Changes of Lesion Morphology and Texture during Neoadjuvant Chemotherapy in Breast Cancer

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Purpose:

Neoadjuvant chemotherapy (NAC) has become increasingly used in treatment of breast cancer. MRI, with its high sensitivity, high spatial-resolution and 3D coverage, has been proven as the optimal modality for response monitoring. We have previously analyzed pre-treatment tumor morphology features using quantitative algorithms, and tried to select classifiers to predict the response. In the current study, we extended the work to analyze the change of features during the course of therapy, and investigated whether the change of some parameters were associated with different response patterns, thus may potential serve as response indicators.

Methods:

38 patients (29-75 yo) enrolled from Jan 2004 to Aug 2006 were included in this study. They received 2-4 cycles of AC followed by the second-line Taxane regimen. All patients received at least 4 MRI examinations, a baseline MRI prior to any treatment (B/L), a follow-up after 1 or 2-cycle of AC (F/U-1), and second follow-up after 4 cycles of AC (F/U-2). For those who were not responding well to AC, they were switched to taxane after 2 AC, and the F/U-2 was after receiving 1 cycle of taxane. After finishing all treatments, patients received a final MRI before surgery. By pooling all the patients together, we investigated the patients' response to AC regimen alone, and the response to the full course treatment. The response to AC was determined by the size reduction measured from the MIPs (Fig.1). The responder was defined as >15% 1-D reduction in F/U-1, or >30% in F/U-2 after 4 AC. After receiving the full treatment protocol, patients received surgery and based on the pathological response, they were categorized into two groups. The Complete Responder (CR) included pCR (pathological complete response) and minimal residual disease with scattered cells or foci, and Partial Responder (PR) as those with bulk residual disease. Of 38 patients, 25 were AC Responders (AC_R), 13 were AC non-responders (AC_NR). Among the AC_R group, 15 reached CR (G1: R_CR), 10 were PR (G2: R_PR); in AC_NR group, 7 achieved CR (G3:NR_CR) and 6 with residual bulk disease (G4: NR_PR). The lesion ROI was analyzed using the fuzzy C-means algorithm, and the results were confirmed by an experienced radiologist. Then 8 morphological features including volume, surface, NRL (Normalized Radial Length) Mean, NRL Entropy, NRL Ratio, Sphericity, Compactness, and Roughness, 10 GLCM texture features and 14 LAWS' texture energy features were obtained to describe the morphology/texture properties for each case.

Results:

For each analyzed feature, the baseline value and the percentage change in follow-ups to the baseline were analyzed. Unpaired t-tests were utilized to compare parameters between groups. Among those 32 features, 'homogeneity' showed consistent changes among responders during the entire treatment course. Fig 1 demonstrates two cases with relatively high/low homogeneity index. Fig.2 shows the group comparison between AC_R and NR. This index was significantly higher in the baseline of AC_R than AC_NR (p=0.008). In the F/U-1, the values in the AC_R group decreased significantly (p=0.002), and that in the AC_NR group increased slightly but not significant. In F/U-2 the values continued to decrease in the AC_R group. The results suggested that a homogeneous lesion is more likely to respond to AC, and shows decreased homogeneity with treatment.

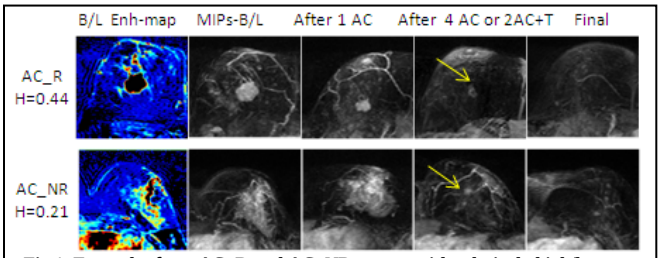

Fig 1. Examples from AC_R and AC_NR groups with relatively high/low homogeneity index. Color-coded enhancement maps and MIPs are shown.

By definition of the response in the AC_R group, the lesion volume decreased in F/U-1 compared to B/L (p=0.02). Three other morphology features (p=0.006-0.013) and five GLCM features (p=0.002-0.008) also showed significant changes with smaller p values. In patients who finished 4 cycles of AC, all 32 features showed significant difference between B/L and F/U-2. Two texture features, gray level difference (p=8E-5) and homogeneity (p=5E-4), were particularly sensitive to therapy-induced changes, showing a great percentage change in F/U compared to B/L with very small p values, suggesting their potential role as response indicators.

When separating all patients into four groups based on AC response and the final pathological response, only those who still had substantial disease in F/U-2 were analyzed. The percentage change between the B/L, F/U-1, and F/U-2 are shown in Fig 3. Interestingly, all patients in G-1 (N=11) showed decreased homogeneity in F/U-1 (mean=19%, range=0-61%) and further decrease in F/U-2 (mean=47%, range=1%-80%). All patients in G-4 (N=6) showed increased homogeneity (mean=38%, range 11%-67%) in F/U-1. When switched to Taxane, the value began to decrease for both G-3 and G-4 suggesting that patients started to respond to the new drug.

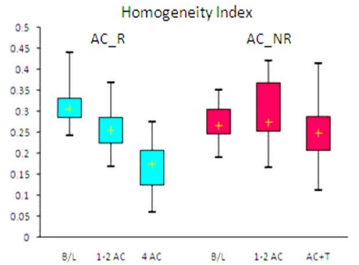

Fig 2. Homogeneity index in AC_R & NR.

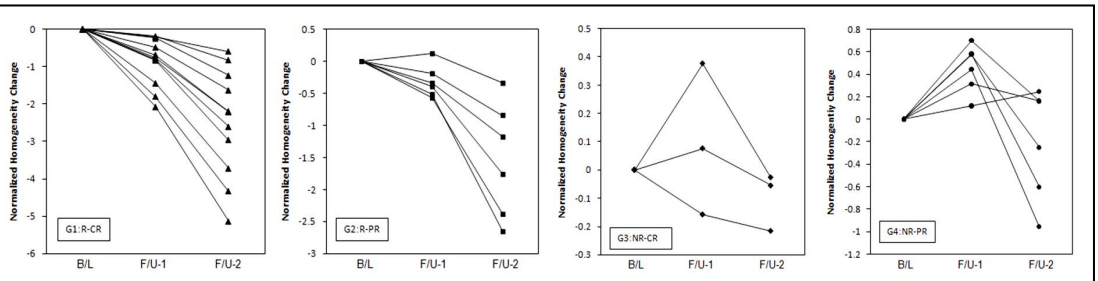

Fig 3. The percentage change of Homogeneity index compared to the baseline in 4 different response groups.

Discussion:

In this study we investigated the change of lesion morphology and texture features during the course of neoadjuvant chemotherapy treatment. The size reduction is the ultimate proof of response. However, some other features might show greater changes compared to the size, thus provide a more sensitive indicator to predict response. Due to complexity of the large data metrics, it was not easy to identify which combination of features, at which follow-up time point, might have the highest predicted value for the final response. We presented the initial evaluation results of each analyzed features individually, only as a single parameter. It was found that for cancers that were responding, the homogeneity index would decrease, and for the non-responders this index would remain at the same level. The results suggested that this feature might be useful to be built into the response prediction classifier. The commonly used RECIST criterion (based on 1-D tumor size reduction) may be subjective and inaccurate, the additional computer extracted information representing other lesion morphology and texture changes may be combined with the size reduction to achieve a higher accuracy in monitoring and predicting neoadjuvant chemotherapy response. As more and more therapeutic agents are available, imaging may provide very useful information to help select an optimal treatment protocol with the least toxicity. There is a wealth of information contained in imaging, and they should be explored. The computer-based morphology and texture analysis of the lesion may be applied to obtain some information objectively and effectively.

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