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Quantitative MR Imaging Features Associated with Pathologic Complete Response to Neoadjuvant Chemotherapy in Breast Cancer Patients.

Jorge E Jimenez[1], Ph.D., Abeer H. Abdelhafez[2], M.D., Joshua P. Yung[1], Ph.D., Nabil A. Elshafeey[2], M.D., Gaiane M. Rauch[2], M.D., John D. Hazle[1], Ph.D.

[1]Department of Imaging Physics, UT MD Anderson Cancer Center, Houston, TX.
[2]Department of Abdominal Imaging, UT MD Anderson Cancer Center, Houston, TX

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Introduction

Neoadjuvant chemotherapy has been established as the standard of care for patients with locally advanced breast cancer[1]. It has been shown that tumor infiltrating lymphocytes (TIL) is highly correlated with response to neoadjuvant chemotherapy[2]. Consequently, TIL is one of the primary markers to help predict a good response to chemotherapy from a bad response[3]. Unfortunately, TIL measurements can suffer from biopsy sampling bias, which can compromise the confidence in the prognosis.

It has recently been demonstrated that tumor imaging characteristics of magnetic resonance imaging (MRI) could also reflect the genetic profile of breast cancers[4]. Therefore, features from computerized texture analysis of breast cancers MR images are expected to be useful in the prediction of therapy response[5].

Finding additional therapy response biomarkers that can improve clinicians' confidence has the potential to dramatically improve patient care.

Aim

Identify quantitative MR imaging features associated with pathologic complete response (pCR) to neoadjuvant chemotherapy (NACT) to potentially improve prediction of treatment response in breast cancer patients.

Method

This IRB approved retrospective study included 72 biopsy-proven HER 2 positive and triple negative (TN) breast cancer patients. Patients who received NACT, had pretreatment dynamic contrast enhanced (DCE) MRI and pretreatment biopsy-based pathological assessment of the tumor infiltrating lymphocytes (TIL) were included in the study. Patients were classified into pCR, and non-pCR groups based on post-operative pathology, where pCR was defined as absence of residual invasive component in tumor bed. DCE-MR images were obtained from a variety of GE and Siemens platforms. Lesion segmentation and image feature subtraction was done using FDA approved software QuantX.

Feature analysis was done using MATLAB. We first evaluated the Pearson linear correlation between individual imaging features and the pCR classifier. Next, we used minimum redundancy maximum relevance (MRMR) and binary decision trees to rank the importance of the remaining features. Finally, we linearly combined the top five imaging features into a single imaging signature number.

Method

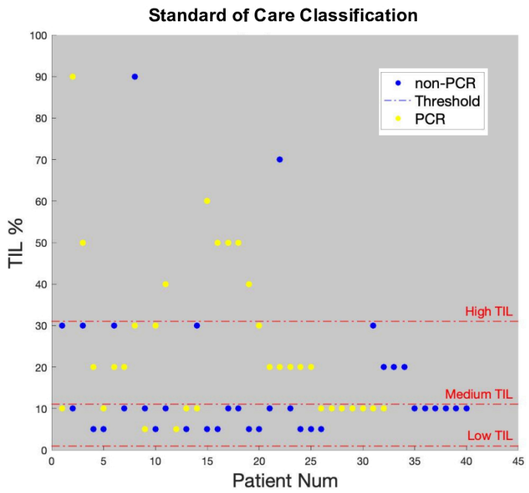

Figure 1 *Graphical visualization of TIL Population distribution based standard of care classification scheme: Low TIL (0-10%), Medium TIL (11-30%) and Hight TIL (>30%). Biopsy bias is attribute to the discrepancy between pCR and High TIL.*

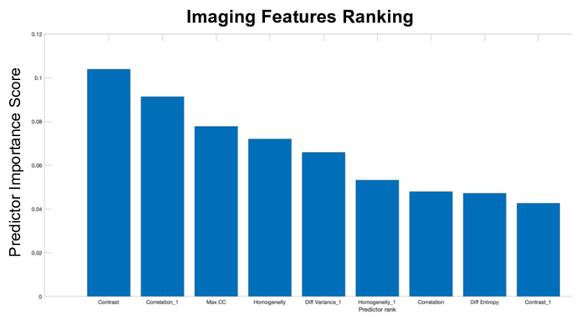

Figure 2 *We found 26 statistically significant quantitative imaging features out of the 145 subtracted features. The top 5 most relevant imaging features were: Contrast, Correlation, Maximal Correlation Coefficient, Homogeneity, and Difference Variance.*

Results

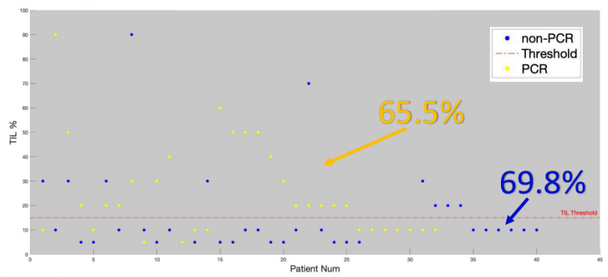

Figure 3 *TIL results scatter plot showing all lesions and their corresponding (tumor infiltrating lymphocytes) TIL percentage. A threshold of 15% was used to differentiate between high and low TIL. Standard of care predicts high TIL as pCR and low TIL as non-pCR. This model provides accuracy of 65.5% for pCR and 69.8% for non-pCR.*

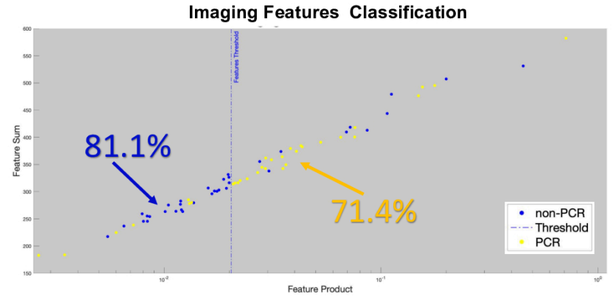

Figure 4 *Visualization of image classification model using the five most relevant imaging features. This model provides accuracy of 71.4% for (pathologic Complete Response) pCR and 81.1% for non-pCR.*

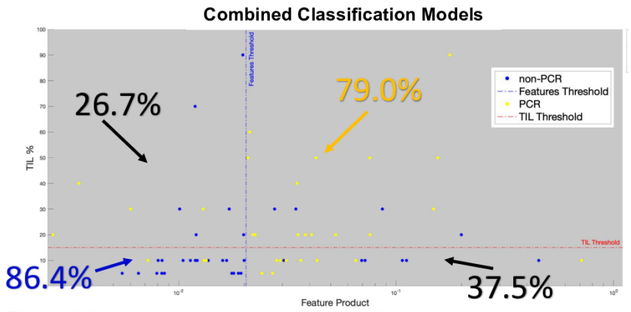

Figure 5 *Combined scatter plot of imaging features and pathology results. Lower left quadrant shows patients who are expected to have non-pCR in both models. Top right quadrant shows patients who are expected to have pCR in both models. Remaining quadrants shows areas where patients are expected to have pCR by at least one model. The combined model provides accuracy of 79.0% for pCR and 86.4% for non-pCR.*

Discussion

Image based features have the potential to provide additional information in the pathologic report. The results of our study showed that imaging features are independently associated with pCR in breast cancer. The more statistically significant biomarker matches recent literature findings, particularly: homogeneity and contrast.

Even though we were able to generate a classification model using five imaging features, definite selection of features requires further analysis. It is important to take into consideration that no population differentiation between HER 2 positive and triple negative cases were made. It is expected that predictor importance scores would change within a single cancer type. However, we currently do not have a large enough sample size to make statistically significant conclusions at a sub-cancer level.

A judicious selection of imaging features in combination with an appropriate regression model could further improve prognosis accuracy. Furthermore, adding more than five features to a model could also increase the classification robustness. Lastly, more sophisticated classification algorithms such as Naive Bayes, decision tress, support vector machine, etc. could also be used to develop better models.

Image feature analysis could become a powerful tool in breast cancer NACT prognosis at the cost of little computing time of the already acquired MR images.

Conclusions

Our study showed that quantitative imaging features can produce similar classification accuracy to pathologic information from biopsy. Combining the imaging features with pathology information could improve prognostic prediction confidence for NAC treatment response in breast cancer patients.

References

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