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MRI evaluation of residual tumor size after neoadjuvant endocrine therapy vs. neoadjuvant chemotherapy

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ABSTRACT

Aim: To investigate if there is any difference in evaluation of residual tumor size after neoadjuvant chemotherapy (NAC) and neoadjuvant endocrine therapy (NAE).
Methods: Seventy-eight tumors in 57 patients were prospectively enrolled. Residual tumor sizes in contrast-enhanced MRI after NAC and NAE were compared with those measured on surgical specimen by using linear regression analyses. The line slope values >1 indicates overestimation by MRI. Differences in types of shrinkage patterns: concentric shrinkage (CS) and dendritic shrinkage (DS) were also investigated.
Results: Fifty lesions were treated with NAC and 28 lesions were treated with NAE. Shrinkage patterns were CS in 33 lesions and in 45 lesions. The slopes values were 0.75 ($R = 0.92$) and 0.70 ($R = 0.90$) for NAC and NAE, respectively, and no significant difference was observed ($p = 0.46$). However, they were 1.02 ($R = 0.92$) and 0.68 ($R = 0.92$), respectively for CS and DS with significant difference ($p < 0.01$). The difference between CS and DS was found only in a subgroup with size by MRI >20 mm.
Conclusion: Contrast enhanced MRI enabled fairly accurate measurement in NAE as well as in NAC.

1. Introduction

Neoadjuvant chemotherapy (NAC), which is conducted before surgery, is now commonly adopted to treat breast cancer [1]. Initially, neoadjuvant chemotherapy was indicated in patients with locally advanced or inflammatory breast cancers, then indication has become to include initially operable breast cancer that is not a candidate for breast conserving surgery or that would get some benefit from tumor volume reduction [2]. Advantages of this therapeutic approach are: early treatment of micrometastatic disease, assessment of tumor response to specific chemotherapeutic regimens *in vivo* and analyses of biological markers that may predict the response.

Randomized trials comparing neoadjuvant chemotherapy and postoperative adjuvant chemotherapy have shown similar survival benefit, and preoperative chemotherapy has allowed more patients to have successful breast-conserving treatment [3]. Moreover, complete pathological response of primary breast cancer to neoadjuvant chemotherapy is a surrogate marker for patient outcome [3]. Evaluation of tumor before surgery has been conducted by some modalities including mammography, ultrasound and MRI. MRI is recognized as the most reliable method for detection of residual tumor after NAC [4–7].

Recently, neoadjuvant endocrine therapy (NAE) is gradually adopted in addition to NAC [8]. NAE is considered to be another therapeutic option for a tumor that is highly sensitive to endocrine treatment, especially in elderly population [9]. NAE is often selected for cases of less aggressive cancer than NAC [10], and their similarity and difference in MRI evaluation after presurgical systemic therapies have not been much investigated and still remains to be clarified. Discrepancy was sometimes observed after NAC between assumed residual tumor size evaluated by MRI and that confirmed by resected specimen [7,11]. Patterns of shrinkage, i.e., concentric shrinkage (CS) or dendritic shrinkage (DS) [12], and status of human epidermal growth factor receptor related 2 (HER2), i.e., positive or negative [13], were reported to have some roles for correct evaluation by MRI. Confirmation on MRI evaluation of residual tumor size after NAE has large clinical importance for selection of further therapeutic options.

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Table 1
Lesion characteristics: NAC vs. NAE.

	NAC lesions $n=50$	NAE lesions $n=28$	
Mean age (range)	51 (34–76)	59 (39–80)	$p<0.01$
Clinical tumor stage			$p=0.10$
T1	27 (54%)	9 (32%)	
T2	16 (32%)	17 (61%)	
T3	2 (4%)	1 (4%)	
T4	5 (10%)	1 (4%)	
Nodal status			$p=0.84$
Negative	31 (62%)	18 (64%)	
Positive	19 (38%)	10 (36%)	
Histological subtype			$p=0.04$
IDC NOS	48 (96%)	24 (86%)	
ILC	0 (0%)	1 (4%)	
IDC + ILC	1 (2%)	0 (0%)	
Metaplastic carcinoma	1 (2%)	0 (0%)	
Mucinous carcinoma	0 (0%)	3 (11%)	
Histological grade			$p<0.01$
Grade 1	3 (6%)	12 (43%)	
Grade 2	31 (62%)	14 (50%)	
Grade 3	16 (32%)	2 (7%)	
Receptor status			$p<0.01$
ER and/or PR (+) HER2 (+)	8 (16%)	0 (0%)	
ER and/or PR (+) HER2 (−)	25 (50%)	28 (100%)	
ER and PR (−) HER2 (+)	6 (12%)	0 (0%)	
ER and PR (−) HER2 (−)	11 (22%)	0 (0%)	
Ki-67 labeling index			$p<0.01$
Low (<15%)	7 (14%)	23 (82%)	
Intermediate (16–30%)	8 (16%)	2 (7%)	
High (>31%)	10 (20%)	0 (0%)	
n.a.	25 (50%)	3 (11%)	
Final pathological status			$p<0.01$
Non-CR	39 (76%)	27 (96%)	
CR	12 (24%)	1 (4%)	

Abbreviations: NAC: neoadjuvant chemotherapy; NAE: neoadjuvant endocrine therapy; n.a.: not accessed. ER: estrogen receptor; PR: progesterone receptor; HER2: human epidermal growth factor receptor related 2; IDC: invasive ductal carcinoma; NOS: not otherwise specified; ILC: invasive lobular carcinoma; CR: complete response.

Table 2
Lesion characteristics: CS vs. DS.

	CS lesions $n=33$	DS lesions $n=45$	
Mean age (range)	54 (34–80)	55 (34–76)	$p=0.58$
Clinical tumor stage			$p=0.10$
T1	13 (39%)	23 (51%)	
T2	18 (55%)	15 (33%)	
T3	1 (3%)	2 (4%)	
T4	1 (3%)	5 (11%)	
Nodal status			$p=0.89$
Negative	20 (61%)	28 (65%)	
Positive	13 (39%)	17 (35%)	
Histological subtype			$p=0.31$
IDC NOS	30 (91%)	42 (93%)	
ILC	0 (0%)	1 (2%)	
IDC + ILC	0 (0%)	1 (2%)	
Metaplastic carcinoma	1 (3%)	0 (0%)	
Mucinous carcinoma	2 (6%)	1 (2%)	
Pathological grade			$p=0.28$
Grade 1	9 (27%)	6 (13%)	
Grade 2	16 (48%)	29 (64%)	
Grade 3	8 (24%)	10 (22%)	
Ki-67 labeling index			$p=0.77$
Low (<15%)	12 (36%)	18 (40%)	
Intermediate (16–30%)	3 (9%)	7 (16%)	
High (>30%)	3 (9%)	7 (16%)	
n.a.	15 (45%)	13 (29%)	
Final pathological status			$p=0.13$
Non-CR	25 (76%)	40 (89%)	
CR	8 (24%)	5 (11%)	

Abbreviations: CS: concentric shrinkage; DS: dendritic shrinkage; ER: estrogen receptor; PR: progesterone receptor; HER2: human epidermal growth factor receptor related 2; IDC: invasive ductal carcinoma; NOS: not otherwise specified; IDC: invasive ductal carcinoma; ILC: invasive lobular carcinoma; CR: complete response.

Therefore, we made a prospective study for size evaluation of residual tumor by MRI at the end of presurgical systemic therapies of NAC and NAE, and compared the results with pathological specimen. They were analyzed in terms of differences between NAC and NAE, and also between shrinkage patterns of CS and DS.

2. Materials and methods

2.1. Patients and therapeutics

This study was approved by institutional review board and informed consent was acquired by all subjects enrolled. Seventy-nine pathologically confirmed breast cancer in 58 female patients (34–80 years old, average 54 years) were prospectively enrolled from June 2008 to February 2010, however, one tumor of progressive disease in one patient was excluded, because our study also included analysis of shrinkage cases. Therefore, 78 carcinomas in 57 patients were included for further analysis. They were treated with NAC or NAE and surgically resected thereafter at our hospital. Therapy was decided by the patient with informed consent after discussion with breast surgeons and medical oncologist. Many were based on St. Gallen Consensus Guideline 2007 or 2009 [10,14].

NAC was defined as usage of standard chemotherapeutic agents of taxane or anthracycline and their derivatives without any endocrine therapy. NAE was defined as application of endocrine therapy without chemotherapy except cyclophosphamide. The basic regimen of NAC was a combination of docetaxel (75 mg/m^2) and cyclophosphamide (600 mg/m^2) for 3–6 cycles in every 3 weeks. For NAE, letrozole was administered with addition of some

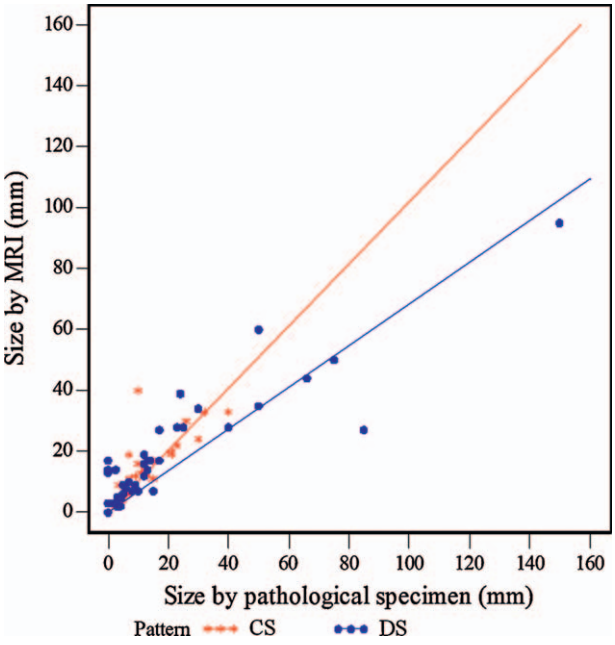

Fig. 1. Linear relationship between MRI measurement compared with that on pathological specimen. By therapeutic regimens, no significant interaction between NAC and NAE was observed ($p=0.46$). NAC: neoadjuvant chemotherapy; NAE: neoadjuvant endocrine therapy.