MRI Functional Parameters in Breast Cancer:T2*, ADC and Contrast Agent Uptake

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Purpose: Dynamic Contrast Enhanced (DCE) and diffusion-weighted imaging (DWI) of the breast are widely accepted as powerful clinical tools in cancer screening, staging and treatment management. However, the value of functional MRI parameters in predicting treatment response remains sub-optimal (1). In recent years, T2* relaxation time has been proposed as an imaging biomarker to evaluate intra-tumoural hypoxia associated with tumour aggressiveness and response to therapy (2,3). In this study, we explore the relationship between T2* and other functional parameters in DWI and DCE of the breast in order to advance the understanding of clinical role of this biomarker.

Methods: Ten breast patients with histologically confirmed breast tumours were examined at 3T (Magnetom Skyra, Siemens Healthcare, Erlangen, Germany) prior to treatment. The MRI protocol includes: i) Diffusion-weighted imaging (DWI) (TR/TE=8900ms/87ms, b-values=50, 900s/mm^2, voxel size=1.16x1.16x4mm^3), ii) 10-echo gradient-echo sequence (TR/TE=2500ms/4.92ms, echo spacing=4.92ms, voxel size=0.85x0.85x4mm^3) matching the DWI slices, and iii) a dynamic series of 7 (3D fat-suppressed T1-weighted gradient-echo sequences (DCE-MRI) (TR/TE=5.07ms/1.68ms, FA=18deg, voxel size=0.88x0.88x1mm^3). This work was approved by the Ethics Committee.
T2* and Apparent Diffusion Coefficient (ADC) maps were calculated on a pixel-by-pixel basis using in-house software. Images were registered using a rigid body registration technique (in-house software, IDL 8.2, Bolder, USA). Each tumour was outlined on a single slice comprising lesion's maximum cross section, using DCE-MRI images showing peak tumour enhancement. Signal intensity on the pre and peak contrast images was measured and relative Enhancement Factor (rEF) was calculated according to the formula: $[(SI_{peak\text{-}contrast}\text{-}SI_{pre\text{-}contrast})/SI_{pre\text{-}contrast}]x100$. Values of T2*, ADC and rEF were recorded pixel-by-pixel for each tumour and Kendall's tau rank correlation coefficient was used to analyse the correlation between T2* and the ADC and rEF metrics. A two-tailed *p-value* <0.05 was taken to be significant.

Results: Considering the 10 patients investigated, the largest cross-section of the tumours contained 247 ± 176 pixels (mean ± standard deviation, range 49 to 580 pixels), and a total of 2470 pixels. Tumours comprised: 1 grade I invasive ductal carcinoma (P8), 4 grade II invasive ductal carcinomas (P1, P2, P7, P10), 2 grade II invasive lobular carcinomas (P5, P6), 3 grade III invasive ductal carcinomas (P3, P4, P9).
Considering the patients individually, significant correlations were found between T2* and ADC for 8 patients, 5 of them positive correlations and 3 inverse correlations (Figure 1a). There was less inter-subject variability in correlations between T2* and rEF: in 8/10 patients these two parameters were positively correlated (Figure 1b). In one patient (P5), no correlations between T2* and the other functional parameters was found. Large inter-subject variability was also observed in correlations between ADC and rEF (Figure 1c).
Considering all pixels from all lesions globally, T2* values and ADC values are weakly but significantly correlated (tau=0.12, p-value<0.001), however the correlation between T2* and rEF is not significant (tau=-0.038, p-value=0.05). A weak but significant correlation was also demonstrated for rEF and ADC values (tau=-0.16, p-value<0.001), suggesting that these parameters are also weakly associated. Figure 1d-e-f shows the mean values of ADC, T2* and rEF and the standard deviation for all 10 cases; substantial variations of the functional parameters occur within tumours. Figure 2 shows different relationships between functional parameters in different lesions (patients P3 and P7).

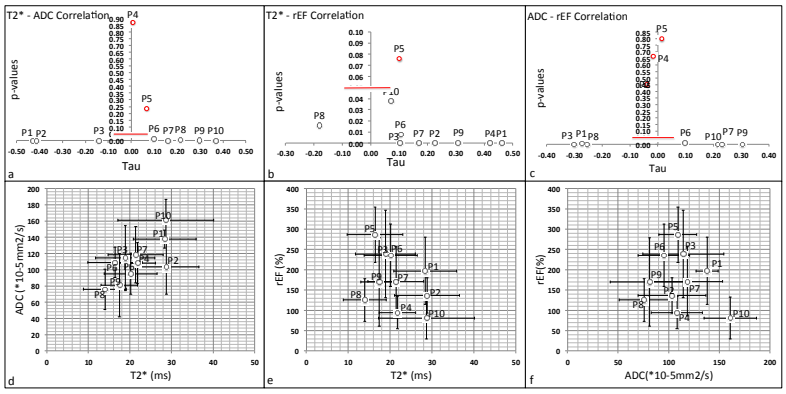

Figure 1: P-values as a function of Tau showing the correlation between T2*-ADC (a), T2*-rEF (b) and ADC-rEF (c). (d,e,f) Mean T2*, ADC and rEF with their corresponding SDs show substantial variability of the functional parameters within tumours.

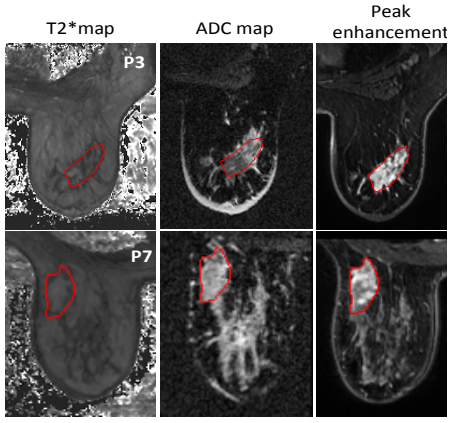

Figure 2: T2* map, ADC map and peak enhancement image of two subjects (P3, P7) with grade III and grade II invasive ductal carcinomas respectively. Intra-tumoural variations for all parameters are observed. Negative and positive correlations between T2*-ADC for P3 and P7 respectively and positive correlations between T2*-peak enhancement are seen for both subjects.

Discussion: McPhail et al. found lower R2* values to be associated with hypoxia and fibrosing in animal models of breast cancer (2) but Li et al. found R2* values to be poor predictors of clinical response to neoadjuvant chemotherapy in breast lesions (3). In their work, they considered tumours in their totality, and did not account for regional variations. In this work we demonstrated a trend for a local rise in T2* in areas of contrast-enhancement. Although this result is in broad agreement with the inverse correlation between the area under the CA concentration curve and R2* described by Li et al (3), this relationship is only present when each tumour is considered individually. In fact the tumours with highest enhancement (P5, P6, P3) present relatively low values of T2* and no more than a weak positive correlation between T2* and rEF values. The highest T2* values (P1, P2, P10), associated with high ADC and low rEF, are low grade tumours (grade II invasive ductal carcinoma). This suggests T2* is affected by many other parameters beyond the presence of de-oxyhaemoglobin in blood. We also demonstrated considerable variability in the association between T2* and ADC for breast lesions in this small patient population, suggesting these are independent parameters.
Analysis of the correlation between functional parameters may be affected by image distortion, registration algorithms, and possible correlations between the characteristics of different pixels within the same image, but is nevertheless an important tool to probe tumour heterogeneity. Only a larger study, appropriately powered, can provide information on the predictive power of T2* (R2*) measurements. Our study shows however that the relationship between T2* and other functional parameters differs within this small patient population, and may prove to be an independent biomarker, thus deserving further investigation.

References:

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