Single MIP Image Evaluation for Predicting Pathologic Response in Patients Receiving Combination Neoadjuvant Immunotherapy/Chemotherapy: A Reader Study

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Introduction

Breast Magnetic Resonance Imaging (MRI) is the most accurate and reliable imaging modality for breast tumor analysis prior to and following neoadjuvant therapy (NAT).[1] Its ability to evaluate breast cancers based on angiogenesis-related contrast enhancement is a key factor in its higher accuracy compared with mammography and sonography.[2] However, traditional MRI evaluation, which is primarily reliant on volumetric measurement changes, still has limitations in predicting NAT response. Pooled sensitivities range 0.65-0.91, while specificities range 0.81-0.88.[3] Additionally, most studies use MRI complete response (mCR) for prediction of pathologic complete response (pCR) with moderate accuracies in the 70-80% range.[4-7] In contrast, data on breast MRI for predicting neoadjuvant immunotherapy response (NAI) is limited with studies often relying on experimental quantitative methods.[8-11] Given the potential for confounding inflammatory effects related to immunotherapy, we hypothesized that breast MRI might have decreased accuracy in predicting pCR. To test this, we pooled the results of four combination neoadjuvant immunotherapy/chemotherapy (NAIC) trials at our institution to evaluate the diagnostic accuracy of mCR for the prediction of pCR. We also hypothesized that evaluation of single maximum-intensity-projection (MIP) image would have similar accuracy in pCR prediction and designed a reader study to test this premise.

Methods

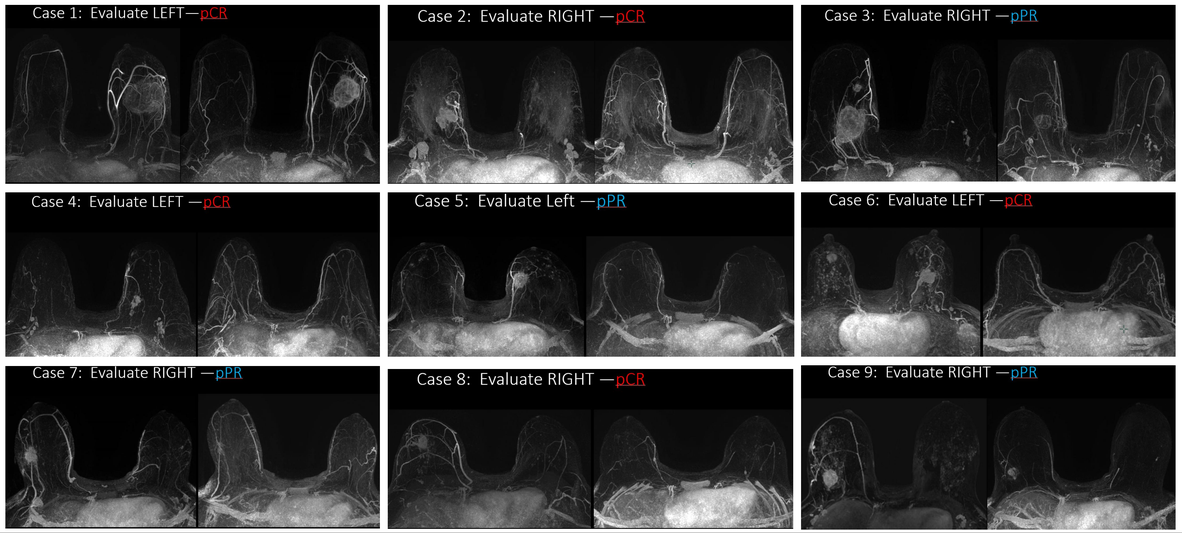
Four single-institution NAIC trials were evaluated retrospectively for MRI and pathologic responses. Immunotherapy treatments in each trial included the following: dendritic cell vaccination (DCV) for HER2+ (ER/PR-) breast cancer patients, DCV for HER2+ patients (ER/PR - or +), Interferon-gamma (IFG) for HER2+ patients (ER/PR - or +) and talimogene laherparepvec (TVEC) vaccination for ER/PR/HER2- (TNBC) patients. Immunotherapy was administered prior to or concurrent with standard chemotherapy according to each individual protocol. Retrospective analysis was performed on all patients in these trials with pre and post-treatment, pre-surgical MRIs. Patients who didn't complete a baseline and/or post-treatment MRI were excluded. Diagnostic reports were evaluated to determine MRI complete response or not (mCR vs non-mCR) in comparison to pCR vs non-pCR.

Next, early vs late phase MRI MIP analysis was performed with three breast-fellowship trained radiologists blinded to MRI and pathologic reports. The readers categorized cases as mCR vs non-mCR based on single, random-ordered, early or late-phase MIP subtracted T1 post-contrast images. Diagnostic accuracy was calculated, and inter-reader agreement was evaluated using Kappa analysis.

Results

A total of 77 patients were included, with 154 cases (early and late) utilized for reader analysis. This included 20 patients with triple negative breast cancer and 57 patients with HER2+ breast cancer. Pathologic complete response was achieved in 44/77 (57%). Average time from post-NAIC MRI to surgery was 32.5 days (range 4-87). MRI reports categorizing mCR as a true predictor of pCR demonstrated 75% accuracy (95% Confidence Interval, CI, 68-82%) with sensitivity 89% (CI 80-94%) and specificity 58% (CI 45-70%). Averaged results from the MIP reader study demonstrated accuracy of 70% (CI 62-77%, reader accuracies 68-71%), not significantly different than the MRI report (kappa 0.620). Sensitivity averaged 81% (range 76-81, CI 71-88) and specificity 56% (range 52-64, CI 43-68%). Average reading time was 6.6 seconds per case. Comparison of diagnostic accuracy for early vs late MIP evaluations yielded similar results (accuracy 73% vs 68%) which were not significantly different (CI 61-82% vs 56-78%, respectively).

Case Examples (pre and post-NAIC MIP for each case)



Conclusion

Post-NAI/NAC pre-surgical MRIs demonstrated moderate accuracy in predicting pCR, despite the potential for confounding inflammatory changes with immunotherapy in the neoadjuvant regimen. The results of our study in patients receiving NAIC were similar to previously reported accuracies in patients receiving NAC only. In addition, accuracy was similar when evaluating a single early-phase MIP image, which could support investigation into abbreviated studies in the future.

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