Correlation of dynamic contrast-enhanced MRI parameters and clinical outcome for locally advanced breast cancer patients

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Introduction

Patients with locally advanced breast cancer are preferably managed with neoadjuvant chemotherapy (NAC) to decrease the tumour size and increase the possibility for breast conservation surgery. A proportion (60-70%) of patients receiving such treatment will respond, although only about 35% classified as complete and partial responders (1, 2). The rest will have a worse outcome, and should be identified as early as possible. The value of dynamic contrast-enhanced (DCE) MRI for prediction of the efficiency of neoadjuvant chemotherapy on clinical outcome has not been fully assessed. The purpose of this study was therefore to evaluate the DCE-MRI characterization of locally advanced breast cancer prior to and after treatment, and correlate these characteristics to the clinical status of the patients 5 years after neoadjuvant chemotherapy.

Experimental

This study included 24 women with locally advanced breast cancer scheduled for neoadjuvant chemotherapy. DCE-MR images in the sagittal plane were acquired using a 3D spoiled gradient echo sequence (RF-FAST) with a temporal resolution of 57 sec, using a clinical 1.5T MR system (Picker Inc.). Pixel by pixel analyses were performed to evaluate changes in the distribution of contrast enhancement in the entire tumour volume using in-house IDL based software. The tumour area was determined by tracing all pixels with more than 50% contrast enhancement after 2 min. The relative signal intensity (RSI) distribution histograms were analysed as described by Mayr et al (3). The 10th percentile of RSI from all imaged slices in each tumour was found. Normalized area under the curve (AUC) based on the enhancement curve from last time point before injection and all subsequent time points were also calculated. Multivariate data analyses including Kohonen neural network (KNN) and probabilistic neural network (PNN) were used to predict outcome. KNN was performed based on mean RSI, mean AUC, in addition to the statistical measures for variance, kurtosis and skew for both of these parameters (i.e. total input 8 variables). PNN was performed by selecting the 149 pixels with highest intensities from DCE-MRI (raw time-intensity curves). All pixels were described by 9 time-intensity points, and were related to clinical outcome (5 years survival) in the PNN. Network training was performed by leave-one-out cross validation.

Results and discussion

Nine patients were alive, while 15 patients did not survive five years after neoadjuvant chemotherapy. The patients were divided into responders and non-responders based on the clinically assessed therapy response (RECIST). This grouping showed no correlation to survival (Fig.1A). When dividing the patients into responders/non-responders based on MRI determined change in tumour volume during treatment, no distinct difference was seen (Fig. 1B). However, when focusing on the result from PNN of the DCE-MRI results before NAC (Fig.1C) the prediction of survival is highly significant ($p<0,001$). This finding indicates the importance of developing robust statistical analyses for DCE-MRI data, in order to interpret the correlation to clinical outcome. Although the result is somewhat dependent on the ROI selection criteria and the threshold (% correct pixels/patient) one wishes to choose for a correct prediction, the approach yields consistent results. Fig. 2 demonstrates the distribution of patient groups (alive or dead 5 years after NAC) based on the unsupervised Kohonen network analyses of DCE-derived parameters obtained before start of NAC.

Conclusion No correlation between simple RSI or AUC analyses of DCE-MRI data and clinical outcome for the breast cancer patients was found. When using the clinical data based on volume reduction measurements, still no correlation appeared related to clinical outcome. However, results from the multivariate data analyses demonstrated that simple statistical measurements of DCE-MRI related parameters may have a correlation with clinical outcome.

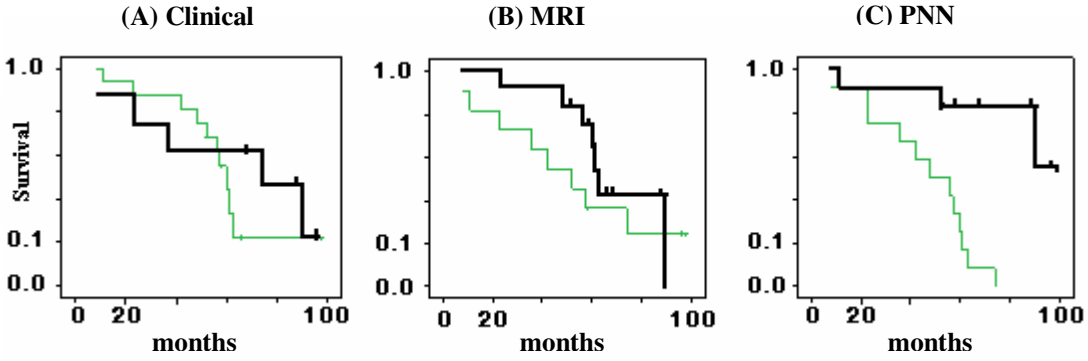

Figure 1: Clinical outcome correlation to overall survival (OS) obtained by Kaplan- Meier diagram. No clear grouping based on the clinical determined response to therapy (A) based on the RECIST criteria (stable and progressive disease (normal line) or complete and partiell response (bold line)), (B) OS curves base on MRI determined tumor volume reduction > 30% (bold line) and ≤ 30% (normal line), and (C) OS curves based on PNN calibration of DCE-MRI results correlated to clinical outcome with dead (normal line) and alive (bold line) patients 5 years after NAC.

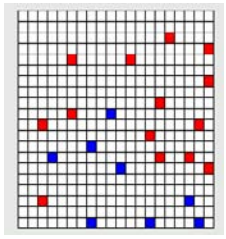

Figure 2: Kohonen neural network analysis of DCE-MRI derived parameters obtained prior to neoadjuvant breast cancer treatment (n=24) illustrates that the patient groups (dead (red) or alive (blue) 5 years after NAC) form distributions related to the statistical variables measured.

References

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