Comparison of MR Lesion Morphology and Contrast Enhancement Kinetics in Patients with Recurrent Breast Cancer and Non-recurrent Lymph Node Positive vs. Negative Breast Cancer

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Purpose:

With earlier diagnosis and improved standard care for breast cancer, the 5-year survival in patients with local cancer has reached 98% [American Cancer Society, Cancer Facts & Figures 2006]. Now with many new therapeutic agents become available, the prognosis is expected to improve further. However, some patients still show early recurrence, which might be related to a more aggressive tumor genotype or phenotype, or poor care. Since angiogenesis is required to support tumor growth, a tumor with a higher angiogenesis may facilitate the spread of cancer cells, thus show earlier recurrence. We have been following a group of patients, and in this study we conducted a follow-up to identify patients with recurrence. We investigated whether the primary tumor in patients who had early recurrence vs. those who were cancer free had different morphology or enhancement kinetic patterns. To further stratify the non-recurrent patients based on their risk, they were separated into lymph node positive vs. negative groups. For each patient the primary lesion was identified, and the morphology was characterized using features described in BI-RADS MRI lexicon. The enhancement kinetics was measured, and from which several parameters based on the original percent enhancement, wash-out slope, as well as pharmacokinetic parameters were analyzed. These morphologic and enhancement parameters were compared among three groups.

Methods:

62 patients (30-83 yo, median 58) who had histological-confirmed breast cancer, with MRI done between Nov 2000 to Dec 2003 were reviewed. The MRI was performed on a Philips Eclipse 1.5T MR scanner, using a dedicated bilateral breast coil. The protocol included pre-contrast images from the concerned breast, and bilateral axial dynamic contrast enhanced imaging using the 3-D gradient echo based RF-FAST sequence. The temporal resolution was 42 second for each acquisition, including 4 pre-contrast and 12 post-contrast images. All patients received surgery after MRI. The histological reports were reviewed to obtain the cancer type and the lymph node status. There were 6 recurrences, confirmed by chart review or contacting patients. The remaining 56 patients were cancer-free, and 28 of them had positive lymph node at the time of diagnosis, the other 28 had negative nodes. The characteristics of primary tumor were analyzed. The size was measured on contrast enhanced MRI. The longest and perpendicular dimension was measured, then converted to 1-D size. The morphological appearances were classified into mass and non-mass enhancements. The shape of a mass lesion was determined as round, oval, lobulated or irregular. These kinetic parameters were analyzed: the % enhancement at 1-min (E1), 2-min (E2), 7-min(E3), and the slope between 7 and 2 min (E3-E2). Furthermore it was analyzed with the Toft's 2-compartmental model to obtain K^{trans} and k_{ep}.

Results:

Among the 6 recurrence cases, three had positive and three had negative lymph nodes. The comparison of lesion morphology is summarized in Table 1. LN(+) group had more irregular mass lesion (19/28, 68%) compared to LN(-) group (12/28, 43%), fewer round mass (4/28, 14% vs. 10/28, 36%), and more non-mass like lesions (3/28 vs. 0/28). The size and enhancement kinetic parameters in 3 groups are also summarized in the table. The size in the LN(+) group was bigger compared to LN(-) group (1.8 vs. 1.5 cm), but not significant (p = 0.12). The % enhancements at 1-min(E1) and 2-min(E2) were about the same, but the wash-out slope was significantly faster in the LN(+) group, with p= 0.021. After analyzing the enhancement kinetics with the pharmacokinetic model, the parameter K^{trans} was higher in the LN(+) group, with borderline significance (p=0.068), and similar as the wash-out slope the k_{ep} was faster in the LN(+) group (0.48 vs. 0.38), with a significant p= 0.01. The mean values of these parameters in the recurrence group are also listed in the table, which was comparable with the other two groups. Since there were only 6 cases in the recurrence group, the statistical comparison with the other two groups did not reach the significance level. The fact that 3 lymph node negative patients developed early recurrence was uncommon, which was more likely due to substandard treatment. Figure 1 shows images from such a patient. She had a confirmed cancer and one other area also showing a strong enhancement with suspicious kinetics, but biopsied to be benign fibrocystic changes. This patient received lumpectomy. Despite the positive ER and PR, patient refused to receive further radiation or hormonal treatment following surgery. She developed recurrence 4 years later in the lateral side, consistent with the area with fibrocystic changes. If she received further treatment, the local recurrence may have been better controlled.

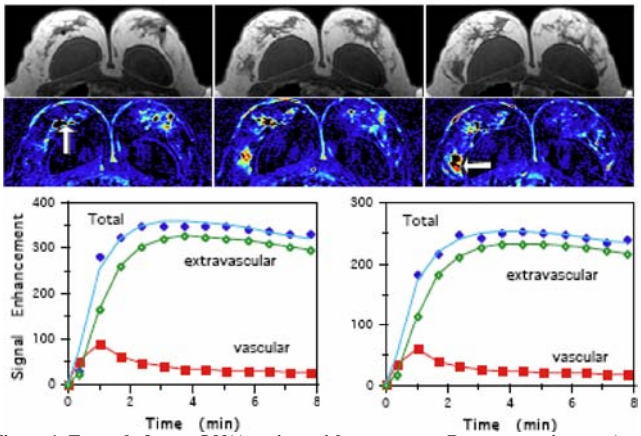

Table 1: Comparison of tumor morphology, size and enhancement kinetic parameters

	LN (-) N=28	LN (+) N=28	p-value	Recur. N=6
Mass-round	10/28 (36%)	4/28 (14%)	NS	3/6 (50%)
Mass-irregular	12/28 (43%)	19/28 (68%)	NS	3/6 (50%)
Mass (oval)	1/28	2/28	NS	0
Mass-lobulated	4/28	0	NS	0
Focus (< 5mm)	1/28	0	NS	0
Non-Mass	0	3/28	NS	0
Size(cm)	1.5 ± 0.8	1.8 ± 0.9	0.12	2.1 ± 0.7
E1	126 ± 37	125 ± 29	0.9	156 ± 77
E2	151 ± 34	146 ± 37	0.6	185 ± 83
E3-E2	**0.6 ± 4.3**	**- 3.7 ± 5.1**	**0.021**	- 4 ± 4
K^{trans}	273 ± 101	338 ± 154	0.068	327 ± 173
k_{ep}	**0.38 ± 0.11**	**0.48 ± 0.16**	**0.010**	0.44 ± 0.1

NS: Non-significant

Figure 1. Example from a LN(-) patient with recurrence. Pre-contrast images (top raw), color-coded enhancement maps (middle raw), and enhancement kinetics measured from the cancer (anterior to the implant) and benign fibrocystic changes (lateral). After lumpectomy the patient refused radiation or hormonal treatment, and found recurrence 4 years later.

Discussion:

In this study we compared the lesion morphology and enhancement kinetic parameters in patients who later developed recurrence vs. those who were disease free. The features in the recurrence group were comparable to those in non-recurrent group. We further compared these parameters in lymph node positive vs. negative non-recurrent cancers. LN(+) cancer were more likely to have irregular lesion, whereas LN(-) cancer were more likely to show round mass. The LN(+) group had a stronger wash-out and faster k_{ep} than the LN(-) cohort, suggesting that lesions with a higher angiogenesis are more likely to have positive nodes. These results are consistent with the previously reported findings between LN(+) and LN(-) cancers regarding their tumor histology, grade, size and enhancement kinetics [1-3]. Since we only followed this group of patients for 3-6 years, this was too short to find many recurrence cases. The MRI morphology or enhancement kinetics could not predict recurrence. One possible reason for early recurrence may be the substandard treatment or care, as the case illustrated here. As anti-angiogenic therapy (such as bevacizumab) is showing promising treatment outcome, this analysis may be applied to select patients who are more likely to benefit from this new therapeutic agent.

References: [1] Massurakis et al. Br J Radiol. 1997; 70:446-51. [2]. Szabo et al. Eur Radiol. 2003; 13:2425-35. [3]. Tuncbilek et al. Eur Radiol. 2005; 53:199-205.

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