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Mammographic size of ductal carcinoma *in situ* does not predict the presence of an invasive focus

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Abstract

A proportion of women thought to have ductal carcinoma *in situ* (DCIS) on mammography and a core biopsy showing DCIS only, in fact have an invasive focus on surgical excision. This study aims to identify the percentage of such patients who harbour an invasive focus and to ascertain features which can predict the presence of invasion. 140 patients had a core biopsy diagnosis of DCIS without invasion. All patients had their core biopsy graded and mammography was performed on 128 patients. Mammographic findings were classified by a radiologist blinded to the surgical findings into normal, mass/distortion or microcalcification. The extent of the microcalcifications was measured. The core biopsies were graded into high, intermediate or low grade DCIS groups. The core biopsy and radiological findings were compared to see if they could predict the presence of invasive disease at surgical excision. Of the 140 patients, 61 (44%) had an invasive focus. 8 (47%) of 17 patients with normal mammography had an invasive focus. 4 (36%) of 11 patients with a mammographic mass had evidence of invasion. Of the 100 patients with mammographic microcalcifications 48 (48%) had an invasive focus. In the 10 patients with low grade DCIS on core biopsy, 3 (30%) had an invasive focus. Comparative studies in patients with intermediate and high grade DCIS, were 7 of 18 (39%) and 51 of 112 (46%), respectively. Thus, 44% of women thought to have DCIS only on preoperative investigation had an invasive focus. In contrast to previous expressed opinions, neither mammography or grade were predictive. We have not identified any factor capable of predicting a higher likelihood of an invasive focus.

Keywords: Breast; Ductal carcinoma *in situ*; Mammography; Microcalcifications

1. Introduction

Prior to the introduction of mammography, ductal carcinoma *in situ* (DCIS) was an infrequently documented lesion representing 1–2% of all new carcinomas [1], and was usually detected as a clinically palpable mass and/or Paget's disease of the nipple. In screening centres, DCIS now accounts for 15–20% of detected cancers [2].

DCIS is now commonly detected as mammographically demonstrated foci of microcalcification. Calcium deposition in central luminal necrotic debris in high grade 'comedo' DCIS coalesces to form rod-like calcifications, which are seen mammographically. Granular microcalcifications represent the isolated deposits of calcifications in necrotic debris [3]. Punctate microcalcifications are calcium deposits seen typically in low-grade DCIS. With the introduction of core biopsy, a diagnosis of DCIS can be established preoperatively [4]. Unfortunately, a proportion of patients in whom DCIS only is identified in the diagnostic core biopsy will have a co-existing invasive focus present in the definitive resection specimen. This factor has stimulated debate on the correct surgical management of the axilla in patients with a pre-operative diagnosis of DCIS only. Those who have an invasive focus on the resected specimen will need further axillary surgery for staging. Thus, the identification of an invasive focus in an area interpreted as pure DCIS by imaging will impact on surgical strategy. This study aims to identify radiological or core biopsy factors that could predict the presence of such an invasive focus.

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2. Patients and methods

The inclusion criteria for entry into the study were symptomatic and screening patients with a definite diagnosis of pure DCIS without invasion on core biopsy, who had undergone mammography from 1995 to 1998. Mammographic findings were classified by a radiologist blinded to the surgical findings as normal, mass/distortion or microcalcifications. The calcifications were morphologically classified as either linear or granular. The extent of the lesion was determined by direct measurement of the image in the unmagnified preoperative mammogram and recorded in mm.

Stereotactic core biopsies were performed on suspicious mammographic abnormalities whereas freehand core biopsies were performed on lesions not seen on mammmography, but with clinical changes. Three to five core biopsies were taken depending on the extent of the lesion. The core biopsy specimens were routinely processed, paraffin wax embedded and 4 μm thick sections stained with haematoxylin and eosin at three levels. All cases in the study had DCIS only on core biopsy. The core biopsies were graded as low, intermediate or high nuclear grade DCIS [5].

Patients with lesions less than 40 mm in maximum extent on mammography were offered breast conservation, whereas those with lesions greater than 40 mm were advised to undergo mastectomy. If the lesion were situated in the upper outer quadrant or a mastectomy were being performed, then axillary node sampling was carried out at the same time.

The resected breast tissue was oriented, using sutures, by the surgeon. The specimen was X-rayed intact to permit comparison of the lesion with the pre-operative mammogram. On receipt in the laboratory, the fresh specimen was inked to facilitate microscopic recognition of the surgical edges. The extent of the DCIS in the resected breast tissue was measured in mm in each case by histological examination of the tissues. Block selection and disease extent measurement was facilitated by whole and sliced specimen radiography, large block histology and extensive conventional block sampling.

The lesion was considered completely excised when a circumferential microscopic margin of 10 mm or more of normal breast tissue was present [6].

2.1. Statistical analysis

To determine whether any pre-operative feature could be used to predict the presence of an invasive focus in the subsequent excision specimen, correlations were sought between the mammographic findings, core biopsy histologic of features and the presence of invasive carcinoma. Univariate analysis using Chi-squared tests was performed using Stat View 4.1 on an Apple Macintosh computer. A P value of < 0.05 was considered significant.

Table 1
Risk of invasion by mammographic features[a]

Mammographic features	No. of cases	Occult invasion (%)
Normal	17	8 (47)
Mass/distortion	11	4 (36)
Microcalcifications	100	48 (48)
No mammogram	12	1 (8)
Total	140	61 (44)

[a] $\chi^2 = 3.59$, $P = 0.31$.

3. Results

There were 140 patients with a preoperative histological diagnosis of DCIS only on core biopsy diagnosis between 1995 and 1998. The median age was 55 years (range 29–83 years). Mammography was available for review in 128 cases. The mammographic features included microcalcifications in 100 cases, of which 62 were linear and 38 were granular. The microcalcifications ranged from 5 to 100 mm (median 29 mm). 11 patients had parenchymal distortion or mass lesions on mammography. There were 17 patients with normal imaging.

112 patients had DCIS classified as high grade, 18 as intermediate grade and 10 as low grade disease on preoperative core biopsy. Of the 140 patients, 61 (44%) had an invasive focus in the subsequent complete excision specimen. 8 (47%) of the 17 patients with DCIS on core biopsy, but with normal mammographic findings had invasive disease in the excised lesion. 4 patients (36%) with parenchymal distortion on mammography were found to have occult invasion (Table 1).

Of the 100 patients with microcalcifications on mammography, occult invasion was found in 48 cases (48%). There was no correlation between calcification cluster size and risk of an invasive focus (Table 2).

Of the 10 patients with low-grade DCIS on core biopsy, 3 (30%) were found to have invasive carcinoma. This was the case with 7 of 18 (39%) and 51 of 112

Table 2
Risk of occult invasion by extent of the microcalcifications[a,b]

Extent (mm)	No. of cases	Occult invasion (%)	No. of cases with nodal metastases
$\leqslant 10$	21	9 (43)	1
11–20	14	7 (50)	0
21–30	15	4 (27)	1
31–40	7	4 (57)	0
41–50	8	4 (50)	1
51–60	8	6 (75)	1
$\geqslant 61$	27	14 (52)	6
Total	100	48 (48)	10

[a] $\chi^2 = 2.04$ $P = 0.92$, for occult invasion associated with the mammographic size of calcifications.

[b] $\chi^2 = 6.20$ $P = 0.40$, for nodal metastasis associated with the mammographic size of calcifications.

Table 3
Risk of occult invasion by grade of the core biopsy[a]

Core biopsy grade	No. of patients (%)	Occult invasion (%)
Low	10 (7)	3 (30)
Intermediate	18 (13)	7 (39)
High	112 (80)	51 (46)
Total	140	61 (44)

[a] $\chi^2 = 0.46$, $P = 0.80$.

(46%) patients with a preoperative diagnosis of intermediate and high-grade DCIS, respectively. However, this trend for a higher risk of invasive disease with high-grade DCIS on preoperative core was not statistically significant (Table 3). This may be due to the small numbers of patients.

Of the 48 patients with an invasive focus within an area of microcalcifications present on mammography, 10 were found to have nodal metastases (Table 2). Seven occurred in patients whose lesions were more than 50 mm in maximum extent. In only a single instance did lymph node metastasis occur in association with a lesion less than 10 mm in dimension.

4. Discussion

Preoperative identification of invasion in malignant disease of the breast is important because lymph node staging procedures are required in invasive disease. Axillary staging is vital for prognostication, in conjunction with histological grade of invasive carcinoma and tumour size, and acts as a guide for adjuvant treatment. Conversely, patients with pure DCIS have a very low risk of nodal involvement and should not undergo axillary surgery [7].

With the advent of mammographic screening and the use of automated gun core biopsy, preoperative histological diagnoses of DCIS have become more common. However, at therapeutic surgery, a proportion of these patients will have an invasive focus. Indeed, in this series this proportion is high (44%). If nodal surgery is not carried out at the initial procedure, these patients will require axillary surgery at a later date. However, the sensitivity of core biopsy in identifying invasion within a DCIS lesion is only 20% [8]. It would be useful, therefore, to identify preoperative factors which could predict the presence of occult invasion within a DCIS lesion, thus allowing axillary surgery in those who require it as a one-stop surgical procedure.

Studies on the natural history of DCIS suggest that the risk of developing an invasive focus in lesions left within the breast is higher in high-grade than in low-grade lesions [10]. It has also been shown that high nuclear grade of DCIS combined with the presence of necrosis predicts an increase risk of local recurrence after wide local excision of DCIS lesions [11]. These and other data suggest that high-grade DCIS is more likely to contain an occult invasion than low-grade DCIS [2,9]. It has also been suggested that high grade DCIS is more likely to be correlated with high-grade invasive disease. A number of recent studies have shown an association between the grade of invasive breast cancer and the grade of the surrounding DCIS [12,13]. Our study confirms such a correlation (Table 4).

Table 4
Comparison of grade of the core biopsy with the grade of invasion[a]

Core biopsy grade	Grade 1 invasive	Grade 2 invasive	Grade 3 invasive
Low	3	0	0
Intermediate	2	5	0
High	5	15	31
Total	10	20	31

[a] $\chi^2 = 25.2$, $P < 0.001$. Of the 61 patients with occult invasion, 51 were found to have high grade DCIS on initial core biopsy. Of these, 31 were found to have grade 3 and 13 grade 2 invasive cancer on surgical excision.

Lagios found a correlation between histological size and the risk of occult invasion [2]. In his series occult invasion in DCIS lesions less than 50 mm was unusual. Mammographic prediction of the size of the DCIS is generally reliable for high grade 'comedo' disease [3]. It has been widely assumed that the mammographic estimation of lesion size predicts for the risk of occult invasion. Indeed this series demonstrates that mammographic findings and mammographic estimation of size of DCIS do not predict occult invasion. This may be related to the identification of small foci of high-grade DCIS mammographically which are commonly seen in the United Kingdom in mammographic screening practice. There is a trend towards an increased risk of occult invasion if the core biopsy shows high-grade DCIS compared with those patients with a core biopsy containing low grade DCIS. Although this is not statistically significant, this excess of high-grade small lesions may, at least in part, explain the difference in this series and previous studies. The difference in risk of invasion between those patients with low- and high-grade DCIS on core biopsy does not, however, appear to be great enough to influence the choice of axillary surgery. We also conclude that mammographic predictors of disease extent and the mammographic features themselves should not be used to identify which patients with a core biopsy result of pure DCIS without invasion require axillary staging surgery.

Recently, there has been an increase in the detection of DCIS with micro-invasion on pathology specimens. Currently, there is disagreement regarding the incidence of axillary metastasis from DCIS with micro-invasion [14]. Sentinel node biopsy is a minimally invasive

procedure; it may be carried out when the final histology for the primary tumour is not available at the time of the breast procedure.

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