Dynamic contrast-enhanced MRI in Triple Negative Breast Carcinomas: is there a distinct imaging phenotype?

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Introduction:

Triple negative breast carcinomas are a subset of breast cancers which are oestrogen (ER) and progesterone (PR) receptor negative, and HER2 receptor negative, and for which treatment options are often limited. There is accumulating evidence that TNBC are biologically distinct and are associated with more aggressive clinical and histopathological characteristics [1]. However imaging features of these tumours are relatively underexplored. This study examines DCE-MR (Dynamic contrast enhanced MR) imaging characteristics of these TNBC compared to a traditionally more favourable prognostic group, ER+/ PR+/HER2- breast cancers.

Patients and Methods:

83 women with primary breast cancer (median age 46 years; range, 26-72; T2-4, N0-1, M0) underwent DCE-MRI prior to neoadjuvant chemotherapy and were identified as ER-/PR-/HER2- or ER+/PR+/HER2- from core biopsy specimens. Initial diagnostic T_1-weighted and T_2-weighted MRI sequences were obtained through the centre of the tumour. Proton density-weighted gradient recall echo images were acquired first (TR 350ms, TE 4.7ms, flip angle (α) 6˚) for four slices (three through tumour and one through the contralateral normal breast). Dynamic T_1-weighted images (TR 11ms, TE 4.7ms, α 35˚, 256^2 matrix) were then acquired at the same slice positions as the proton density-weighted images. Intravenous Gd-DTPA 0.1mmol/Kg bw was injected at 4ml/s during the fifth acquisition time point. Dynamic T_2*-weighted images (TR 30ms, TE 20ms, α 40˚, 128^2 matrix, central slice) using 0.2mmol/kg IV Gd-DTPA, were then acquired. Images were analysed using specialist MRI software (MRIW version 4.3, ICR, UK) [2]. DCE-MRI analysis was performed using Toft's pharmacokinetic model [3] and a modified Fritz-Hansen assumed arterial input function. Values for K^{trans} (inflow transfer constant; min^{-1}), v_e (leakage space; %), k_{ep} (outflow rate constant; min^{-1}) and $IAUGC_{60}$ (initial area under the gadolinium time curve over 60 seconds; $mM.s^{-1}$) and rBV (relative blood volume; arbitrary units (AU)), MTT (mean transit time; s) and rBF (relative blood flow; AU) were calculated for whole tumour ROIs. Values for these parameters were compared across receptor status and with other known prognostic variables using the Mann-Whitney U test. ROC (Receiver Operating Characteristic curve) analysis was used to determine the parameter best able to identify the triple negative phenotype.

Results:

37 patients were assessable in total, 16 of whom were ER-/PR-/HER2- and 21 of whom were ER+/PR+/HER2-. 22 patients with other receptor phenotypes were excluded, 12 were unable to undergo MRI, full receptor status was not available in 11 and 1 patient's tumour was not visible on MRI. TNBC comprised 19% of the total study population with a median age of 42.5 yrs (range 34-57) and median tumour size 60mm (range 40-100). In the ER+/PR+/HER2- group, the median age was 49 yrs (range 26-70) and median tumour size 50mm (range 25-150).

Median k_{ep} values were significantly higher in TNBC with lower median values observed for v_e and shorter MTT in TNBC (Table 1).

MRI parameter	ER-/PR-/HER2-	ER+/PR+/HER2-	Significance
K^{trans}	0.19	0.23	p=0.575
v_e	0.33	0.39	p=0.001
k_{ep}	0.70	0.56	p=0.044
$IAUGC_{60}$	12.59	14.17	p=0.596
rBV	215.51	132.96	p=0.533
rBF	5.68	2.98	p=0.252
MTT	44.27	47.69	p=0.007

Table 1

There was no correlation between age and any MRI kinetic parameters. When assessed according to grade, k_{ep} values were higher in high grade BC (0.82 vs 0.51, p=0.019). When stratified according to tumour size and nodal status, values for v_e were lower in larger TNBC (0.33 vs 0.41, p=0.009) and for node negative BC (0.33 vs 0.41, p=0.004). k_{ep} was higher in TNBC but the differences did not reach statistical significance. In node positive BC rBF was higher in TNBC (5.87 vs 1.96, p=0.046) and MTT shorter (43.69 vs 47.28, p=0.008). v_e was the best predictor of triple negativity (sensitivity 81%, specificity 76%, area under ROC curve 0.80).

Discussion:

The increased cellularity and scant stromal content of triple negative breast cancers are depicted by lower values of the DCE-MRI parameter v_e [4]. Furthermore, increased values of k_{ep} reflecting the rapid return of contrast into the vasculature suggests that capillary permeability may also be higher in TNBC [5]. These findings suggest that novel targeted therapies, in particular, those directed at tumour vasculature may be beneficial in patients with triple negative breast carcinomas.

References:

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