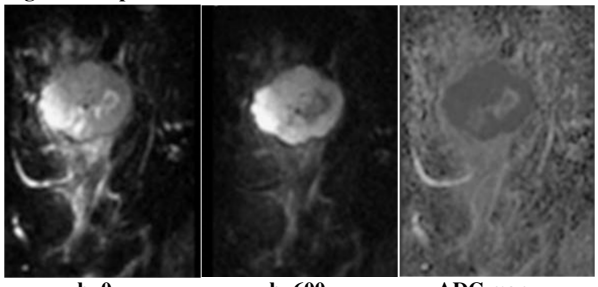
Background: Diffusion-weighted imaging (DWI) provides information about tissue microstructure and has shown promise as a potential biomarker of early treatment response in breast cancer [1,2]. One limitation of single shot echo-planar imaging (ssEPI) DWI is that the spatial resolution is typically much lower than the standard T1-weighted acquisition used for DCE-MRI, which may affect the ability of DWI to detect treatment-related changes. Our group has optimized a high-resolution ssEPI reduced-FOV DWI (HR-DWI) acquisition for breast imaging. The sequence utilizes a 2D spatially-selective echo-planar RF excitation pulse and a 180-degree refocusing pulse to reduce the FOV in the phase-encode (PE) direction [3]. The HR-DWI sequence reduces off resonance effects and has shown improved image quality compared to standard DWI in breast [4]. A preliminary study demonstrated that the lower tumor percentile HR-DWI ADC metrics were more strongly associated with final tumor volume change in breast cancer patients undergoing neoadjuvant chemotherapy [5]. In this work we investigated the association between tumor pathologic complete response (pCR), a clinical measure of tumor response, and early changes in tumor ADC metrics measured with HR-DWI.

Methods: Twenty patients with invasive breast cancer were scanned with HR-DWI before (pre-treatment) and after one cycle (early-treatment) of neoadjuvant taxane based treatment as part of an ongoing IRB approved study at our institution. All patients gave informed consent. Imaging was performed on a 1.5T GE Signa scanner LX (GE Healthcare) using an 8 channel bilateral phased array Sentinelle breast coil (Invivo, Gainesville, FL). HR-DWI acquisition parameters were: TR/TE: 4000ms/64.8ms, FOV: 140x70 mm, matrix: 128x64, NEX: 16, b=0,600 s/mm^2, voxel size: 4.8mm^3. DCE-MRI data were also acquired for all patients at the pre-treatment and early treatment time points. For DWI data analysis, ADC maps were calculated and one tumor region of interest (ROI) was defined on the HR-DWI slice estimated to contain the largest tumor area. Mean tumor ADC as well as 5th, 15th, 25th, 50th, 75th, and 95th percentile ADCs were calculated and evaluated as predictors of pCR. DCE-MRI measured tumor volume change between the pre-treatment MRI and early treatment MRI was similarly evaluated for comparison. The association between early change predictors (HR-DWI ADC metrics and tumor volume) and pCR was evaluated using receiver operating characteristic analysis to obtain the area under the curve (AUC) for the full cohort of patients, and also for the subset of 14 patients that were both hormone receptor positive (HR+) and human epidermal growth factor receptor 2 negative (HER2-). Triple negative (HR-, HER2-) and HR-HER2+ tumor subtype subsets were not evaluated due to limited sample sizes in those groups.

Results: Figure 1 shows representative high-resolution diffusion weighted images acquired at baseline for a patient with a large invasive breast cancer. Table 1 shows the AUCs for the early HR-DWI ADC predictors and tumor volume change predictor for the full cohort and the HR+/HER2- subset. For early percent change in tumor ADC a trend of increasing AUC with decreasing percentile ADC was observed, suggesting that early change in tumor lower ADC percentiles have better associations with pCR outcome than tumor mean or higher percentile ADCs. Additionally, at the early treatment time point the AUCs for the lower percentile tumor ADC were higher than for the early tumor volume change. These effects were stronger when only the HR+/HER2- subset was considered.

Figure 1: Representative HR-DWI



b=0 b=600 ADC map

Table 1

Early Treatment Change	full cohort (n=20)	HR+, HER2- (n=14)
ADC Predictors	**AUC**	**AUC**
% Change Mean ADC	0.61	0.55
% Change 5th percentile	0.67	0.75
% Change 15th percentile	0.67	0.70
% Change 25th percentile	0.65	0.65
% Change 50th percentile	0.65	0.60
% Change 75th percentile	0.59	0.55
% Change 95th percentile	0.57	0.55
MRI Tumor Volume Predictor	**AUC**	**AUC**
% Chng Tumor Volume	0.59	0.40

Discussion and Conclusions: Early treatment changes in tumor lower percentile HR-DWI ADCs were most strongly associated with pCR, a clinically relevant treatment outcome measure. This work expands upon and is consistent with a preliminary study of HR-DWI in breast cancer that suggested that lower percentile tumor ADC values might be more sensitive to early treatment changes [5]. The higher AUCs found for early changes in ADC metrics versus early tumor volume suggest that HR-DWI may be of value in evaluating early breast tumor response to neoadjuvant chemotherapy. These results also suggest that characterization of early change in breast tumor ADC metrics may be affected by the tumor genetic subtype. Studies are ongoing to evaluate the ability of HR-DWI to predict clinical outcome in a larger population.

References: [1] Pickles MD et al, Magn Reson Imaging, 2006 [2] Nilsen L et al, Acta Oncol, 2010 [3] Saritas EU et al, Magn Reson Med, 2008 [4] Singer L et al, Academ Radiol (2011) [5] Wilmes LJ et al, Academ Radiol (2013)
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