

# Comparison of morphological and functional imaging in tumour response evaluation in patients with locally advanced breast cancer receiving neoadjuvant chemotherapy

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## Purpose

To study the role of clinical examination (CE), morphological imaging [mammography, gray scale ultrasonography (USG) and contrast enhanced magnetic resonance imaging (CE-MRI)] and functional imaging [diffusion-weighted MRI (DW-MRI) and single-voxel in vivo proton MR spectroscopy at 1.5T and color Doppler ultrasonography] in assessing the response to neoadjuvant chemotherapy (NACT) in patients with locally advanced breast cancer (LABC).

## Methods

In a prospective study 25 patients with LABC scheduled for NACT were evaluated using clinical examination and the imaging studies prior to and after 3-4 cycles of chemotherapy. Institute ethics committee approved the study. NACT regimen was Cyclophosphamide, Epirubicin and 5-Fluorouracil (CEF) or Docetaxel and Epirubicin (DE). The tumour response was assessed according to its morphological and functional parameters. Individual imaging tumor responses was compared with histopathological response. Intraclass correlation coefficient (ICC) analysis was used to evaluate the agreement between the residual tumour size predicted by clinical examination and imaging studies and that measured by pathology. Receiver operating characteristic (ROC) curve analysis was used to evaluate the diagnostic accuracy, in terms of predicting pCR and responders. Spearman's rho correlation was used to compare the percentage change of ADC and tCho values and tumour diameter as measured by MRI after chemotherapy. Entire statistical analysis was done using SPSS software. P value < 0.05 was considered significant.

## Results

The mean age was 42.6 years. The mean pre-NACT diameter of tumour by CE, mammography, ultrasonography and MRI was 7.2±2.2, 4.6±2.3, 4.8±2.2 and 5.6±1.9 cm, respectively and post-NACT tumor diameter by CE, mammography, ultrasonography and MRI was 3.5±3.2, 2.8±1.9, 3.3±3.3 and 2.9±2.4 cm, respectively. Seven patients had pathological complete response. The mean diameter of residual tumour was 3.2±3.2 cm on final histology. MRI showed the highest reliability (ICC=0.88) for predicting residual tumour size when compared all other imaging modalities. The mean pre-NACT ADC was 1.15±0.19x10<sup>-3</sup> mm<sup>2</sup>/s and mean post-NACT ADC increased to 1.429±0.247x10<sup>-3</sup> mm<sup>2</sup>/s yielding an significant increase of 24.3% (p=0.004). The mean ADC increase was 37% in responders as compared to 16% in non-responder (p=0.028). The best pre-treatment ADC cut-off with which to differentiate between responders and nonresponders was 1.114x10<sup>-3</sup> mm<sup>2</sup>/s, which yielded a sensitivity and specificity of 67% and 56% respectively. The mean value of pre-NACT total choline (tCho) was 3.56 mmol/ kg, and the mean value of post-NACT tCho was 2.954 mmol/ kg.

There was significant decrease in tCho in patients with pCR (p=0.018) and responders (p=0.008) after chemotherapy. Using ROC analysis cut-off values of 22.9% for tCho were obtained to differentiate between responders from non-responders with a sensitivity and specificity of 100% and 67%. MR spectroscopy and CE-MRI had the highest sensitivity (100%) to predict response to

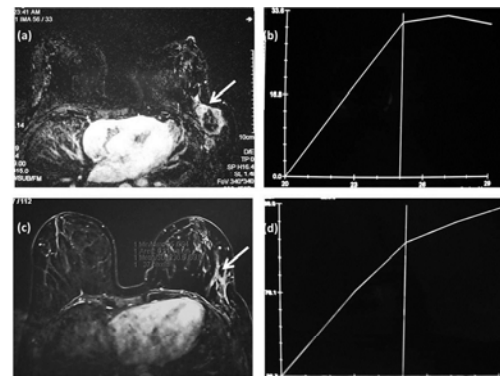


Figure 1: Pre- and post-NACT Contrast-Enhanced fat suppressed subtracted T1W axial sequence MRI of a patient with complete response. (a): Pre-NACT MRI shows 4x4 cm well defined mass involving the axillary tail of left breast (arrow). (b): Pre-NACT MR Time-signal intensity curve shows Type II pattern. (c): Post-NACT MRI shows no definite mass lesion (arrow)(d): Post-NACT Time-signal intensity curve shows Type I pattern.

chemotherapy while colour Doppler (78%) and MR time-signal intensity response (77%) had the maximum specificity to predict response to chemotherapy. Colour Doppler had the highest sensitivity (71%) to predict pCR and MRI had highest specificity (95%) to predict pCR. Figures 1, 2 and 3 show the tumor responses by CE-MRI, MR spectroscopy and DW-MRI, respectively.

## Discussion

Pathological complete response is the ultimate goal for NACT as it strongly correlates with a favourable prognosis. This requires an accurate assessment method to identify the response to NACT as it helps in early recognition of non-responders and thus facilitates an earlier change to a more effective chemotherapy and also give information about type of chemotherapy to given after surgery. Response to NACT can be assessed by clinical examination, mammography, Ultrasonogram (gray and colour Doppler), and MRI and MR spectroscopy. Of the imaging technique we used to measure the tumour response, MRI showed the best overall agreement (kappa=0.64) between the final predicted response and the pathological response. Similar superiority of MRI over these imaging techniques and clinical examination has been reported in literature (1). The best pre-treatment ADC cut-off with which to differentiate between responders and non-responders was 1.11x10<sup>-3</sup> mm<sup>2</sup>/s, which yielded a sensitivity and specificity of 67% and 56%, respectively. A similar report also showed ADC cut-off and but with a higher specificity (71%) and sensitivity (94%) to predict responders. In our study, tCho showed significant decrease after chemotherapy in patients with pCR and responders. Meisamy et al (2) showed changes in tCho concentration after 24 hours of the first dose of primary systemic therapy.

## Conclusion

In patients with LABC undergoing NACT, MRI has the maximum specificity to predict pCR and has highest reliability for predicting residual tumour size. The functional imaging can supplement morphological imaging modalities in predicting tumour responses to chemotherapy and may have a promising role in future in tumour response evaluation.

## Reference

1. Shin HJ, et al. Br J Radiol. 2011 Jul; 84(1003): 612–20; Meisamy S, et al., Radiology. 2005 Aug; 236(2):465–75.

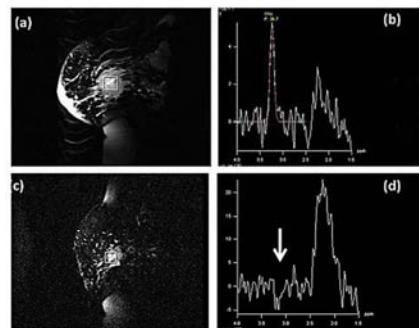


Figure 2: MR spectroscopy of a responder (a-d) and non-responder (e-h). (a&b): Pre-NACT Sagittal contrast-enhanced fat-suppressed MR image (a) of a responder with (b) Single-voxel spectra showing a Cho resonance peak at 3.2 ppm. tCho peak integral was 29.6 arbitrary units (AU). (c&d) Post-NACT sagittal CE-MR image (c) of the above patient with (d) no tCho peak at 3.2 ppm (arrow).

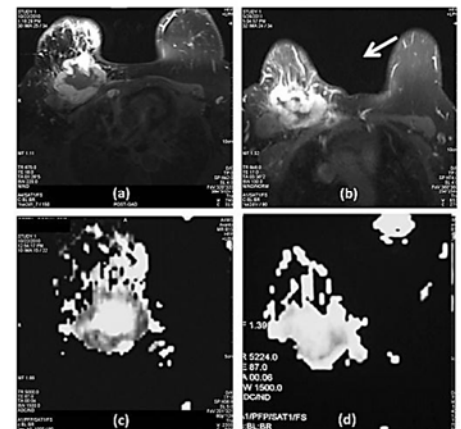


Figure 3: Pre- and post-NACT DW-MRI of a representative patient with breast carcinoma (a): Pre-NACT T1W post-contrast image shows 8x6 cm mass lesion in upper central part of right breast with central necrosis (arrow). (b): Corresponding Pre-NACT ADC map showing restricted diffusion with mean ADC value of 1.438x10(-3) mm(2)/s. (c): Post-NACT T1W post-contrast MRI shows 7x6 cm mass lesion with increase in central necrosis (arrow)(d): Corresponding post-NACT ADC map also shows decrease in area of restricted diffusion with mean ADC value of 1.562x10(-3) mm(2)/s.