MR imaging in predicting pathological response of inflammatory breast cancer and non-inflammatory breast cancer with skin involvement following neoadjuvant chemotherapy

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Background and Purpose

Inflammatory breast cancer (IBC) is a very aggressive form of breast carcinoma marked by rapid disease progression and early distant dissemination. It is very rare, only accounting for 1-5% of all breast cancers. IBC is diagnosed based on the clinical presentation not pathological findings. The typical features are discerned based on the 'classical' skin changes, such as ulceration, edema, peau d'orange and satellite skin nodules. On the other hand, not all cancers with skin involvement are classified as inflammatory cancer. Non-inflammatory breast cancer with skin involvement is a separate entity, which has been categorized in a grey area of the TNM nomenclature with questionable staging as T4 tumor. In the 2nd edition of the TNM Supplement, it was defined that for a lesion to be classified as T4b, the previously mentioned clinical (macroscopic) features must be present. Microscopic invasion of the dermis alone, without the accompanying classical clinical signs is not sufficient for placing a lesion in the T4b category. Survival for patients with IBC has improved with the routine use of anthracycline-based chemotherapy. The combination of neoadjuvant chemotherapy (NAC), mastectomy, and radiotherapy results in local control in 80% of patients. In this study we analyzed and compared the MR imaging features between these two different types of breast cancer. The response to NAC was evaluated and correlated with histopathological findings to compare the prediction accuracy in these two cancer types.

Materials and Methods

A review of all breast cancer patients receiving neoadjuvant chemotherapy in our institution from 2003 to 2007 was conducted, and found 25 IBC who fit the clinical diagnostic criteria, and 12 non-inflammatory cancers that showed skin involvement on MRI. MRI was performed at 1.5T. All patients received bi-weekly Doxorubicin and Cyclophosphamide (AC) as the first-line regimen, followed by either 2 additional cycles of AC, or being switched to a taxane-based regimen. The second-line taxane based regimen consisted of Paclitaxel or Nab-paclitaxel combined with Carboplatin. HER-2-positive patients also received trastuzumab and some HER-2-negative patients also received bevacizumab. All patients had pre-treatment baseline breast MRI and at least 2 follow-up during the course of therapy, and a final MRI after completing all treatments. Following NAC, a definitive surgery was performed. The residual disease on histopathological examination was recorded into one of three categories: 1) No residual malignancy, no sign of cancer cells; 2) No residual invasive cancer, DCIS present; 3) Residual invasive cancer. The pathological complete response (pCR) is defined as no invasive cancer, including categories 1) and 2). The response on MRI is evaluated based on the 1-dimenional size reduction, non-responder (NR, <30%), partial response (PR, >30%), and clinical complete response (CCR, no visible enhancement, or low enhancement comparable to that of normal glandular tissues).

Results

Table 1 summarizes imaging features. IBC had larger tumor size than non-IBC (6.6 ± 3.2 cm vs 3.6 ±1.3 cm, $P < 0.05$). The non-mass tumor morphology was more frequently encountered in IBC (14/25, 56% vs. 2/12, 17%, $P < 0.05$). Most cancers showed the malignant type enhancement kinetics with wash-out. The axillary lymph nodes were found in 48% and 42% patients in IBC and non-IBC group, not different. The tumor response is summarized in Table 2. The pCR rate was 50% in both groups. The MRI-evaluated response (NR, PR, and CCR) did not show significant difference between these two groups. The prediction accuracy of MRI findings by correlating with the histopathological results is summarized in Table 3. The overall accuracy was 75% in IBC and 84% in non-IBC group. The false negative rate is higher in the IBC (5/24, 21%) compared to non-IBC (1/12, 8%). Combining true negative and false negative results (11/16, 69% vs. 5/6, 83%), the accuracy of MRI in predicting pCR was not significantly different between both groups (P=0.6).

Table 1. Imaging Features Inflammatory vs. Non-inflammatory Cancer

	*Tumor size (cm)	*Non-mass Lesion	Malignant kinetics	Axillary Nodes
Inflammatory Cancer (N= 24)	6.6 ± 3.2	14/25 (56%)	14/15 (93%)	12/25 (48%)
Non-inflammatory Cancer (N= 12)	3.6 ± 1.3	2/12 (17%)	8/8 (100%)	5/12 (42%)
All patients (N= 36)	5.6 ± 3.0	16/37 (43%)	22/23 (96%)	17/37 (46%)

***denotes significant difference between both groups (P < 0.05).**

Table 2. Tumor Responses Determined by MRI and Pathology

	NR	PR	CCR	pCR
Inflammatory Cancer (N= 24)	1 (4%)	7 (29%)	16 (67%)	12 (50%)
Non-inflammatory Cancer (N= 12)	0 (0%)	6 (50%)	6 (50%)	6 (50%)
All patients (N= 36)	1 (3%)	13 (36%)	22 (61%)	18 (50%)

NR: Non-responder; PR: Partial Response, CCR: Clinical Complete Response pCR: pathologic complete response, No significant difference between groups.

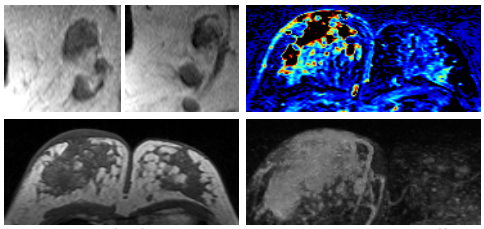

Figure 1. One case of inflammatory breast cancer showing diffuse non-mass type tumor infiltration in the right breast with skin thickening, skin enhancement and, axillary lymph nodes metastasis.

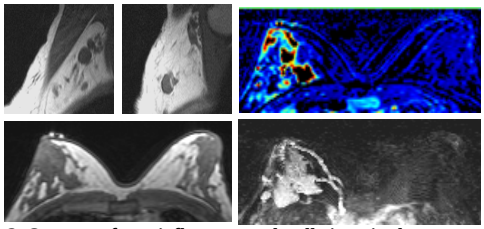

Figure 2. One case of non-inflammatory locally invasive breast cancer showing multiple masses in the right breast with focal skin enhancement and axillary lymph nodes metastasis

Table 3. Overall Diagnostic Performance of MRI

	True negative*	True positive	False negative*	False positive
Inflammatory Cancer (N= 24)	11 (46%)	7 (29%)	5 (21%)	1 (4%)
Non-inflammatory Cancer (N= 12)	5 (42%)	5 (42%)	1 (8%)	1 (8%)
All patients (N= 36)	16 (44%)	12 (33%)	6 (17%)	2 (6%)

***Combining true negative and false negative, pCR prediction accuracy was not different ($P = 0.6$), inflammatory cancer had higher false negative.**

Conclusion

IBC and non-IBC with skin enhancement are breast cancers of two different entities. Using MRI, these two cancers showed significantly different imaging features, including tumor size and tumor morphology. IBC was more likely presented with bigger tumor and non-mass type infiltration. Most non-IBC tumors (10/12, 83%), however, are smaller and mass type lesions, an evidence showing the less aggressiveness of this cancer. Although IBC had more aggressive tumor morphology, the tumor response to current neoadjuvant chemotherapy combining AC and taxane-based regimens was not significantly different from that of non-IBC. The accuracy of MRI in predicting response also did not show significant difference.

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