DIFFUSION-WEIGHTED MRI FOR THE EARLY RESPONSE ASSESSMENT OF NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER: DOES PERFUSION EFFECT INFLUENCE ADC MAP ACCURACY?

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Target Audience
We intend for this to be useful for clinical radiologists and MR physicists with an interest in the field of diffusion-weighted MR imaging in breast cancer.

Purpose
Diffusion-weighted MR imaging (DWI) has shown promise in demonstrating early treatment response in patients receiving neoadjuvant chemotherapy (NACT) for breast cancer. Perfusion may confound accuracy of the apparent diffusion coefficient (ADC) value when DWI is acquired with low-diffusion b-values, although it has been suggested that acquiring DWI after contrast-enhanced sequences (CE-MRI) may suppress this effect. Here, we explore this in the context of early response assessment to NACT, by comparing tumour size changes and ADC values with appropriate selection of diffusion b-values to include/exclude perfusion effects.

Methods
Breast MRI scans were reviewed from patients receiving NACT between October 2008 and January 2012. Patients underwent imaging pre-, mid- (at around three months, after three or four cycles of NACT) and post-treatment (at around six months, after six to eight cycles of NACT and just prior to surgery) on Avanto and Aera 1.5T MRI systems (Siemens, Erlangen, Germany). DWI was acquired with a free-breath single-shot fat-suppressed (SPAIR) echo planar sequence with b-values of 0, 100 and 800 s/mm² in three orthogonal directions after a 9-minute CE-MRI sequence. Two ADC maps were calculated using an ADC map plugin within OsiriX; ADC_{0,100} from b-values 0 and 800 s/mm² (incorporating potential perfusion) and ADC_{100,800} from b-values 100 and 800 s/mm² (excluding potential perfusion). Regions of interest (ROIs), verified by a consultant radiologist, were defined around the largest area of homogeneity in the whole tumour at its largest diameter on T1 contrast-enhanced images, avoiding necrotic/cystic areas and the MRI-compatible coil artifact. ROIs were transferred to the ADC maps and the mean ADC values were measured. Pre to mid NACT changes in mean ADC values and tumour size were compared with eventual radiological response/non-response, defined as >50% reduction in tumour long-axis diameter between pre and post-NACT scans, using a Mann-Whitney U test in IBM SPSS (version 20). Receiver operating characteristic (ROC) curves were calculated for each early response measurement and compared using Vassar Stats.

Results
Of the 34 patients (mean age 47.6 years) who underwent MRI scans between these dates, 4 were excluded due to complete radiological response by mid-treatment. Of those remaining, 23 were responders and 7 were non-responders. Pre to mid NACT changes in the mean values for both ADC_{0,100} and ADC_{100,800} were strongly significant between responders/non-responders (p=0.003 and p=0.001 respectively), whereas pre to mid NACT changes in long-axis measurement only just reached significance (p=0.042). ROC area-under-curve values for long axis measurement, ADC_{0,100} and ADC_{100,800} were 0.652, 0.863 and 0.882 respectively. When compared to long axis measurement the ROC curve for ADC_{0,100} just failed to reach significance (p=0.055), whereas the ROC curve for ADC_{100,800} was significantly better than the long axis measurement (p=0.038).

Discussion
DWI offered a more accurate early response assessment to NACT than long axis measurements in these patients, in line with previous studies. Despite reports that residual contrast agent suppression may improve slightly the performance of the fitted ADC value, even when DWI is acquired after CE-MRI, results here suggest increasing the minimum b-value to avoid perfusion effects may have a small benefit. Limitations of this work include a relatively small sample size, particularly the number of non-responders, and the subjective definition of ROIs to avoid areas of tumour heterogeneity. Increasing tumour heterogeneity during the treatment cycle was also problematic, as our method of ROI generation became increasingly challenging with eventual radiological response/non-response, defined as >50% reduction in tumour long-axis diameter between pre and post-NACT scans, using a Mann-Whitney U test in IBM SPSS (version 20). Receiver operating characteristic (ROC) curves were calculated for each early response measurement and compared using Vassar Stats.

Conclusion
DWI offers a better early response assessment to NACT in breast cancer than tumour size changes. Removing potential perfusion effects by utilising a low b-value of at least 100 s/mm² may improve slightly the performance of the fitted ADC value, even when DWI is acquired after CE-MRI.

References