Kinetics and morphology of biopsy-proven DCIS on preoperative MRI: can we predict occult invasive disease?

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Purpose

Since the advent of screening mammography, the incidence of ductal carcinoma in situ (DCIS) has increased dramatically, now accounting for up to 20% of screen-detected breast cancers.[1] The treatment for DCIS is surgical excision, historically by mastectomy, and more recently by breast-conserving surgery. Non-surgical treatment of DCIS is the subject of current investigation, however the feasibility of such options is heavily dependent on imaging to identify and exclude subjects with occult invasive disease. Recent studies have shown that magnetic resonance imaging (MRI) has relatively high sensitivity for DCIS (88 - 92%)[2,3] and invasive ductal carcinoma (91-95%),[4,5] but few studies aim to distinguish between the two. We retrospectively examine our institutional database for women with an initial diagnosis of pure DCIS in order to evaluate the ability of breast MRI to predict presence of invasive disease based on final surgical pathology. Our goal is to estimate risk for occult invasive disease when diagnosis of DCIS is already established.

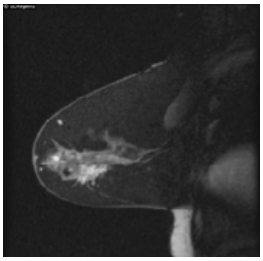

Figure 1: Example of clumped enhancement.

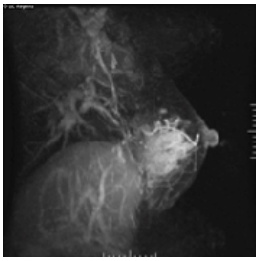

Figure 2: Example of segmental distribution.

Methods

We performed a comprehensive search of our institution's pathology and radiology archives spanning 2000-2007 to identify women diagnosed with pure DCIS on core biopsy who has also obtained a preoperative MRI. Neoadjuvant therapies, including preoperative chemotherapy, hormone and statin therapy, were excluded. Patients with a diagnosis of microinvasive disease at biopsy, history of ipsilateral invasive cancer in the past 2 years, or ipsilateral breast surgery within 6 months were also excluded. Inclusion required that final surgery occur within 6 months of the core biopsy in order to avoid the possibility of disease progression. A breast MR-trained radiologist blinded to the surgical results was given the location of the primary lesion as marked by biopsy clip or the estimated biopsy location. The reader was asked to categorize the lesion according to the ACR MRI-BIRADS lexicon (Figure 1 and 2) and estimate the likelihood of occult invasive disease. Final results were compared to surgical histopathology.

Results

Over the 8-year period, 54 biopsy-proven pure DCIS lesions in 51 patients were retrospectively identified which fit all entrance criteria. Final surgery consisted of lumpectomy in 57% (29) and mastectomy in 43% (22). Within this population, 13 (25%) patients with 14 lesions were found to have invasive disease at final surgery. Mean size of DCIS and invasive carcinoma, if present, was 44 ± 8 mm and 9 ± 4 mm, respectively. When asked to rate probability of invasive disease on the preoperative MRI, the reader categorized 23 cases (45%) as "no invasive cancer," 22 of which were accurately categorized and one of which contained a 2 mm grade II invasive ductal carcinoma (Table 1). Radiologist sensitivity for invasive disease was 92% (95% confidence interval (CI): 64-100%), specificity 58% (CI: 41-74%), positive predictive value 43% (CI: 25-63%), and negative predictive value 96% (CI: 78-100%) (Table 2).

Upon examination of individual lesions, there was a statistically significant correlation between initial enhancement pattern and presence of invasion (P=0.003). Whereas lesions with no, slow, or medium enhancement were associated with benign or purely in situ histology at surgery, those with rapid enhancement were associated with some component of invasive disease. Two invasive carcinomas measuring 2 mm (invasive ductal) and 3 mm (invasive lobular) were not visualized due to lack of discrete enhancement at the biopsy site. The former is described above and accounts for the single false negative in this study. The scan containing the latter was categorized under "possible" invasive disease by the reader because of diffuse background enhancement. Surprisingly, no statistically significant correlation to delayed enhancement pattern (plateau, persistent, washout) was identified, partially due to the low rate of washout in this small population (only 2 cases found). As expected, correlation between invasive disease and type of lesion (mass or non-mass) was also statistically significant (P=0.018). Of 5 masses detected, 4 contained invasive cancer. Among non-mass enhancement characteristics, segmental distribution and clumped or reticular enhancement patterns were more often associated with presence of invasive carcinoma, however these variables did not reach statistical significance.

Discussion

Despite a diagnosis of pure DCIS on initial core biopsy, a large percentage (one out of four patients) was found to have invasive disease at surgery in this retrospective study. Our initial results suggest radiologist prediction is highly sensitive for presence of occult invasive disease, although specificity is poor. Upon examination of individual lesions, rapid initial enhancement and/or the presence of a mass raise the possibility of occult invasive disease. However these factors alone do not entirely account for the radiologist's prediction. Several additional factors are incorporated, at least one of which appears to be background enhancement. Overall, the high negative predictive value in this study suggests that a negative preoperative MRI may allow stratification of patients into low and high risk groups for occult invasive disease. This has immediate ramifications for surgical planning, and ultimately for establishing diagnostic criteria that can be used to identify candidates for non-surgical treatment of DCIS.

References

[1] Ernster et al. JAMA; 1996:913-8. [2] Menell et al. The breast journal; 2005:382-90. [3] Kuhl et al. Lancet; 2007:485-92. [4] Bluemke et al. JAMA; 2004:2735-42. [5] Berg et al. Radiology; 2004:830-49.

Acknowledgement

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	Reader assessment		
Surgical pathology	Invasion	No invasion	Total
Invasion	12	1	13
No invasion	16	22	38
Total	28	23	51

Table 1: Reader estimate of presence of occult invasive carcinoma based on preoperative MRI, compared to final surgical pathology. One 2 mm invasive carcinoma was missed.

Sensitivity	92% (64-100%)
Specificity	58% (41-74%)
ROC area	0.75 (0.64-0.86)
Likelihood ratio (+)	2.2 (1.5-3.3)
Likelihood ratio (-)	0.13 (0.02-0.89)
Odds ratio	16.5 (2.4-nd)
Positive predictive value	43% (25-63%)
Negative predictive value	96% (78-100%)

Table 2: Performance, reader assessment of occult invasive disease (p=0.003). Results are listed as n (95% confidence interval). nd: not derivable