Comparative Analysis of Morphological MR Imaging Features in Human Epidermal Growth Factor Receptor (HER-2/neu Receptor) Positive and Negative Invasive Ductal Carcinoma

G. Agrawal[1], J-H. Chen[1,2], H. Yu[1], D-B. Hsiang[3], R. Mehta[4], O. Nalcioglu[1], and M-Y. Su[1]

[1]Tu & Yuen Center for Functional Onco-Imaging, University of California Irvine, Irvine, CA 92697, United States, [2]Department of Radiology, China Medical University Hospital, Taichung 404, Taiwan, [3]Deparrtment of Surgery, University of California Irvine, Irvine, CA 92697, United States, [4]Department of Medicine, University of California Irvine, Irvine, CA 92697, United States

Purpose

HER-2/neu is over-expressed in 20-25% of invasive breast cancers, and it is associated with an aggressive tumor phenotype and reduced survival rate before the targeted therapy Trastuzumab became available. Currently the HER-2 status of a tumor is a critical determinant for treatment using HER-2-targeted antibody Herceptin [1]. Her-2 positivity is significantly associated with high histologic grade, T2 stage and positive axillary lymph nodes [2]. No studies have been reported analyzing the MR imaging features with respect to HER-2/neu overexpression in invasive breast cancers. We hypothesize that the association of HER-2 overexpression with aggressive phenotype might show differences in MRI features. In this study we compared the morphological MR imaging features and the enhancement kinetic patterns between HER-2 positive and negative invasive ductal breast cancer.

Methods

Breast MRI of 67 patients with histologically proven invasive ductal carcinoma, including 30 patients with HER-2 positive lesions and 37 patients with HER-2 negative lesions were retrospectively reviewed. MRI was performed using a 1.5 T Phillips Eclipse MR scanner with a standard bilateral breast coil. The imaging protocol consisted of spin echo T1W sagittal unilateral pre-contrast images, and axial bilateral dynamic contrast-enhanced images using a 3D SPGR (RF-FAST) pulse sequence including 4 pre-contrast and 12 post contrast frames. After the dynamic scan was completed, subtraction images, enhancement maps and maximum intensity projection (MIP) were generated .The evaluation was based on the morphologic and enhancement kinetic features defined in the ACR BIRADS-MRI lexicon. Lesion morphology included focus/foci (smaller than 5mm), mass, and non mass-like enhancement patterns. Shape, margin, and internal enhancement patterns were also assessed. The evaluation of enhancement kinetic curve was based on initial (within the first 2 minutes or when the curve starts to change), and late phases. The initial enhancement phase is categorized into fast, medium, and slow. The delayed enhancement phase is described as persistent, plateau, and wash-out. The involvement of lymph node was evaluated on MRI. Homogeneous hypointense round shape node(s) visible in the axillary region on pre-contrast non-fat-sat T1-weighted images was read as a positive node, i.e. suspicious of malignancy. The size and whether there are multiple nodes were evaluated, and compared between the two groups.

Results

Two HER-2 negative patients had bilateral lesions, therefore a total of 39 lesions. Twenty seven of HER-2 positive (27/30) and thirty three of HER-2 negative (33/39) lesions were mass type lesions. Among these, 11/27 (41%) HER-2 positive and 5/33 (15%) HER-2 negative masses were multifocal. Rim enhancement was seen in 9/27 HER-2 positive and 8/33 in HER-2 negative lesions. Three HER-2 positive and five HER-2 negative lesions showed non mass-like enhancement patterns. Enhancement kinetic pattern was reviewed in 38 HER-2 positive and 42 HER-2 negative lesions. 34/38 lesions in HER-2 positive group and 36/42 lesions in HER-2 negative group showed fast initial phase followed by wash-out or plateau. While 4/38 lesions in HER-2 positive group and 5/42 lesions in HER-2 negative group showed moderate initial phase patterns. The lymph node status was evaluated based on sagittal view pre-contrast MR scan (Fig.1). 9/30 HER-2 positive patients showed positive nodes, while there were 7 cases (7/37) in HER-2 negative patients. 8 cases in HER-2 positive group (8/9, 89%) had nodes larger than 1cm on MRI, while only three cases in HER-2 negative group (3/7, 43%) were larger than 1 cm. 7/9 (78%) had multiple lymph nodes seen on MRI in HER-2 positive group, while 2/7 (29%) had multiple lymph nodes in HER-2 negative group.

Table 1. Comparison of morphology, enhancement kinetics, and lymph nodes status between patients with HER-2 +/- lesions

	HER-2 positive	HER-2 negative
Mass-type pattern	27/30 (90%)	33/39 (85%)
Multi-focal mass	11/27(41%)	5/33 (15%)
Rim Enhancement	9/27 (33%)	8/33 (24%)
Fast-initial kinetics	34/38 (89%)	36/42 (86%)
Axillary nodes	9/30 patients	7/37 patients
Nodes > 1cm	**8/9 (88%)**	**3/7 (43%)**
Multiple nodes	**7/9 (78%)**	**2/7 (29%)**

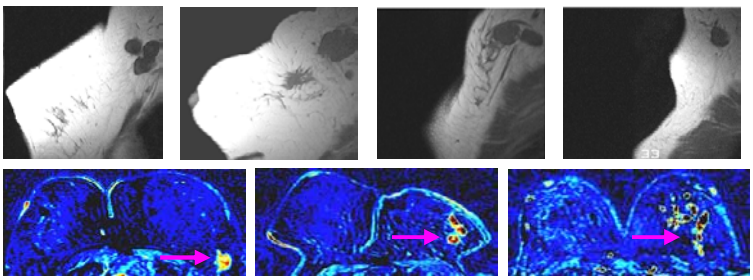

Fig. 1. Top row show HER-2 positive IDC cases with lymphadenopathy. Bottom row show three different HER-2 positive IDC cases; solitary mass on left image and right two images demonstrating multi-focal masses.

Discussion

Breast MRI did not demonstrate significant differences in lesion morphology, size, shape, margin, enhancement pattern or kinetics between HER-2 +/- groups. Based on MRI, HER-2 positive cases were more likely to show multifocal lesions, and with multiple and larger lymph nodes. Since MRI is based on contrast enhancement, which is more directly associated with angiogenesis, and the fact that VEGF or other angiogenic factors are independent of HER2 neu overexpression [3] might explain the lack of significant differences between HER-2 positive vs. negative cases. On the other hand, the appearance of larger and multiple lymph nodes in patients with HER-2 overexpression indicated a more aggressive phenotype. This may be associated with overall increased tumor viability and a significant increase in the population of viable hypoxic cells [4]. Our results suggested that pre-operative MRI may be more helpful for HER-2 positive patients to detect the presence of multi-foci lesions, which may help in selecting a better management protocol.

References: [1] Nahta et al .Cancer Lett. 2006 232(2):123-38. [2] Poltinnikov et al Am J Clin Oncol. 2006 Feb;29(1):71-9.[3] Vogl et al Histopathology. 2005 Dec;47(6):617-24. [4] Dragowska et al. Mol Cancer Res. 2004 Nov;2(11):606-19

Acknowledgement: This study is supported in part by NIH CA 90437 and CBCRP #9WB-0020.