Utility of pre-treatment MR derived vascular, shape and texture parameters in the prediction of response to neoadjuvant chemotherapy in a cohort of breast cancer patients

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Introduction Predictive biomarkers of treatment response are currently being sought to allow individualised treatment strategies. Imaging features such as shape (round, irregular), enhancement (homogeneous, heterogeneous), and kinetic curve assessment (persistent, plateau and washout) have been used to aid in the classification of breast lesions (ACR BI-RADS MRI Lexicon). These same features may also help to highlight those patients who are likely to be poorer responders to their initial treatment. The aim of this work was to determine if there were any associations between pre-treatment MR derived quantitative descriptors (shape, enhancement and kinetic curve assessment) and response to neoadjuvant chemotherapy (NAC).

Methods Patients were scanned prior to NAC on a 3.0T HDx scanner (GE Healthcare). In each case a 3D dynamic dataset was acquired utilising VIBRANT. Shape, texture and model free vascular kinetics (empirical) parameters were acquired. Semi-automated ROI's were generated on each slice that demonstrated malignant tissue throughout the breast from an early arterial phase. Texture and shape analysis were undertaken purely from this early arterial phase. For the texture analysis multiple 2D datasets were averaged to provide a pseudo 3D analysis. This averaging approach was felt to be unsuitable for shape analysis, consequently, a 2D approach was adopted whereby only the ROI with the largest cross sectional area was interrogated. For kinetic analysis the signal intensities from the individual ROI's were averaged for each individual temporal phase prior to analysis. Following NAC patients underwent either mastectomy or wide local excision followed by histopathological analysis. Patients were dichotomised according to treatment response (complete response or residual disease). To determine which lesion descriptor, or combination of, best predicted eventual treatment response parameters were entered into a logistic regression analysis model (LRA). As a comparator clinical data (histological grade, histological type, hormonal status, HER2 status, tumour size, age) were also entered into the LRA model. Model performance was assessed via summary statistics and ROC analysis.

Results All data, both MR and clinical, was available in 73 patients. Following histopathological analysis residual disease was identified in 64 patients while 9 patients had had a complete response. Model prediction, histological results, TP, FP, TN, FN rates, summary statistics and ROC AUC results for the various LRA models and the number of variables within those models are presented in Table I. As can be seen from Table I poor model performance was noted when clinical (9 FP), vascular (8FP), texture (8FP, 3FN) and shape (6FP) parameters were used in isolation. However, the model prediction accuracy improves when the parameters are combined [vascular (final slope, AUC@30sec), texture (f2, f5), shape (none), clinical (ER status)] resulting in only 2FP cases. Nevertheless this model with 5 variables seems over parameterised. Ideally for the 9 complete responders noted the maximum number of variables in the model should be no more than 3. Consequently, a reduced model was developed by omitting the vascular parameters at the expense of increasing the number of FP cases to 3.

LRA model (variables in model)	Model prediction	Histopathology +ve	Histopathology -ve	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)
Clinical (1)	+ve	64	9	100% (92.9 – 100)	0% (0 – 37.1)	0.835 (0.700-0.970)
	-ve	0	0			
Vascular (2)	+ve	64	8	100% (92.9 – 100)	11% (5.8 – 49.3)	0.767 (0.634-0.901)
	-ve	0	1			
Texture (6)	+ve	61	8	95.3% (86.0 – 98.8)	11% (5.8 – 49.3)	0.873 (0.781-0.966)
	-ve	3	1			
Shape (2)	+ve	64	6	100% (92.9 – 100)	33.3% (9.0 – 69.1)	0.766 (0.584-0.947)
	-ve	0	3			
Vascular, texture, shape (7)	+ve	63	4	98.4% (90.5 – 99.9)	55.6% (22.7 – 84.7)	0.920 (0.834-1.00)
	-ve	1	5			
Vascular, texture, shape, clinical (5)	+ve	64	2	100% (92.9 – 100)	77.8% (40.2 – 96.1)	0.938 (0.839-1.00)
	-ve	0	7			
Vascular, texture, shape, clinical reduced (3)	+ve	64	3	100% (92.9 – 100)	66.7% (30.9 – 91.0)	0.917 (0.787-1.00)
	-ve	0	6			

Conclusions This work has demonstrated that pre NAC clinical data was a poor predictor of eventual treatment response. Further, MR vascular, texture and shape parameters while providing high sensitivity for eventual treatment response had very low specificity. By combining vascular, texture and shape MR parameter with clinical data a LRA model with both high sensitivity and specificity was obtained. However, this model may have been over parameterised and was therefore modified by only including clinical and texture parameter at the expense of a lower specificity. The final LRA model indicated that patients with baseline characteristics of positive ER status and elevated texture parameters f2 (contrast) and f5 (inverse difference moment) are more likely to have residual disease at the end of NAC. If the results of this final LRA model, based purely on pre treatment data, had been used to individualise patients treatments then 64 (87.7%) patients would have been corrected streamed into a more aggressive treatment option, 6 (8.2%) would have been correctly left on the standard treatment and 3 (4.1%) would have been incorrectly exposed to a more aggressive treatment regime.

Future Work Increase this patient treatment response database to establish if pre-treatment MR and clinical parameters can predict eventual response to NAC.

Abbreviations ROC receiver operating characteristic, TP true positive, FP false positive, TN true negative, FN false negative