

Assessing breast cancer response with DCE-MRI: Are signal intensity/time curves adequate?

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Introduction: Neoadjuvant chemotherapy (NAC) has a long established role in the treatment of locally advanced breast cancer¹. Although most patients respond to NAC, there is a continued need to identify non-responders early on in their treatment, to enable timely changes in treatment to occur. It is well-established that quantitative DCE-MRI parameter changes, in particular K^{trans} , after 2 cycles of therapy can predict for both disease-free and overall survival¹, as well as pathological and clinical response². However, quantitative parameters are not routinely used because they are time-consuming to calculate, requiring expensive software and interpretive expertise. In the clinic, signal intensity-time curve (SITC) analysis is recommended for lesion characterisation, and preliminary data have shown that changes in curve shape are associated with pathological response to NAC³. In this study we evaluated the relationship between SITC shapes and K^{trans} before and after 2 cycles of NAC and the relative ability of SITC shapes and K^{trans} to predict pathological response and long term patient benefits.

Methods: 73 women with breast cancer underwent DCE-MRI before (pre-treatment) and after (post-treatment) two cycles of NAC as part of two prospective studies. MRI was performed with a 1.5T Siemens Symphony scanner (Erlangen, Germany) using a bilateral breast coil. Sagittal proton density-weighted (PDw) GRE images were acquired followed by 40 matched sets of dynamic T1-weighted (T1w) images, 1 set every 12 seconds for a total imaging time of 8 minutes. 0.1mmol/kg Gd-DTPA (Magnevist: Bayer-Schering, Newbury, UK) was injected intravenously using a power injector. The PDw and T1w dynamic series of images were analyzed using MR Imaging Workbench software (v4.3; Institute of Cancer Research, London, UK)⁴ with whole tumour regions of interest drawn on T1-w subtraction images. Quantitative DCE-MRI analysis was performed using the Tofts model⁵ employing a modified Fritz-Hansen arterial input function^{6,7}. Median transfer constant (K^{trans} , min^{-1}) values were calculated for each voxel within ROIs of up to 3 tumour slices. Signal intensity time curves (SITC) of the central tumour slice were created and scored by two radiologists in consensus employing a published 1-5 point scheme⁸ (Fig 1). Pathological response at the end of chemotherapy was assessed by examination of surgical excision specimens.

The primary outcome variables were central MRI slice SITC shape and change in shape in response to NAC. Correlations between SITC shape and K^{trans} values were undertaken using multinomial regression. χ^2 testing was used to assess curve shapes and curve shape changes in their ability to predict pathological outcome (pathological response (pR) and pathological complete response (pCR) rates). Survival curves were estimated using the Kaplan-Meier method and significance determined using log rank tests for both disease-free and overall survival (DFS & OS).

Results: At baseline the majority of patients had a curve shape of 4 or 5 ($n = 28$ and $n=17$ respectively). 37 of the 58 evaluable patients (64%) had changes in SITC shape after 2 cycles of NAC of which 35 had decreased. Of those who had a decrease, 15 (43%) had a change of 1 point and 20 (57%) had decreases of >1. Curve types were significantly associated with K^{trans} values at baseline ($\chi^2 = 43.3$, $p = 0.000$) and after two cycles of NAC ($\chi^2 = 60.5$, $p = 0.000$). Changes in curve type and K^{trans} were significantly associated ($\chi^2 = 53.5$, $p = 0.000$). Baseline SITC shape correlated with pCR rate ($p=0.029$); tumours with curve shape 5 were more likely to obtain pCR (29%) compared to those with curve shape 3 (fast wash-in only: 8%). The post 2 NAC cycles SITC shape was also associated with pR rate ($p=0.02$); curve shapes of 3-5 were less likely to go onto develop pR (9%) compared with curve shape 2 (slow wash-in only: pR rate = 27%). Changes in curve shape of >1 point were likely to develop pathological and clinical response ($p=0.005$); a 50% pCR rate was seen amongst those who had a decreased curve shape of 3.

Overall survival (Fig. 2) was significantly greater for reductions in curve shape >1 point ($p = 0.048$) but did not show a significant difference to those who had reductions in curve shape of only one point ($p = 0.47$). DFS was not associated with curve shape changes. Correspondingly, changes in K^{trans} also showed significant differences in OS ($p = 0.029$) but not in DFS ($p = 0.13$).

Discussion: Real world barriers have impeded the adoption of quantitative DCE-MRI to assess the therapy effectiveness of neoadjuvant chemotherapy for locally advanced breast cancer. Radiologists already use signal intensity-time curve shapes for characterising breast lesions: this study shows that SITC are highly correlated to an important DCE-MRI parameter (K^{trans}) before and after 2 cycles of chemotherapy, and that SITC shape and K^{trans} changes are also highly correlated. Furthermore, both baseline and changes in SITC shapes can predict the probability of pathological benefit as well as patient survival. Whilst quantitative DCE-MRI parameters remain the optimal standard, the easier to use signal intensity time curves may have wider clinical applications.

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