Impact of Factors Affecting the Accuracy of Breast MRI in Determining Residual Tumor Size Following Neoadjuvant Chemotherapy

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Background and Purposes: Neoadjuvant chemotherapy (NAC) is increasingly being used to down-stage inoperable cancers or to facilitate better outcomes in breast-conservation surgery. Because of the heterogeneous nature of breast cancer, each individual patient may respond differently to NAC, and an accurate assessment of residual disease is important for surgical planning. Many studies have suggested the superior role of MRI in assessing residual tumor size after NAC when compared with other modalities [1, 2]. Most of these studies, however, focused on the overall accuracy but did not investigate the factors that may affect the accuracy [3, 4]. Improved knowledge about the detection accuracy of residual disease after NAC by imaging is crucial to help the planning of an optimal surgery to achieve a tumor free margin. This can reduce the re-excision rate and minimize local recurrence. The purpose of this study is to investigate the role of multiple factors, including tumor characteristics, NAC regimens, MR systems, and time to operation, in affecting the accuracy of MRI evaluation of residual tumor size following NAC treatment.

Materials and Methods: This was a retrospective analysis. A total of 98 patients (28 y/o to 82 y/o, mean 49 y/o) were identified. All patients had a final follow-up MRI within 90 days of the definitive surgery, and had both MRI and pathological tumor size available for analysis. The NAC regimens include a combination of doxorubicin and cyclophosphamide (AC) and taxane. MRI studies were performed on a 1.5T (N=51) or a 3T (N=47) MR scanner. In pathological examination, if no invasive tumor was found within all examined slides, a diagnosis of pathological complete response (pCR) was made. The longest dimension measured in MRI and pathology was used in analysis. The tumor size discrepancy between pathology and MRI was calculated as the absolute difference between these two measurements. Separate univariate linear regression models were formed to assess the association between MRI and pathological tumor size discrepancy (as the outcome variable) and clinical predictors. Multivariate linear regression was applied using the backward selection method to model the mean size difference as a function of clinical predictors.

Results: The distribution of each considered predictor is summarized in Table 1. They include tumor type, tumor morphology (mass vs. non-mass), grade (4-6 as low/medium vs. 7-9 as high), ER and HER2 status (positive vs. negative), the use of MRI scanner (1.5T vs. 3T), chemotherapy (AC+taxane vs. AC without taxane). **True negative** diagnosis (CCR by MRI and pCR by pathology) was achieved in 39 patients by MRI. **False negative** diagnosis of MRI (CCR by MRI but pathology showed residual tumor) was noted in 16 patients. Of these 16 patients, the tumor size in pathology range from 0.3 to 14 cm with mean±SD of 2.5±3.7 cm. There were 38 **true positive** diagnoses, and 5 **false positive** diagnoses (MRI showed 0.4 to 1 cm lesions but final pathology showed pCR). Overall the sensitivity, specificity, positive predictive predicating value, negative predicting value, and accuracy of MRI were 70.4%, 88.6%, 88.4%, 70.9%, and 78.6% respectively. The baseline MR tumor size was 3.9±2.1cm, which decreased to 0.9±1.5 cm after NAC. The final pathological residual tumor size was 1.5±2.4 cm. The mean difference between final MRI and pathology was 1.0±2.0 cm. MR underestimated the residual tumor size by > 5 mm in 27 patients, and overestimated in 14 patients. In Table 1, individual linear regression models showed significant predictors including tumor type (p<0.0001, the strongest), morphology (p=0.0039), ER (p=0.012), and MR scanner (p=0.038). Multivariate regression analyses demonstrated that only tumor type, tumor morphology, ER status, and HER-2 were independent predictors (p=0.0004, 0.0017, 0.0235 and 0.0287, respectively; F-statistic for the overall model, p<0.0001). Figures 1-3 show 3 case examples diagnosed by MRI (B/L and 2 FU). The fat-sat pre-contrast images (top row) and subtraction images (bottom row) are shown.

Table 1: Univariate linear regression models for prediction of MR diagnostic accuracy

Clinical Characteristic	Observed absolute difference between MRI and Pathological Residual Tumor Size (cm)		Regression Model Coefficient of Determination	Regression Model Slope Parameter
	Mean	SD	R^2	p-value
Tumor type			0.227	**< .0001**
IDC (N=85)	0.7	1.20		
ILC (N=10)	2.3	2.85		
IDC and ILC (N=3)	5.6	7.31		
Tumor morphology			0.084	**0.0039**
Mass lesion (N=74)	0.7	1.00		
Non-Mass-like lesion (N=23)	2.1	3.59		
Tumor grade			0.037	0.0579
4-6 (N=40)	1.5	2.79		
7-9 (N=57)	0.7	1.11		
ER status			0.064	**0.0117**
Positive (N=56)	1.4	2.51		
Negative (N=42)	0.4	0.67		
HER-2 status			0.078	0.0780
Positive (N=40)	0.3	0.50		
Negative (N=57)	1.5	2.50		
MR Scanner			0.044	**0.0383**
1.5T (N=51)	0.6	1.48		
3.0T (N=47)	1.4	2.39		
Chemotherapy regimen			0.013	0.2672
AC+Taxane (N=63)	0.8	2.16		
Taxane without AC (N=35)	1.3	1.66		
Days from final MRI to surgery	3.62	18.3	0.000	0.9842

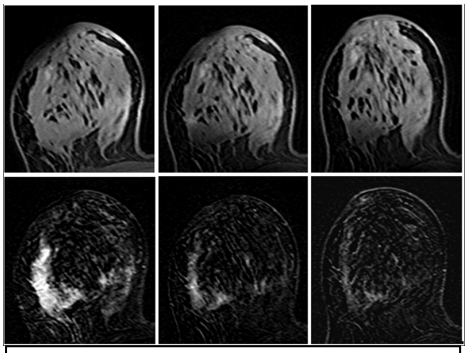

Figure 1. A 41 y/o woman with an ER(+)/HER2(-) IDC. Baseline MRI shows a 7.9 cm non-mass-like lesion. Post-NAC pathology shows a 1.0 cm residual tumor.

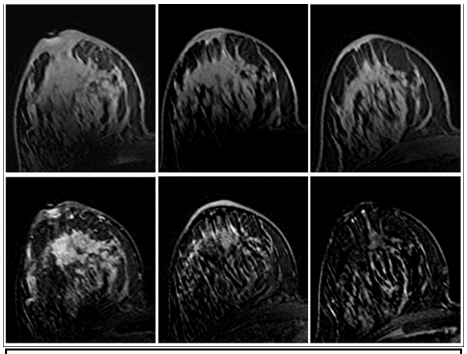

Figure 2. A 31 y/o woman with an ER(+)/HER2(-) IDC. Baseline MRI shows a 5.5 cm non-mass-like lesion. Post-NAC pathology shows a 5.0 cm residual tumor.

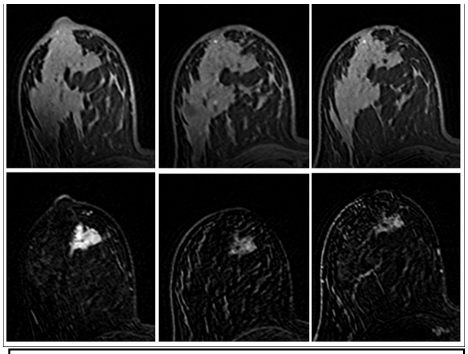

Figure 3. A 49 y/o woman with an ER(+)/HER2(-) lobular cancer. Baseline MRI shows a 3.8 cm mass that shrinks to 2.3 cm; and pathology shows a 5.0 cm residual tumor.

Discussion: Multivariate regression analysis showed that the tumor type, morphology, ER, and HER-2 status were independent predictors of MRI diagnostic accuracy. MRI diagnosis is less accurate in cancers with lobular component, cancers presenting non-mass-like enhancements, and cancers with ER positive and HER-2 negative status. The results from this study may provide useful information for surgeons and patients to choose optimal surgical plan based on post-NAC MRI findings.

References: [1] Partridge SC. AJR Am J Roentgenol. 2002; 179: 1193–1199. **[2]** Bhattacharyya M. Br J Cancer. 2008;98:289 –293. **[3]** Shin HJ. British J of Radiol. 2011;84: 612–620. **[4]** Kwong M. Cancer J. 2006;12:212–221.

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