An investigation of histological and DCE-MRI correlates of intrinsic susceptibility contrast relaxivity (R_2*) in human breast cancer

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Introduction

Intrinsic susceptibility contrast (R_2*) yields unique quantitative image contrast in visceral tumours whose imaging correlates are relatively underexplored. Theoretically, R_2* is related to blood oxygenation, blood volume, blood haematocrit and other physical and physiological parameters (Howe). This study aims to assess the dynamic contrast enhanced MRI (DCE-MRI) correlates of breast cancer T_2* relaxivity (R_2*).

Methods

23 untreated patients with solid, non-necrotic and non-infiltrating invasive ductal carcinoma were imaged. This subgroup was chosen because in infiltrating/septal spreading disease, intact breast septae can cause increases in R_2* and necrosis causes a paradoxical decrease in R_2* [1]. A spoiled multiple gradient echo T_2*w sequence (TE 5-75ms, TR 100ms, α=40°, sl 8mm, 256^2 matrix, single slice) was used to acquire data for R_2* calculation (performed using an IDL® least-squares fitting routine). Following this, a T_1w DCE-MRI sequence with 0.1mmol/kg Gd-DTPA dose (4 slices with one matched to the R_2* position, TE 4.7ms, TR 11ms, α=35°, 256^2 matrix) and a T_2*w DCE-MRI sequence with a 0.2mmol/kg Gd-DTPA dose (single slice, TE 20ms, TR 30ms, α=40°, 128^2 matrix) were run. T_1w DCE-MR images were processed using MRIW software and the Tofts' model[2] (Institute of Cancer Research, London) to give quantitative and semi-quantitative parametric maps: K^{trans}, k_{ep}, v_e, maximum Gd concentration (MaxGd), maximum amplitude (MaxAmp), mean gradient and washout gradient. A gamma-variate fit was performed on the T_2*w DCE-MR images to give relative blood volume rBV, relative blood flow rBF and mean transit time MTT. Regions of interest (ROI) were drawn around the tumour on the MR images. Median values for each parameter were recorded.

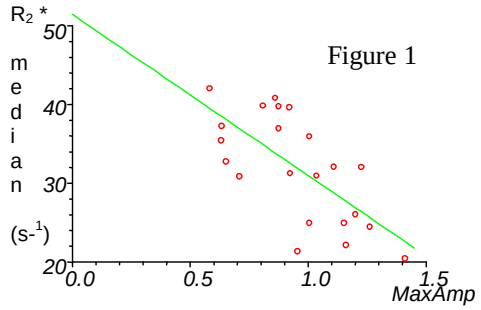

Figure 1

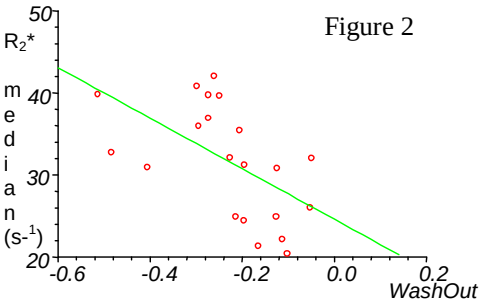

Figure 2

N=23	Median R_2*	95th centile R_2*
Pathology		
CA-IX (+/-)		
Tumour grade	**P=0.015**	**0.0001**
MRI Morphology		
Size		
T_1W DCE-MRI		
Mean Gradient		
Max Amp	**0.0004 (r = -0.684)**	**0.002 (r = -0.624)**
Wash-out	**0.008 (r = -0.56)**	**0.02 (r = -0.52)**
Modelling Failures		
K^{trans}		
v_e		
Max Gd		
Rate Constant k_{ep}		
T_2* DCE-MRI		
rBV	**0.003 (r = -0.6)**	**0.03 (r = -0.46)**
rBF	**0.003 (r = -0.6)**	**0.03 (r = -0.5)**
MTT		
Only significant correlations are shown		

Histological variables (CA-IX staining and tumour grade) were acquired from biopsies or surgical specimens.

Univariate analyses were carried out, dividing histological features from morphology and DCE-MRI kinetics. Correlates were first sorted with median R_2* and if significant, then with 95th centile R_2* values. Continuous variables (all MRI parameters) were analysed with linear regression and discrete variables (histological grade) with a 2-tailed Mann-Whitney test set with a significant value set at $p<0.01$. Multivariate analyses were then carried out on the most significant variables from the univariate analysis.

Results

Significant results are given in the Table. With univariate analysis, a significant negative correlation was found between median R_2* and tumour grade (p=0.015: R_2* 95th centile p=0.0001). Significant inverse correlations were found between median R_2* and rBV and rBF (p=0.003, 95th centile p=0.03 for both), Maximum amplitude (p=0.0004: figure 1, R_2* 95th centile p=0.002) and washout gradient (p=0.008: figure 2, R_2* 95th centile p=0.02). On multivariate analysis, MaxAmp and wash-out were the only significantly correlated parameters (p = 0.0079 and 0.0006 respectively).

Discussion

There is a strong but inverse association between tumour grade and R_2*. This is a potentially a very useful result since in general, MR imaging does not predict histological tumour grade in breast cancer. The inverse correlations between R_2* and MaxAmp and washout as well as blood volume and flow strongly indicate that the R_2* contrast is dominated by blood volume, blood flow and capillary permeability. The multivariate analysis shows that as explanatory variables, the maximum amplitude and wash-out are dominant.

References

[1] Taylor, N.J *et al.*,*Proc. I.S.M.R.M. 10th Ann. Meet. 2002* p2126

[2]Tofts, PS and Kermode, AG. *JMRI* 1997;7:91